Outcomes of Pharmacist Interventions for Management Antiepileptics Drug Using in Patient with Epilepsy at Setthathirat Hospital in LAO PDR.

Saysamooth Phanouvong

A Thesis Submitted in Partial Fulfillment of Requirements for

degree of Master of Pharmacy in Clinical Pharmacy

May 2023

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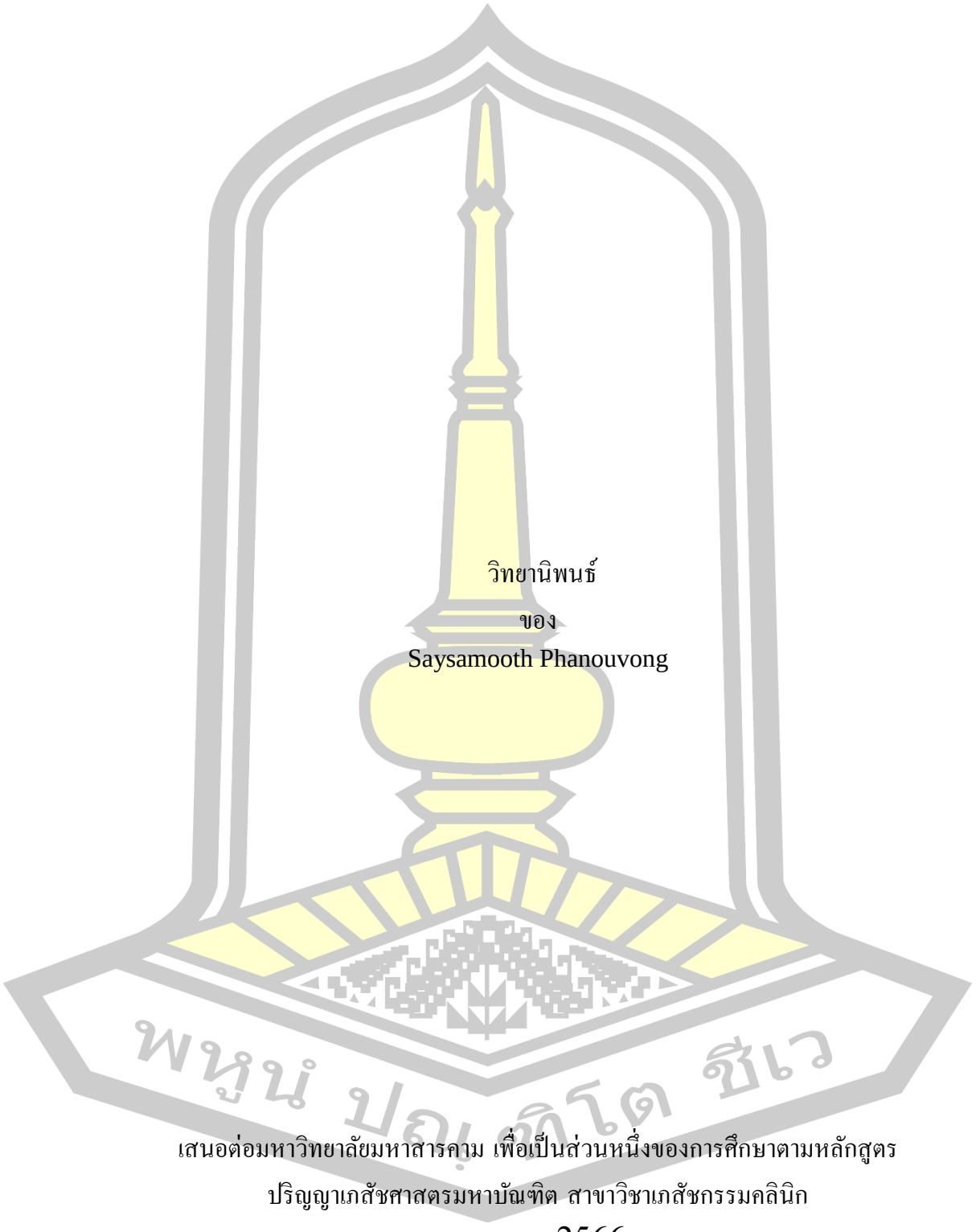

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Saysamooth Phanouvong

เสนอต่อมหาวิทยาลัยมหาสารคาม เพื่อเป็นส่วนหนึ่งของการศึกษาตามหลักสูตร

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TITLE Outcomes of Pharmacist Interventions for Management Antiepileptics Drug Using in Patient with Epilepsy at Setthathirat Hospital in LAO PDR.

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ABSTRACT

The objective of this study was to establish and develop a multidisciplinary team for epilepsy management at an outpatient clinic at the department of neurology, Setthathirath hospital, LAOS PDR. The study was a mixed-method research including qualitative interviews and quasi-experimental study. The duration of study was carried out between November 2021 to August 2022. Descriptive statistics constitute numbers, percentages, mean, and standards including gender, age, education, occupation, marital status, the residence of the patient, monthly income of patients, family history of epilepsy, seizure frequency, number of AEDs, type of epilepsy, type of AEDs, comorbidities, seizure type, medication history. Descriptive statistics constitute numbers, percentages, mean, and standards including gender, age, education, occupation, marital status, the residence of the patient, monthly income of patients, family history of epilepsy, seizure frequency, number of AEDs, type of epilepsy, type of AEDs, comorbidities, seizure type, medication history. Wilcoxon Signed Rank Test was implemented for statistical analysis. Measuring clinical outcomes as efficacy outcomes were: patients' adherence, patients' knowledge, seizure frequency, Drug-related problems drug (interaction, adverse action, over dosage), and quality of life. Qualitative interviews were Individual and focus group interviews. The face-to-face interviews were based on 6 healthcare professionals: 2 doctors, 2 nurses, and 2 pharmacists. The major themes that emerged from the interviews consisted of healthcare professionals' experiences of current practice problems with antiepileptic drug therapy, and healthcare professionals' perspectives on ways to improve services. The focus group interview interviewed 6 healthcare professionals including 2 doctors, 2 nurses, and 2 pharmacists. The major themes were the collaborations among healthcare professionals and the expectations of pharmacists' roles. The results from the qualitative interviews were used to develop the intervention of a quasi-experimental study, called "multidisciplinary team for management antiepileptic therapy". The study compared 68 patients before and after the intervention. There were 24 males and 44 females.

The patients were aged 18-39 years old. The patients have education at the level of secondary 30.9%. Most of them are single 54.4%. Followed by high school and university level (29.4%). Most patients lived in out-town 72.1%. The main occupation of the patient was selling the product 36.8%, followed by a career Government officer 17.6%. The comorbidities of the patient were hypertension at 7.4% with depression at 2.9%. The most favored regimen was monotherapy 95.6%. The mean percentage of pill count in month 3 (90.17 ± 4.55) was statistically significantly higher than the first visit 0 (58.15 ± 27.31), ($p < 0.0001$). The mean percentage of pill count in month 3 (90.17 ± 4.55) was statistically significantly higher than the first visit 0 (58.15 ± 27.31), ($p < 0.0001$). The mean score of the antiepileptic drug knowledge for patients in the pre-test and the post-test in visit (month 0) were 6.00 ± .45 and 9.58 ± 1.12 (p-value = 0.000). The outcome showed a statistical difference after receiving an intervention. The most frequent DRPs were drug interactions 10 (14.7%), Failure to receive drugs 9 (13.2%), weight gain 4 (5.9%), alopecia 2 (2.9%), headache 2 (2.9%), over dosage 2 (2.9%), allergy 1 (1.5 %), behavior change 1 (1.5%). After the provision of a multidisciplinary team managed, The DRPS decreased respectively. Most patients had frequencies seizure more than 3 times/month 20 patients. After the provision of a multidisciplinary team, the frequency of seizures decreased 3 times/month in (month 3) 7 patients and visit month 6, respectively. There were statistically significant differences ($p < 0.01$). There were significant differences ($p<0.05$) in these 7 domain functions: mood, work limitations, social limitations, memory problems, physical treatment effects, cognitive treatment effects, and seizure worries. But in 3 domain functions: energy, mobility, and general QOL There were no statistically significant differences ($p \geq 0.05$). There were significant differences ($p<0.01$) in overall scores of QOLIE-10 between the 6 months before and after the 6 months of the provision of a multidisciplinary team.

Conclusion: A multidisciplinary team can manage patients with epilepsy by improving medication adherence, patients' knowledge, seizure frequency, Drug-related problems, and quality of life in patients with epilepsy in Laos. As part of the healthcare team, pharmacists need to engage at every stage to monitor the patient’s response and determine the most effective treatment.

Keyword : Epilepsy, medication adherence, patients' knowledge, seizure frequency, Drug-related problems, quality of life, Multidisciplinary

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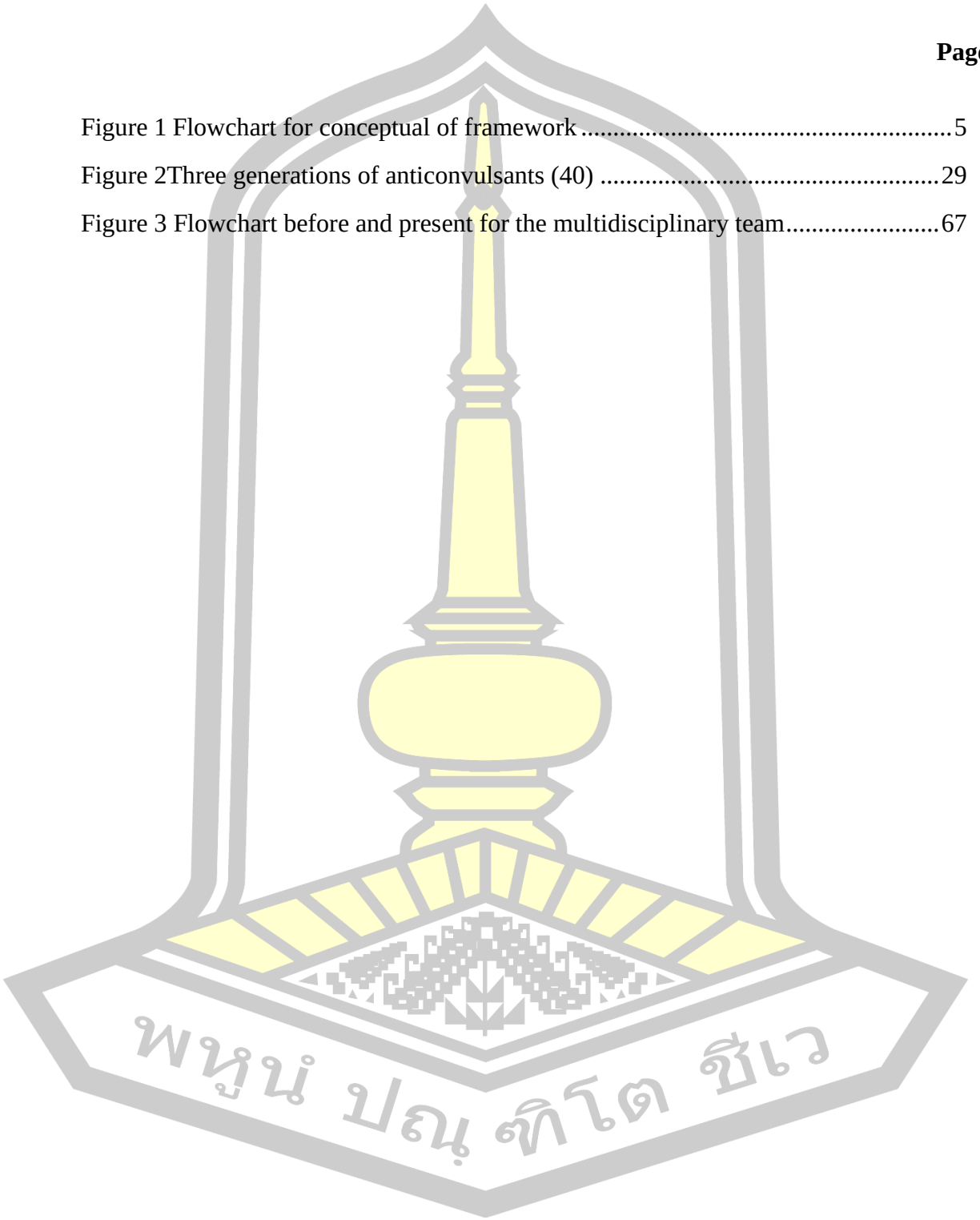


CHAPTER I
INTRODUCTION

1.1 Background and rationale of the study

Epilepsy is a chronic brain disorder that affects about 70 million people worldwide. (1) Epilepsy affects about 1% of the population in Southeast Asia region; thus, there are approximately 15 million people with epilepsy in the region. Only 10-20% of all people living with epilepsy (PWEs) receive appropriate treatment; communities in the Southeast Asia continue to believe in many myths and misconceptions about epilepsy. (2) Its treatment is complex and may involve the use of antiepileptic drugs (AEDs), a special diet, immunotherapy, and neurostimulation. (3) Pharmacotherapy is the primary choice for the treatment of epileptic disorders (4) and antiepileptic drugs, either alone or combined with other antiepileptics. Although polytherapy is often required to keep patients seizure-free, it is often cited as a cause of undesirable quality of life effects, such as adverse reactions and drug interactions. Pharmacists are important health professionals in counseling and monitoring patients with epilepsy (PWE) because they are easily accessible and know about pharmacotherapy, health education, and management of chronic diseases. (5,6)

Patients need to be treated with drugs over a long period causing various drug related problems (DRP). (7) Adverse reactions were reported with older antiepileptic drugs (phenytoin carbamazepine phenobarbiturate) such as drowsiness, slow thinking, weight gain, glaucoma, swollen gums, rash, hepatitis, etc. (8) Adverse reactions from newer antiepileptic drugs were found, such as movement disorders and psychotic symptoms from gabapentin, hyponatremia from oxcarbazepine, weight loss from topiramate, etc. (9) It was found that most anti-epileptic drugs primarily pass the enzyme CYP450. Therefore, when administered with drugs through the same drug elimination mechanism may cause interactions with other drugs (oral contraceptives, oral anticoagulants, immunosuppressants, and chemotherapeutic agents, etc.). (10) It was found that 42.7 % of epilepsy patients had recurrent seizures after discontinuing drug use by themselves because of lack of understanding. (11)

Since epilepsy is a chronic disease that requires patients to be treated with medication for a long time causing various problems and also it has a narrow therapeutic index causing closely patient monitoring. Some studies reported that pharmacists can play a major role in resolving drug-related problems and improve patients with epilepsy by decreasing drug-related problems and increasing medication adherence and patient knowledge. Pharmacist can educate and counsel patients and caregivers concerning drug knowledge in order to increase the effectiveness of treatment. (5,6,12,14,45,46,59,60,61,63,66)

More studies showed that patients getting better therapeutic outcomes when pharmacist-managed antiepileptic drugs therapy is provided such as an opened randomized controlled longitudinal and two-arm parallel prospective study on pharmaceutical care intervention improves adherence to the antiepileptic medication at outpatient clinics in the University of Uyo Teaching Hospital, Uyo, Akwa Ibom State and the University of Calabar. The study shows that there was a statistically significant difference in medication adherence scores between the control and intervention groups over time, the mean medication adherence score of the intervention group increased. Therefore, shows that pharmaceutical care services implemented by a clinical pharmacist significantly improved the adherence to antiepileptic drugs in patients with epilepsy. (12)

A systematic review of published studies describing clinical services performed by pharmacists for the patient with epilepsy, which identified 4463 studies, and 5 studies were following inclusion criteria. All those studies showed that the pharmacists‟ interventions were able to prevent problems related to the use of medicines, improve patients‟ knowledge about epilepsy, improve patients‟ quality of life and agility in daily activities, and increase medication adherence of patients with epilepsy. Those studies showed that the pharmacists are involved in clinical services that can improve the treatment outcomes and the epilepsy-related health of patients. (13)

A prospective study by Kanjanasilp et al. The study found a total of 111 DRPs in the period before the provision of pharmaceutical care and 61 DRPs in the period after the provision of pharmaceutical care. The seizure frequency reduced after the provision of pharmaceutical care. This study showed that Pharmaceutical care practice has the potential to increase epileptic patients‟ quality-of-life scores and decrease both the frequency of seizures and the number of drug-related problems. (14)

However, those studies did not assess the multidisciplinary team in this group of patient with epilepsy by the pharmacists, neurologists and nurse.

Some studies have investigated the impact of the multidisciplinary clinic such as a prospective study multidisciplinary management improves anxiety, depression, medication adherence, and quality of life among patients with epilepsy in eastern China. The result showed that the multidisciplinary program significantly increased the number of patients with moderate-to-high AED adherence ($p = 0.006$) and the overall QOLIE score ($p < 0.001$) in the intervention group. Both groups demonstrated a significant increase in the number of patients with a low seizure frequency ($p < 0.001$). (15)

Lao PDR is a small, landlocked country, sharing borders with Vietnam and Cambodia (the former Indochina) and also with Thailand, China, and Myanmar. The overall prevalence of epilepsy was 7.7 cases per thousand inhabitants in 2006. (16)

The treatment gap was 90% or more, the low level of knowledge of epilepsy on the part of health workers may be contributing to the wide treatment gap in Laos. A low availability of antiepileptic drugs throughout the country was reported with an annual importation of phenobarbital allowing to treat around 2% of the patient with epilepsy. (17)

A cross-sectional qualitative study by N. Sengxeu et al. The result of this study shown that head trauma was cited as the main cause of epilepsy by 27.2%. Epilepsy was considered as a contagious disease by 6.6%. Phenobarbital was mentioned in more than 90.0% of cases.

This study showed that an educational intervention should be implemented to improve the knowledge of epilepsy and AEDs for pharmacy-dispensing workers. This could include advice for all pharmacy-dispensing workers in order to improve AED management and follow-up of therapeutic adherence. (18)

In LAOS PDR there is no research in the field of the role of pharmacist evaluation and no multidisciplinary team for epilepsy management. This is the first research of the multidisciplinary team for epilepsy management in LAOS PDR.

Therefore, this study aimed to establish and develop a multidisciplinary team for epilepsy management at an outpatient clinic at the department of neurology, Setthathirath hospital, LAOS PDR.

1.2 Aim of the study

1.2.1 General objective

To evaluate outcome of the multidisciplinary team for epilepsy managed at the outpatient clinic, Setthathirath hospital.

1.2.2 Specific objective

1.2.2.1 To compare the adherence medication of patients with epilepsy before and after received the multidisciplinary team intervention.

1.2.2.2 To compare the knowledge of patients with epilepsy before and after received the multidisciplinary team intervention. (19)

1.2.2.3 To study the consequences of problem-solving of DRP.

1.2.2.4 To compare the seizure frequency of patients with epilepsy before and after received the multidisciplinary team intervention.

1.2.2.5 To compare the quality of life of the patient with epilepsy before and after received the multidisciplinary team intervention.

1.3 The scope of the study

This study was conducted at the outpatient clinic at the department of neurology, Setthathirat hospital, LAOS PDR. The study design is a quasi-experimental study. Patients will be received by the multidisciplinary team for epilepsy management at the outpatient clinic, Setthathirat hospital. The duration of the study will be March to August 2021.

1.4 Definition of specific terms

1.4.1 A multidisciplinary team was a group of different healthcare professionals who specialized in specific disciplines. These teams consist of the epileptologist, pharmacist, and nurse. Their goal, as a team, is to provide the patient with the specific services they require t treatment, medication use, and quality of life.

- Doctors prescribe antiepileptic drugs and duration of therapy, adjust antiepileptic drug dose in each visit.
- Nurses advise on health education for the patient with epilepsy including exercises, daily behavior, how to take medicine, and compliance with medication.
- Pharmacists manage antiepileptic drugs, give knowledge of epilepsy, adherence, ADRs, side effect.

1.4.2 Drug-related problems (DRPs) mean any adverse phenomenon that occurs to a patient as a result of the use of drugs that pose a risk or affect treatment. DRPs focus on see the consequences of problem-solving. Categorizes the problems associated with drug use from the Hepler and Strand (1990) including DI, SE, Improper drug selection. (20)

1.4.3 Intervention is to manage the problems related to drug use of patients by the team such as a nurse, doctor, and pharmacist which a nurse will interview the patient about some characteristics, measure blood pressure and record it in the patient’s book, remind patient to visit in time and advise on health education for epilepsy. The doctor will diagnose, recommend to continues or change antiepileptic drugs, provide short counseling about the disease and the medication used to the patient. The next follow-up is up to the doctor's appointment. The pharmacist will management of problems related to drug use, give advice on how to solving or prevent problems for doctors and treatment, give advice on the disease, medication use, knowledge, and adherence.

1.4.4 Clinical outcomes are:

1. Patients adherence assessment tool was used for the pill count and self-report of how to take medicine.
2. Patient's knowledge assessment tool has used the tool that follows the test by using questions adapt from Siriporn Tiamkao (2007). (19)

3. Seizure frequency was measured every 3 months. (21)

4. Patients' quality of life assessment tool was measured by a test modified from the test by using questions adapted from Joyce. Cramer (2016). (22)

5. Drug-related problems were classified according to Hepler and Strand classification (1990).19 Focus on the consequences of problem-solving, drug-related problems such as management DI, SE, and Improper drug selection. (20)

This research monitored the ADR for each drug as follows by taking a history in conjunction with a doctor's diagnostic:

Phenobarbital adverse reactions such as sedation, nystagmus, dizziness, ataxia, mild drowsiness, amnesia, intelligence decreased, work is done less, unable to perform complex tasks, serious adverse reactions include morbilliform rash changed to steven johnson syndrome or exfoliative dermatitis or hepatitis or bone marrow suppression.

The adverse reactions related to dose-related dosing of carbamazepine include dizziness, drowsiness, anorexia, nausea.

Adverse reactions related to Valproic acid the most common side effects were weight gain, alopecia, gastrointestinal tract, nausea, vomiting, anorexia was reported, and another abdominal discomfort. Adverse reactions related to phenytoin were ataxia, diplopia, drowsiness, encephalopathy, and involuntary movements. (22)

1.5 Conceptual of framework

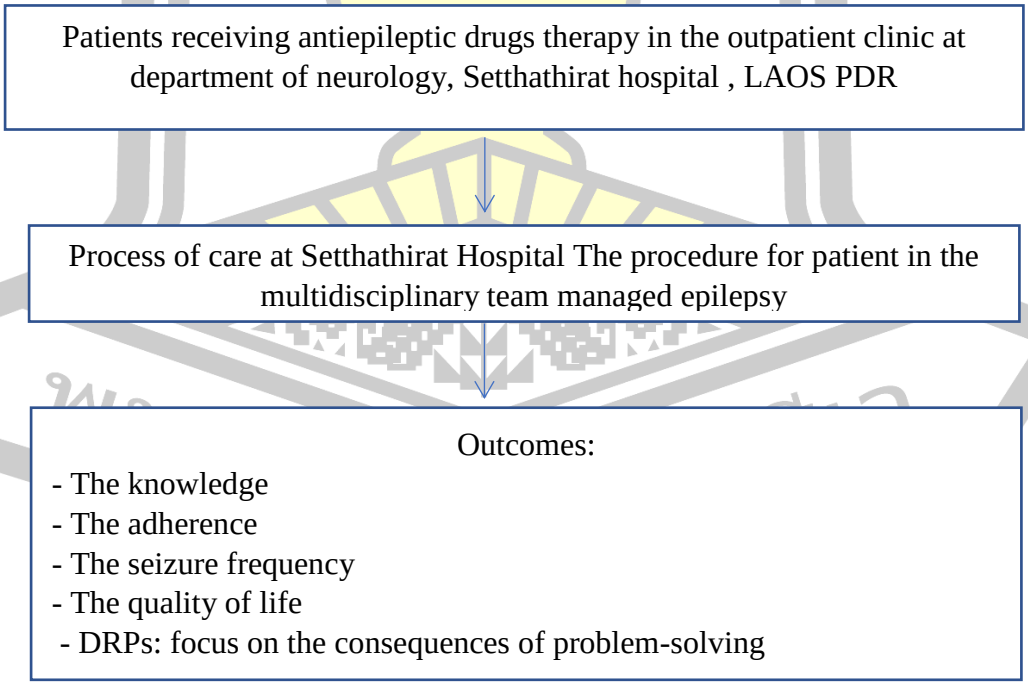


Figure 1 Flowchart for conceptual of framework

1.6 Hypothesis

This study used the directional hypothesis: patients before receive the multidisciplinary team intervention have a different percentage of adherence compared with patients after receiving pharmacist intervention.

H0 is null hypothesis,

H0: μ1>μ2 Ha is alternative hypothesis,

Ha: μ1>μ2 or μ1<μ2=0

μ1 is The score of the adherence for before receive multidisciplinary team intervention.

μ2 is The score of the adherence for after receive multidisciplinary team intervention.

1.7 Expected outcome and benefits

1.7.1 To be the pharmaceutical care model in other diseases/medications in Laos PDR.

1.7.2 To decrease mortality rate, the hospitalization rate of a patient with epilepsy and to reduce the cost of treatment.

1.7.3 Being a source of information for policymakers to enhance pharmacists' roles

CHAPTER II
LITERATURE REVIEW

This research was a study of outcomes of pharmacist interventions or the multidisciplinary team-managed epilepsy at Setthathirat Hospital in LAO PDR. The researcher has set the scope for the literature review and related by covering topics of epilepsy in adults, the multidisciplinary team managed epilepsy, and pharmaceutical care for patients with epilepsy.

2.1. Definition of epilepsy

The word epilepsy comes from the Greek language. The definition of epilepsy is that there are at least two unprovoked seizures 24 hours apart is an epileptic disorder. Patients may have other comorbid such as depression, anxiety, and neuroendocrine disturbances. It is a chronic condition of the brain in which abnormal nervous currents are released simultaneously and cause epileptic seizures causing various consequences neurobiological recognition rule and cognitive, psychological, and social. (24)

The word seizure is a clinical condition with neuronal activity in the cerebral region excessive cortex most will see the symptoms that the patient is suddenly unconscious, muscle spasms all over the body which is a symptom of generalized tonic-clonic or grand mal seizure. Many other signs and symptoms are depending on where are the abnormality in the brain. The term "epileptic seizures" means epilepsy.

2.2. Epidemiology

Epilepsy to be about 1-3% of the world's population. The prevalence of epilepsy in the United States is 1% is the fourth place in the central nervous system, the first is stroke, the second is migraine, and the third is Alzheimer's disease. Most have a high incidence in the first ten years of age and elderly people over 50 years old. According to the World Health Organization (WHO) found that worldwide, there are more than 70 million people with epilepsy each year22,2.4 million people are diagnosed with epilepsy annually. (23)

In America, 120 new cases of seizures were found per 100,000 populations at least 8 % of the general population had at least once in a lifetime. The rate of repeated after having your first seizure within five years found 23-80 % only 40-70 patients diagnosed with epilepsy per 100,000 populations.

Seizures can be caused by the withdrawal of drugs that depress the central nervous system as alcohol or barbiturates, or in periods of acute neurologic illnesses or systemic toxic conditions such as uremia or eclampsia. Some people may develop a seizure from fever but high fever, seizures do not cause epilepsy. The age-adjusted incidence of epilepsy is 44 (40-70) per 100,000 population per year. Each year, there are 125,000 new cases, 30 % are younger than [18]. On the day of being diagnosed with epilepsy. The first seizures usually occur in patients in two age groups are newborn and young children group and the other group is the elderly aged over 65 years.20for the elderly over 65 years, 1.5 % were found. (24)

In Eastern and South-Eastern Asian languages, such as Chinese, Japanese, Korean, Malay, Lao, Thai, Burmese, and Khmer (Cambodia) Epilepsy is associated with madness. (25) In Laos, the overall prevalence of epilepsy was 7.7 cases per thousand inhabitants in 2006. (26)

The mortality rate of epilepsy patients up to 2-3 times that of the general population. There are many causes of death including sudden unexplained death in epilepsy (SUDEP). The patient died from SUDEP 1 per thousand epilepsy patients, despite their good health if the patient is unable to control their seizures, the patient will die from one SUDEP per 150 epilepsy patients. The severity of seizures is the most important risk factor for SUDEP, other risk factors include gender, cause of seizures having epilepsy from a young age sudden death. It was found rarely in pediatric patients but it is the leading cause of death in young adults who cannot control seizures. The mechanism of SUDEP remains unclear but is expected to be the heart-related mechanism. (24)

Patients with epilepsy must have seizures. Patients with seizures may not be diagnosed with epilepsy provoked seizures such as seizures caused by systemic, toxic, or metabolic such as overdose; withdrawal of barbiturates, benzodiazepines, or alcohol. There is a danger to the acute nervous system, such as cerebral hemorrhage; a systemic illness such as hypocalcemia, hypoglycemia, uremia, and eclampsia, or some patients have seizures associated with febrile seizures. These are not called epilepsy but it's just a seizure when the stimulus is removed. The patient will not have a seizure but if there is a stimulus, the patient may have another seizure.

2.3 Etiology

Seizures are caused by abnormal nerve impulses from a group of neurons in the cortical part of the brain simultaneously. Seizures can be caused by several reasons from genetic mutation to traumatic brain injury. Genetic, causes multiple seizures in primary epilepsy generalized, mental retardation, cerebral palsy, head injury, strokes increase the risk of seizures and epilepsy. The elderly often experience seizures from certain brain injuries (focal) from stroke or disease that comes from

neurodegenerative disorders such as Alzheimer's disease[20]. Childhood-onset epilepsy is often caused by genetics. Epilepsy is at an older age. It is often caused by injury to the brain structures as stroke or traumatic brain injury. In 2014, the ILAE categorized six types of causes as follows. (25,27)

1) Genetic
2) Structure
3) Infectious
4) Metabolic
5) Immune
6) Unknown

Certain epilepsy can have more than two common causes (24).

1: Genetic

Genetic etiology is often in infants or children, such as Juvenile Myoclonic Epilepsy (JME). There are mutations in the EF-hand of protein-1 (EFHC1) Dravet Syndrome is related to the mutation of sodium channel, voltage, gated type 1 alpha subunit (SCN1A), and Children Absence Epilepsy (CAE).There are mutations in T-type Ca2 + channels and GABA subunits (24) before 2010, formerly known as primary generalized epilepsy or idiopathic generalized epilepsy (IGE), which is not clear why the cause is Genetic or structural but now that epilepsy is known to be caused by genetics, it is called "genetic epilepsies.

2: Structural etiologies may occur later or genetically which can allow neurological imaging to see abnormalities in that structure for example Mesial temporal lobe epilepsy has sclerosis in the hippocampus Glial scarring is taken MRI images show reduced hippocampus volume and reduced cellular density when biopsy. This type of epilepsy quite resistant and difficult to treat another example is the traumatic brain injury or stroke that may cause brain lesions and cause epilepsy. Before 2010, we called epilepsy caused by this cause "symptomatic epilepsies.

3: Another common cause in the world population is an infection, such as meningitis or encephalitis, tuberculosis, Human Immunodeficiency Virus (HIV), cerebral malaria, cerebral toxoplasmosis, Zika virus, cytomegalovirus, etc. In developing countries, there is a parasitic infection in raw pork in the brain (Neurocysticerosis) causing brain structure injury and cause epilepsy.

4: Metabolic disorders and immunity cause less epilepsy. Examples of epilepsy caused by metabolic disorders such as Lafora disease, due to the abnormal glycogen metabolism, insoluble glycogen inclusion bodies cause epilepsy. In addition, porphyria, uremia, a pyridoxine-dependent seizure can cause.

5: Some of the autoimmune causes of autoimmune diseases include anti-N-methyl-D-aspartate (anti-NMDA) encephalitis, which causes inflammation in the central nervous system and causes epilepsy, both diseases require specific treatment.

6: Also, if the cause of epilepsy cannot be determined, it is called an unknown cause. Before 2010, it was called "cryptogenic epilepsies". It may be because we still do not know the gene that causes it or unable to find abnormal structure and metabolism. In some cases, if the cause of seizures can be determined patients will not need to receive antiepileptic drugs such as causes that affect metabolism or systemic diseases such as metabolic disorders, hypertensive encephalopathy, or drug overdose. If the cause of seizures is not found must have to ask thorough history, physical examination, laboratory tests, and neuroimaging. This is called idiopathic and if there are repeated seizures must receive antiepileptic drugs for treatment during long.

2.4 Risk factors and Seizure triggers. (23,24)

Risk factors are factors that increase the risk of epilepsy but not the cause of the disease, such as premature birth and low weight birth injuries (such as anoxia) with a history of alcohol withdrawal has a history of febrile seizures and a family history of seizures but getting the vaccine (Immunizations) not related to an increased risk of epilepsy.

Stimulating factors include hyperventilation and strobe-inducing absence seizures and genetics-related epilepsy such as Juvenile Myoclonic Epilepsy (JME) and Childhood Absence Epilepsy (CAE), too much sleep, sleep deprivation, sensory stimuli, physical and emotional stress hormonal changes during menstruation puberty, or pregnancy. Drugs that lower the threshold for seizures and stimulate seizures such as high-dose theophylline, alcohol and phenothiazines, antidepressants especially bupropion, street drugs. The occurrence of drug seizures is often correlated with the dose. The patient has a history of previous seizures or the elimination of defective drugs.

Drugs that cause other seizures are shown in Table 1

Table 1Drugs that cause seizures (28)

Antimicrobials β-lactam and related compounds Cephalosporins Imipenem/cilastatin Penicillin and its derivatives Quinolones Ciprofloxacin Enoxacin Nalidixic acid Norfloxacin Isoniazid	Theophylline Anesthetic and antitiarrhythmic agents Class 1B Lidocaine Tocainide β-Adrenergic blockers Esmolol Metroprolol Propranolol Local anesthetics Bupivacaine Metoprolol Chlorprocaine Lidocaine Procaine
Psychotropic agents Antidepressants Amitriptyline Bupropion Desipramine Doxepin Fluoxetine Imipramine Maprotiline Nortriptyline Paroxetine Protriptyline Sertraline Antipsychotics Chlorpromazine Clozapine Haloperidol Perphenazine Thioridazine Trifluoperazine Lithium	Radiographic contrast agents Diatrizoate meglumine Iohexol Iopamidol Ioxaglate sodium Meglumine metrizoate Sodium iothalamate Drugs of abuse Amphetamine Cocaine Phencyclidine Methylphenidate Phencyclidine Methylphenidate Alcohol Barbiturates Benzodiazepines Benzodiazepines Ethchlorvynol Glutethimide Meprobamate Methaqualone Methyprylon Miscellaneous Cyclosporine Flumazenil Ganciclovir

2.5 Pathophysiology

Seizures are caused by excessive nerve stimulation. Seizures are an abnormality of the inhibition of excessive cortical neurons which is shown in the EEG as a sharp wave or spike. In the beginning, there were many cells with abnormal nerve currents. From then, when the inhibition is less than the stimulation of the nervous system causing abnormal abnormalities that spread more. The occurrence of this disorder in some areas of the brain causes focal seizure seizures or if the disorder spreads throughout the brain, there will be a generalized seizure. Clinical manifestations depend on areas with abnormal nerve impulses. The level of disturbances around the area and the intensity of the abnormal nerve impulses. (23,24)

Also, many mechanisms can cause synchronous hyperexcitability, such as:

1: Changes in distribution, number, types, and properties in biophysics. (biophysical) of ion channels in the cell membrane of both voltage-gated and ligandgated cells K +, Na +, Ca2 +, Cl including the mutation of these ion channels.

2: Modification of receptor biochemistry

3: Modulation of second messaging system and gene expression

4: Changes in the concentration of ions outside the cell

5: Changes in neurotransmitters and metabolism of glial cells

6: Modifying the proportions and functions of inhibitory circuits

7: The imbalance of neurotransmitters between glutamate (excitatory) and γaminobutyric acid (GABA) (inhibitory) and neuromodulators (such as acetylcholine, norepinephrine, serotonin).

Antiepileptic drugs can control seizures by increasing the threshold of nerve cells against stimulation by nerve impulses and chemicals which is usually done by stabilization of nerve cell membranes or will limit the spread of abnormal nerve impulses from the origin. This can be done by pressing synaptic transmission and reducing nerve conduction.

Prolonged seizures and continuous exposure to glutamate injuring nerve cells, affect the function of the brain abnormalities especially memory, and causing the neuronal circuit to change permanently. The regeneration of nerve fibers (sprouting) and organized the new projections which cause chronic seizures destruction of the nervous system and brain damage (23,24).

2.6 Classification and clinical manifestations

Seizure classification is important to the choice of antiepileptic drugs. Most of them are divided according to the symptoms that the patient describes as during the symptoms, must ask if there is any warning aura, specific symptoms and symptoms after seizures.

The International League Against Epilepsy has classified seizures and epilepsy since 1981, the International Classification of Epileptic Seizures (ICES, 1981), and 1985 the International Classification of the Epilepsies and Epilepsy Syndromes (ICE, 1985) and revised in 1989. In 1989, the term "epileptic syndrome" was defined as the epileptic syndrome in which (23) identified the type of seizures, causes, anatomy, motivation factor (precipitating factors) age of onset, severity, chronicity, diurnal and circadian cycling, and may also have prognosis by dividing epilepsy according. There are two main types of seizures: generalized seizures and seizures with partial or focal seizures (24). The further classification is further categorized according to the cause and the choice of antiepileptic drugs is mainly chosen according to this type of seizure. Antiepileptic drugs that can treat both types of seizures may be called antiepileptic drugs broadspectrum, the antiepileptic drugs that can treat any type of seizures or specifically referred to as narrow-spectrum anticonvulsants.

The International Classification of Epileptic Seizures uses shared clinical data and brainwave examination results which is divided into two main groups: partial seizures and generalized seizures, as detailed in Table 1.2

Table 2 Classification of seizures and epilepsy in the International Classification of Epileptic Seizures (23).

I.Partial seizures (seizures begin locally)
- A. Simple (without impairment of consciousness)
  - 1. With motor symptoms
  - 2. With special sensory or somatosensory symptoms
  - 3. With psychic symptoms
- B. Complex (with impairment of consciousness)
  - 1. Simple partial onset followed by impairment of consciousness-with or without automatisms
  - 2. Simple partial onset followed by impairment of consciousness-with or without automatisms
- C. Secondarily generalized (partial onset evolving to generalized tonic–clonic seizures)

II. Generalized seizures (bilaterally symmetrical and without local onset)
- A. Absence
- B. Myoclonic
- C. Clonic
- D. Tonic
- E. Tonic–clonic
- F. Atonic
- G. Infantile spasms

III. Unclassified seizures

IV. Status epilepticus

The classification of epileptic seizures and syndromes by the International League Against Epilepsy is as in Table 3.

Table 3 Classification of epileptic seizures and syndromes (23).

Partial seizures (focal, local)
- Simple partial seizures (consciousness preserved)
  - With motor signs (jacksonian)
  - With somatosensory or special sensory symptoms
  - With autonomic symptoms or signs
  - With psychic symptoms
- Complex partial seizures (consciousness impaired)
  - Simple partial onset followed by
  - impaired consciousness Impaired consciousness at onset
- Secondarily generalized seizures
  - Simple partial seizures evolving to generalized tonic-clonic seizures
  - Complex partial seizures evolving to generalized tonic-clonic seizures
  - Simple partial seizures evolving to complex partial seizures evolving to generalized tonic-clonic seizures.

Generalized-onset seizures (convulsive or nonconvulsive)
- Tonic-clonic seizures
- Absence seizures
  - Typical absence seizures
  - Atypical absence seizures
- Myoclonic seizures
- Tonic seizures
- Atonic seizures

Localization-related (focal) epilepsies Idiopathic
- Idiopathic
  - Benign epilepsy of childhood
- Symptomatic
  - Temporal lobe epilepsy
  - Extratemporal epilepsy

Generalized epilepsy
- Idiopathic
  - Benign neonatal convulsions
  - Childhood absence epilepsy
  - Juvenile myoclonic epilepsy
  - Other
- Idiopathic and/or symptomatic
  - Infantile spasms (West syndrome)
  - Lennox-Gastaut syndrome
  - Myoclonic epilepsies

Special syndromes
- Febrile seizures

By changing the name from the original, the author has summarized and compared it as shown in Table 4.

Table 4 Name of seizures changed by ILAE 2010 compared to previous names

Former name	New name
Simple partial seizures	Focal seizures without dyscognitive features
Complex partial seizures	Focal seizures with dyscognitive features
Secondarily generalized tonic-clonic seizures	Bilateral convulsive seizures

Table 5 Semiological Seizure Classification (29)

Auras		Somatosensory Visual Auditory Olfactory Gistatory Autonomic Abdominal Psychic
Autonomic seizures		
Dialeptic seizures		Typical dialeptic seizure
Motor seizures	Simple motor seizure	Myoclonic seizure spasm Tonic-clonic seizure Tonic seizure Clonic seizure Versive seizure
	Complex motor seizure	Hypermotor seizure Automotor seizure Gelastic seizure
Special seizures		Atonic seizure Astatic seizure Aphasic seizure Negative myoclonic seizure Hypomotor seizure Akinetic seizure

However, the selection of antiepileptic drugs is mainly based on the division of ICES seizures.

New seizure classification and epilepsy classification in 2016-2017 by the ILAE (the new 2017 ILAE seizure classification) (27) is divided into 3 levels which are:

1) Seizure type
2) Epilepsy type
3) Epilepsy syndrome

Seizure classification uses the framework to understand triggers and prognosis. The risk of comorbidities such as learning difficulties, intellectual disability, psychiatric features (such as autism spectrum disorder), and mortality risk (such as SUDEP) and most importantly, is a guideline for the selection of antiepileptic drugs for the treatment.

The epilepsy classification section was initiated in the 1960s. It is important to choose a treatment such as anticonvulsants or dietary therapies, surgery, or the development of new devices. However, the epilepsy classification is often proposed to change according to the knowledge of research that changes. Epilepsy syndrome-specific diagnosis is required.

Seizure type is divided into 3 types which are focal onset, generalized onset, and unknown onset, but epilepsy is divided into 4 types:

1. Focal epilepsy has one or more abnormalities in one side of the brain. Patients have the following types of seizures: focal aware seizures, focal impaired awareness seizures, focal motor seizures, focal nonmotor seizures, focal to bilateral tonic-clonic seizures.

2. Generalized epilepsy with seizure type including absence, myoclonic, atonic, tonic, and tonic-clonic seizures.

3. Combined generalized and focal epilepsy (as a newly added category) are both generalized and focal epilepsies. The most common examples are Dravet syndrome and Lennox-Gastaut syndrome.

4. Unknown epilepsy cannot be identified as generalized or focal epilepsies due to insufficient data.

Epilepsy syndrome has a group of seizure types, including electromagnetic waves and imaging features usually related to age at the beginning and in the remission period. Factors that stimulate seizures, diurnal variation, and similar prognosis may have distinctive comorbidities such as intellectual and psychiatric dysfunction, specific electromagnetic waves, and imaging images, for example, childhood absence epilepsy, West syndrome, Dravet syndrome.

2.7 Cause of disease

Diagnosis of this type of epilepsy must be based on clinical symptoms and supported by etiology, divided into 6 types: structural, genetic, infectious, metabolic, immune, and unknown group which affects the choice of treatment methods, for example, structure etiology may consider surgical treatment options if there is further genetic etiology, gene therapy may be performed if caused by infection was able to eliminate the root cause or if immune-related may be treated by targeted immunotherapies. Therefore, knowing the cause of the disease has completely changed the treatment not only limited to antiepileptic drugs only.

For divide seizure type and new epilepsy this time, there is the use of new terminology developmental and epileptic encephalopathy and the words self-limited and pharmacy responsive.

Formerly, the term "epileptic encephalopathy" refers to the epileptic activity causing severe cognitive and behavioral impairments. This may be due to cortical malformation and these symptoms will continue to worsen. These impairments will occur along with the severity of seizures and can occur with all age groups of patients. Later studies have found that epileptic encephalopathy causes cognitive slowing and often worsens (regression). The treatment of epileptic form activity may cause development (improvement consequences). Whether the patient has normal development or developmental delay already. Therefore, the term "developmental and epileptic encephalopathy" should be used. The causes can be both genetic and acquired etiology for developmental and epileptic encephalopathy that have genetic mutations and genes may be called by using that gene name, such as STXBP1 encephalopathy or KCNQ2 encephalopathy, etc.

The term "developmental encephalopathy" is used when developmental impairment does not involve an epileptic activity or makes development worse by seizures.

The term "epileptic encephalopathy" is used when there is no developmental delay (developmental delay) first and not related to a genetic mutation that causes developmental problems and has both developmental and epileptic encephalopathy.

Previously, patients with these disorders were classified as "symptomatic generalized epilepsies" but covered too many different patients such as referring to patient's developmental encephalopathy and epilepsy, epileptic encephalopathy, developmental and epileptic encephalopathies, generalized epilepsy or combined generalized and focal epilepsy, etc. The new classification of seizures and epilepsy requires more specific, so the term has been discontinued.

Formerly, the word "benign" gives the impression that the disease is mild. In reality, the disease is severely affected such as benign epilepsy with centrotemporal spikes (BECTS) is associated with both temporary and long-term cognitive effects.

Therefore, offering the words "Self-limited" and "Pharmacoresponsive" instead of the word benign.

In which the term "Self-limited" means syndrome can be the spontaneous resolution. The term "Pharmacoresponsive" means epilepsy syndrome to be controlled by the use of antiepileptic drugs. At this time, the name has not been changed epilepsy syndrome. That has the word benign but hopefully, next, there will be a change. Besides, the term "malignant" and "catastrophic" are also discontinued as they appear too harsh.

2.8 Symptoms and Signs

During the seizure there were no signs of objective or pathognomonic signs.

2.9 Laboratory Tests

No laboratory tests for epilepsy

Post-GTC or CP seizures may temporarily increase prolactin levels in the blood.

Laboratory examinations may be made to rule out, other causes of seizures that can be treated, such as hypoglycemia (hypoglycemia), changes in the level of electrolytes (altered electrolyte concentrations), an infection that is not epilepsy.

Seizures are classified by their symptoms and the nature of the brain's electrical waves. (electroencephalographic features) can be divided into generalized or partial.

2.10 Diagnosis

The diagnosis of epilepsy and the classification of epilepsy require a detailed history of patients and those who witnessed the episode. Diagnosis requires a history that is accurate, unambiguous and most spectators will provide accurate information for generalized tonic-clonic seizures but for other seizures such as partial, absence often the information is unclear.

Because the seizures that occur tend to be obvious must find the cause of seizures, first especially that may be caused by metabolic and systemic factors which must be separated from the unknown group by taking a history of illness and drug use (medical history), physical examination and inspected by the laboratory Most 60-70 % of the epilepsy is unknown. For patients younger than 25 years and have a family history of epilepsy, often caused by genetic causes.

EEG examination Electroencephalogram (EEG) is used in both the diagnosis and classification of epilepsy. An abnormal EEG occurs when the patient develops a symptom but if examined after the patient has symptoms then 50 % abnormalities and abnormal brain waves are found in people who do not have epilepsy 10-15 %.

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) scans are used when history taking or neurological examination indicates structural abnormalities in the brain such as focal neurologic abnormalities or have a history of partial seizures), MRI can detect lesionsassociated with partial epilepsy better than CT, Positron emission tomography (PET) can find areas with abnormal blood flow or metabolism, suitable for evaluating patients for surgery but the cost of using such tools for diagnosis.

However, be careful of misdiagnosis because some symptoms are similar to seizures, if the treatment does not work, the diagnosis should be reviewed again. Symptoms similar to seizures include25 gastroesophageal reflux, breath-holding spells, migraine, sleep disorders (especially parasomnias), Cardiovascular events, Pallid infantile syncope, Movement disorders, Psychological disorders.

Summary

The prevalence of epilepsy patients is approximately 1-3 % of the world population. There are many main causes such as genetics, structure, infection, metabolic, immune, and unknown. The current seizure classification is divided into generalized seizures and focal seizures which generalized seizures are divided into absence seizures, myoclonic seizures, tonic-clonic seizures, tonic seizures, clonic seizures, atonic seizures. The focal seizures are divided into focal seizures without dyscognitive features, focal seizures with dyscognitive features, and focal seizures with dyscognitive features with bilateral convulsive seizures

The doctor is diagnosing epilepsy to know what kind of seizure patients. Pharmacists need to know the type of seizures of patients to consider the appropriate use of antiepileptic drugs including the dosage and dosage forms. Monitoring of adverse drug reactions, the interaction between drugs using the medication as prescribed by a doctor providing counseling to patients according to the type of seizures to maximize the effectiveness and safety of the anticonvulsant. The classification of seizures is constantly improving and developing. However, the main seizures are still similar and the name seizures have changed, pharmacists need to follow to read the evidence and evidence from old and new journals. Must also be able to assess whether there is a drug that causes seizures. Nowadays, most people have mobile phones to help record the incident while seizure. Therefore, it is very useful to provide information for diagnosis. However, information on pre-seizure symptoms seizures, and post-seizures are very useful in the diagnosis, should advise patients and relatives to observe.

2.11 Guidelines for the treatment of epilepsy

Guidelines for the treatment of epilepsy, there are both medication and non-drug therapies. Antiepileptic therapy has been developed and new drugs are increasing accordingly and have treatment guidelines for many countries and departments. However, there may be some differences, it depends on which country the drug is used and the current treatment methods are based on more empirical evidence.

Drug therapy is usually started on a single dose first. Most of them can control seizures but if the seizures cannot be controlled, a combination of drugs may be given (polytherapy) when concomitant medication is given, the seizure cannot be controlled or caused drug resistance, other non-drug treatments should be considered: surgery, insertion Electric stimulator, use of ketogenic diet and behavior modification.

Pharmacists play an important role in determining which anticonvulsants are appropriate for the type of seizure disorder or epilepsy, selection of drugs that are suitable for the patient's characteristics, adjusting the dose of anticonvulsants, monitoring of seizure control and adverse drug reactions, fostering cooperation in drug use, give advice and consult about disease anticonvulsant and patient practice including finding, solving and preventing problems from drug use.

2.11.1 Treatment goals

The goal of treatment is to control seizures to the best, without any seizure and minimal side effects. However, the control of seizures must be consistent with the quality of life, for those who cannot control the seizures until they are none at all treatment goals may be reduced to a smaller number or frequency of seizures.

2.11.2 Pharmacologic treatment

Initially, the type of seizures and the frequency of seizures must be evaluated and the type of epilepsy correctly, set possible treatment goals, maintenance plan by choosing the main drug according to the type of seizures and seizures and taking into account the characteristics of the patient such as age, sex, co-morbidity, adverse reactions from medication, adherence to Most patients (65%) can control seizures by using only one antiepileptic drug (monotherapy). However, patients may have different responses depending on the type of seizures, such as when using a single drug for 12 months found that GTC without seizures at 48-55 % focal seizure without seizures at all 23-26 % and mixed seizures type without seizures 25-32 % (24). There is a network meta-analysis study to compare the effectiveness of antiepileptic drugs in monotherapy treatment to treat generalized epileptic seizures by comparing it with valproate, lamotrigine, levetiracetam, and topiramate can be used to treat generalized tonic-clonic seizures, tonic seizures, and clonic seizure with as effective as valproate. For phenytoin, it is significantly less effective than valproate statistical significance (OR 0.5; 0.27-0.87). For the absence of seizures, valproate or ethosuximide can be

used to control symptoms. However, ethosuximide can be treated in the absence of seizures only. Therefore, it is used in the event of adverse hepatic reactions from valproate. Also, considering free seizures and withdrawal from therapeutic inefficacy and put them in order. Lamotrigine was found to be the most effective for a seizurefree and withdrawn from ineffective treatment minimal. (30)

When unable to control seizures by using only one antiepileptic drug, may have to use 2-3% antiepileptic drugs (polytherapy) 10 % of patients can control seizures. The rest, 20-25 % were unable to control symptoms of a seizure. Although using more than two drugs together means (drug resistance). In 2009, the ILAE established the definition of drug resistance: failure to control seizures when appropriate antiepileptic drugs were used and then join them together. (31)

For guidelines on the selection of various antiepileptic drugs, classified according to the type of seizures shown in Table 6- 9

Table 6 Guidelines for the selection of GTC antiepileptic drugs

Seizure type	AAN (Krumholz, 2015)	SIGN (HealthCare Improvement Scotland,2015)	NICE(Nunes et al.,2012)	ILAE(Glauser et al.,2013)	Thai (Kanjanasilp,2016)
GTC	Carbamazepine Lamotrigine Oxcarbazepine Phenobarbital Phenytoin Topiramate Valproate	Lamotrigine Valproate	Carbamazepine Lamotrigine Topiramate Valproate Second-line Clobazam Levetirazetam Oxcarbazepine	Adults Carbamazepine Lamotrigine Oxacarbazepine Phenobarbital Phenytoin Topiramate Valproate Children Carbamazepine Phenobarbital Topiramate Valproate	Phenobarbital Sodium valproate Phenytoin Carbamazepine Lamotrigine Topiramate Oxacarbazepine Second-line Levetiracetam Clonazepam Clobazam

Table 7 Guidelines for the absence of seizures and myoclonic seizures

Seizure type	AAN (Krumholz, 2015)	SIGN (HealthCare Improvement Scotland,2015)	NICE (Nunes et al.,2012)	ILAE(Glauser et al.,2013)	Thai (Kanjanasilp,2016)
Absence	Children Lamotrigine	Ethosuximide Lamotrigine Valproate	Ethosuximide Lamotrigine Valproate Second-line Clobazam Clonazepam Topiramate	Children Ethosuximide Lamotrigine Valproate	Sodium valproate Lamotrigine Second-line Clonazepam
Myoclonic	Not mentioned	Lamotrigine Valproate	Valproate Topiramate (severe) Second-line Clobazam Clonazepam Lamotrigine Levetirazetam Piracetam Topiramate	Clonazepam Lamotrigine Levetiracetam Topiramate Valproate Zonisamide	Sodium valproate Second-line Topiramate Lamotrigine Clonazepam Nitrazepam

Table 8 Guidelines for the selection of tonic seizures and atonic seizures

Seizure type	AAN (Krumholz, 2015)	SIGN (HealthCare Improvement Scotland,2015)	NICE (Nunes et al.,2012)	ILAE(Glauser et al.,2013)	Thai (Kanjanasilp,2016)
Tonic	Not mentioned	Not mentioned	Lamotrigine Valproate Second-line Clobazam Clonazepam Levetiracetam Topiramate	Not mentioned	Sodium valproate Second-line Topiramate Lamotrigine Clonazepam Nitrazepam
Atonic	Not mentioned	Not mentioned	Lamotrigine Valproate Second-line Clobazam Clonazepam Levetiracetam Topiramate	Not mentioned	Sodium valproate Second-line Topiramate Lamotrigine Clonazepam Nitrazepam

Table 9 Guidelines for the selection of anticonvulsant type partial with or without secondary generalization

Seizure type	AAN (Krumholz, 2015)	SIGN (HealthCare Improvement Scotland,2015)	NICE (Nunes et al.,2012)	ILAE(Glauser et al.,2013)	Thai (Kanjanasilp,2016)
Partial with or without secondary generalization	Carbamazepine Gabapentin Lamotrigine Oxcarbazepine Phenobarbital Phenytoin Topiramate Valproate	Carbamazepine Lamotrigine Oxcarbazepine Phenytoin Valproate	Carbamazepine Lamotrigine Oxcarbazepine Topiramate Valproate Second-line Clobazam Gabapentin Levetiracetam Phenytoin Tiagabine	Adults: Carbamazepine Phenytoin Gabapentin Lamotrigine Oxcarbazepine Phenobarbital Topiramate Valproate Vigabatrin Children: Oxcarbazepine Carbazepine Phenobarbital Phenytoin Topiramate Valproate Lamotrigine Vigabatrin Elderly: Lamotrigine Gabapentin Carbamazepine Topiramate Valproate	Carbamazepine Phenytoin Sodium valproate Phenobarbital Lamotrigine Topiramate Levetiracetam Oxcarbazepine Second-line Gabapentin Clonazepam Clobazam

Adverse reactions from the use of chronic antiepileptic drugs (chronic ADRs) are osteoporosis caused by the use of antiepileptic drugs carbamazepine, phenytoin, phenobarbital, oxcarbazepine, valproate, after only 6 months of using the drug, bone mineral density reduction can be reduced or prevented by providing calcium and vitamin D supplements to prevent fractures and follow up every 2 years. Another symptom is folic acid deficiency anemia (megaloblastic anemia) for who taking phenytoin, phenobarbital, carbamazepine, primidone, folic acid may also be supplemented by monitoring the levels of homocysteine and folate in the blood (32) or may change to use antiepileptic drugs that have little effect on folate levels, such as lamotrigine, zonisamide. Valproic acid is still in conflict but mechanically, it can inhibit the production of folic acid. (33)

2.11.3 The use of antiepileptic drugs in Comorbid disease

Treatment of epilepsy patients with joint diseases may choose antiepileptic drugs that are good for the joint disease as well for example should choose antiepileptic drugs lamotrigine, carbamazepine, oxcarbazepine for patients with depression. Patients with headache should choose valproate, topiramate since the drug has a preventive effect on headache as well or should be careful of the effect of antiepileptic drugs on the joint disease as well for example patients with depression should avoid the use of drugs levetiracetam, phenytoin, for patients with headache, the use of lamotrigine, felbamate should be avoided, etc.

There are attempts to find empirical evidence that will guide the use of drugs in various diseases as follows: heart disease, lung disease, liver disease, kidney disease, porphyria, organ transplantation, thyroid metabolic disorder, mental disability infection, psychiatric disorder, cognitive impairment, stroke, and brain tumor but since most studies are case series and retrospective analysis were not studied RCTs. Therefore, the selection of drugs is recommended based on the data of the characteristics pharmacokinetics, drug tolerance which uses expert experience. (34)

2.11.4 Switching drugs

If the antiepileptic drug is not effective in controlling seizures or adverse reactions, the drug must be changed. The drug should not be stopped suddenly because it can cause seizures. To start a new antiepileptic drug, gradually increase the dose and gradually reduce the original dose until stopped.

2.11.5 Withdrawal or stop antiepileptic drugs

The use of anticonvulsants may not be necessary for life-long therapy. To stop the drug, some factors indicate that stopping the drug will not cause another seizure for example no seizures for 2-4 years, able to control seizures completely within a year who began to seizure, began to have seizures between the ages of 2-35 yearsand the neurologic examination and EEG normal, for factors relating to poor prognosis at the risk of not being able to control seizures when stopping the drug, despite where the patient can control their seizures or have no seizure at all (seizure-free) or refers to factors that indicate that the patient should not stop the drug such as a history of very frequent seizures, have repeated episodes of status epilepticus, having multiple seizures together and have an abnormal mental function. The AAN has established a stopping guideline for patients without seizures (seizure-free) as follows after assessing the risks and benefits of discontinuation on patients and their social impact can stop the drug according to the criteria prescribed are:

1. No seizures for at least 2-5 years
2. Having only one history of seizures, focal seizure, or primary generalized seizures only one history of seizures, focal seizure, or primary generalized seizures
3. Neurologic exam and normal IQ
4. Normal EEG test

When the drug is stopped, the relapse rate at 1 year is 35% and at 2 years is 29%.

For patients after surgery must take anticonvulsants and when there is no seizure for at least 1-2 years, the drug may be stopped but must be gradually decreased, the dose may be reduced by at least 3-6 months.

2.11.6 Risk factors for repeated seizures

Risk factors for repeated seizures are:

+ Structural CNS lesion
+ Abnormal EEG
+ Partial seizure type
+ Positive family history
+ Postictal motor paralysis

If none of these factors, patients have a 10-15% chance of recurring seizures, if these factors at least 2 and up patients have a 100% chance of having repeated seizures. Therefore, if a patient has these risk factors anticonvulsants should not be stopped due to a high chance of repeated seizures.

2.11.7 Drug interaction

Since most anticonvulsants are changed by various enzymes own antiepileptic drugs and drugs used in combination may also have properties to induce or inhibit enzymes. Therefore, drug interactions may easily occur when used together. Table 10 anticonvulsants which are substrate of enzymes and common enzyme inducers and enzyme inhibitors have been summarized. To be careful in sharing and track interactions that may occur. This could lead to uncontrolled seizures or adverse drug reaction, information common drug interactions are shown in Table 7.

Table 10 Drug interactions of antiepileptic drugs with enzyme inducers and enzyme inhibitors (35,24).

Enzyme	Substrate	Common inducers	Common inhibitors
CYP1A2	Carbamazepine	Carbamazepine, Phenytoin, Phenobarbital, Rifampin	Cimetidine, Ciprofloxacin, Erythromycin, Clarithromycin, Stiripentol
CYP2C9	Phenobarbital Phenytoin Carbamazepine Valproate	Carbamazepine, Phenytoin, Phenobarbital, Rifampicin	Amiodarone, Cimetidine, Fluconazole, Valproate
CYP2C19	Phenobarbital Phenytoin Valproate Lacosamide		Felbamate, Ticlopidine, Topiramate, Zonisamide, Stiripentol
CYP2D6	Zonisamide	Carbamazepine	Stiripentol
CYP3A4	Carbamazepine Tiagabine Zonisamide	Carbamazepine, Eslicarbazepine, Phenytoin, Phenobarbital, Oxcarbazepine, Rifampin, Rufinamide	Amiodarone, Erythromycin, Propoxyphene, Ketoconazole, Stiripentol
Uridine diphosphate glucuronyl transferase	Lamotrigine Carbamazepine Valproate	Lamotrigine Oxcarbazepine Phenobarbital Phenytoin Hormonal contraceptives	Valproate

2.11.8 Nonpharmacologic treatment

There are several treatments for non-drug epilepsy including surgery, vagus nerve stimulation (VNS), ketogenic diet and behavioral therapies, etc.

2.11.8.1 Surgery

It is the primary treatment option for patients with drug-resistant focal epilepsy. In particular, seizures with abnormal brain electrical points at the temporal lobe, about 15 % of patients treated with the drug did not improve need to have surgery. Before the surgery, you must find the position that is lesion by examination MRI, PET, and single-photon emission computed tomography scans and may use EEG and video telemetry monitoring to measure the occurrence of seizures. Most surgeries are cut in the anterior part temporal lobe after surgery about half of the patients recovered from seizures and 1 in 3 had significantly reduced symptoms. The RCT study found that 58 % of the patients who had the surgery had no seizures for at least 1 year when compared to the group did not have surgery, only 8 % had no seizures, there were no seizures at all. (36) In another RCT study, 73.3 % of the surgery group had no seizures at 2 years, while the continued drug group had none of the patients without seizures. (37) Side effects of surgery can affect learning and memory and general intellectual abilities. Patients may have received antiepileptic drugs continuously but may have to reduce the dose. The predictable factor for a good

outcome from surgery is that an MRI is examined, have mesial temporal sclerosis on one side, PET detected anomalies (Even though a normal MRI exam). Electrocardiogram examination found abnormal spots during seizures and decreased abnormalities before surgery and if found that there is a possibility of resistance and immediately operate immediately.

2.11.8.2 Nerve stimulation (VNS)

It is a medical device implanted in the skin of the chest which is approved by the US Food and drug administration as adjunctive therapy. To reduce seizures in pediatric patients older than 12 years and adults with partial-onset seizures which antiepileptic drugs resistant and for treating primary generalized epilepsy (off-label) or used for patients who cannot operate. The mechanism of treatment is not yet clear but human studies show that stimulation of the vagus nerve. This causes the concentration of both stimulating and inhibitory neurotransmitters in the cerebrospinal fluid to change, cause increased blood flow to the brain and stimulate the brain in some areas and cause regulates the nerve impulses that cause seizures and there should be a mechanism related to the locus coeruleus equipment to stimulate relatively safe and may have a positive effect on the patient's mood and behavior and it was not associated with a reduction in seizures. A common side symptom is a hoarseness, pharyngitis, dyspnea, dyspepsia, and nausea, serious side effects include infection, nerve paralysis, hypoesthesia, facial paresis, left vocal cord paralysis, left facial paralysis, left recurrent laryngeal nerve injury, congested urine, and low fever treatment results from VNS at three months. It was found that 23-50 % of patients had a frequency of seizures decreased by at least 50 %. However, VNS treatment does not control seizures all but helps reduce the use of antiepileptic drugs.

2.11.8.3 Ketogenic diet

Most of the ketogenic diet in the treatment of patients with drug-resistant epilepsy especially caused by GLUT1 deficiency ketogenic diet. It is a high-fat food, carbohydrates, and low in protein thus causing acidosis and ketosis but there must be sufficient protein and calories for growth. Most calories or energy obtained from foods such as cream and butter by this group of patients do not eat sugar, urine ketones may need to be tested, provide enough vitamin and mineral substitutes, may provide food containing medium-chain triglycerides instead of fatty foods, and must control the amount of water as well, parents must cooperate and tighter. Most patients cannot tolerate treatment, Long-term side effects are kidney stones, increased risk of fractures, high blood cholesterol, and has growth retardation. There are many forms of ketogenic diets that can make the patient more resistant to treatment such as the modified Atkins diet and the Low Glycemic Index.

2.11.8.4 Behavioral Therapies

Psychological treatment, is effective in treating patients with impulsive seizures with flashing light or visual patterns, reading or listening to the sound (reflex epilepsies), in such a case behavior adjustment will work well.

Conclusion:

Nowadays, the treatment of epilepsy has advanced technology and there are more effective treatments such as surgery but the treatment is still largely used antiepileptic drugs which have more and more new types of antiepileptic drugs. These are drugs that have different mechanisms and there are several treatment approaches. However, this approach contains evidence-based studies empirical. This chooses medication categorized by type of seizures and epilepsy effectively. Pharmacists can be involved in selecting anticonvulsants, dose adjustment, the choice of medication when the patient has various diseases, avoiding the interaction between drugs and the negative effects of anticonvulsants on that disease, monitoring of adverse drug reactions. The key is to emphasize cooperation in the use of drugs because the drug must be used for a long time and give advice, discuss drug withdrawal and drug discontinuation.

2.12 Anticonvulsants and drug selection guidelines

Antiepileptic drugs are divided into three generations. First-generation AEDs into the market during the years 1857-1958 including potassium bromide, phenobarbital (PB) drugs that are structural derivatives of barbiturates such as phenytoin (PHT), primidone (PRM), trimethadione, and ethosuximide (ESM). (38) Second generation AEDs debuted in the years 1960- 1975, these include carbamazepine (CBZ), valproate (VPA), and benzodiazepines such as chlordiazepoxide, diazepam, clonazepam, and clobazam. Its chemical structure is different from that of barbiturates. (38) Third-generation AEDs, is often used for adjunctive use in patients with drug resistance, including vigabatrin, zonisamide, lamotrigine, oxcarbazepine, felbamate, gabapentin, topiramate, tiagabine, levetiracetam, pregabalin, stiripentol, rufinamide, lacosamide, eslicarbazepine acetate (38). There are also new antiepileptic drugs that came out later such as ezogabine (2011), perampanel (2012), brivaracetam (2016), etc.

Some references provide second-generation anticonvulsants: felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, rufinamide, stiripentol, tiagabine, topiramate, vigabatrin and zonisamide, and the third-generation anticonvulsants are eslicarbazepine acetate and lacosamide. (39) or another study held the third generation as follows: brivaracetam, eslicarbazepine acetate, lacosamide, rufinamide, perampanel (40) which the classification of this model also vary. However, this chapter will discuss the details of individual antiepileptic drugs such as

the mechanism of action, dose used, pharmacokinetic characteristics, adverse reactions, and the drug interaction for selection and use as follows phenobarbital, carbamazepine, phenytoin, and valproic acid that use frequently for Setthathirat hospital.

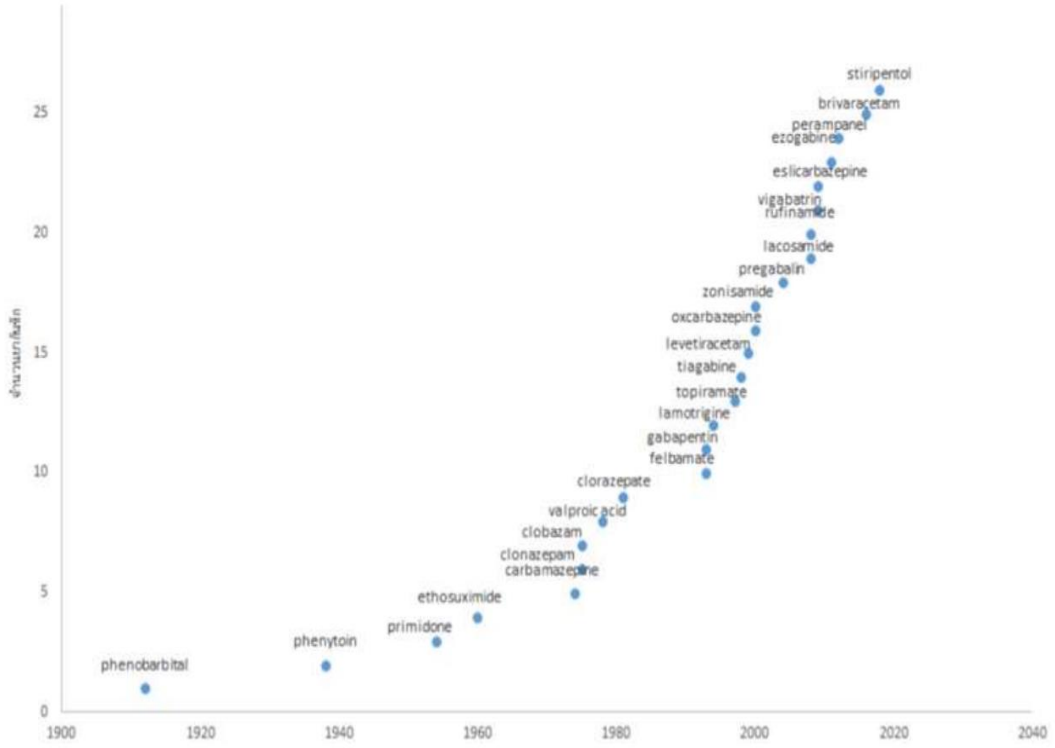


Figure 2Three generations of anticonvulsants (40)

2.12.1 First-generation antiepileptic drugs details are as follows:

- Phenobarbital
- Phenytoin
- Primidone
- Ethosuximide

2.12.2 Second-generation antiepileptic drugs:

- Carbamazepin
- Clonazepam
- Clobazam
- Valproic acid
- Clorazepate

2.12.3 Third-generation antiepileptic drugs:

- Felbamate
- Gabapentin
- Lamotrigine

- Topiramate
- Tiagabine
- Levetiracetam
- Oxcarbazepine
- Brivaracetam
- Zonisamide
- Pregabalin
- Lacosamide
- Rufinamide
- Vigabatrin
- Eslicarbazepine
- Ezogabine
- Perampanel
- Stiripentol

In the hospital, there are only four antiepileptic drugs and the researcher will review the specific drugs that are available in the Setthathirat hospital.

2.12.4 Phenobarbital

It was first used in 1912 and has been used indefinitely but the latter, because there are medications that have fewer side effects and more effective thus making use of phenobarbital is used as an alternative when a single first-line drug is ineffective. Mostly phenobarbital will work in the treatment of partial and generalized tonic-clonic seizures. Although the mechanism of action of the drug is still unknown exact it is estimated that the effect on GABA and making postsynaptic effects of excitatory neurotransmitters such as glutamine reduced.

Pharmacokinetic

Phenobarbital was available as a sodium salt in capsules, tablets, elixir, and injection. The usual dose is used as a maintenance dose in adults is 1-3 mg/kg / d, for infants and children, the normal dose is 3-4 mg/kg. It is usually given once before bedtime to avoid daytime drowsiness. Food makes the absorption slows down but all absorbed quantities do not change. The drug has a very long half-life of about 4 days which leads to a steady-state, it takes a time of about 2-3 weeks, so may require a loading dose to get immediate results the loading dose is 15 mg/kg IV, the dosing rate should not exceed 100 mg/min, giving loading dose by eating by dividing the dose into 3 divided doses 24 hours apart. The drug is almost completely absorbed by mouth and IM injection. The time to reach the maximum drug level is less than 4 hours, The drug binds to protein in the blood in low amounts. The drug is eliminated with first-order kinetics. The drug is transformed by the liver to 30-50% inactive substances by process glucuronidation and sulfation and excreted in the urine.

Adverse drug reactions

Adverse reactions related to the CNS dose are: sedation, nystagmus, dizziness, ataxia, mild drowsiness is usually the beginning of the drug but it will get better in 2-3 weeks but there are some symptoms throughout in these patients may require dose reduction but the major adverse reactions and has a negative effect: behavior, mood, and cognition. In children, it is reversible for hyperactivity and insomnia. 40 % of the elderly were paradoxical excitation. This behavioral change usually occurs during the first 2-3 months of taking the drug. Using valproate or carbamazepine instead can improve these symptoms. Medicines also cause depression and lack of interest or goal which will be better when the drug is stopped. Medicines also have cognitive effects concerning the dose such as amnesia, intelligence decreased, work done less, unable to perform complex tasks.

Serious adverse reactions include morbilliform rash 1-3 %. Some have changed to steven johnson syndrome or exfoliative dermatitis or hepatitis or bone marrow suppression but very rare beware of cross-reactivity with carbamazepine and phenytoin, if allergy occurs, valproic acid may be used instead. The occurrence of megaloblastic anemia with folic acid deficiency was less than 1% and responds to folic acid replacement prolonged use of the drug also affects bones such as osteomalacia.

Drug interaction

Phenobarbital accelerates drug changes in the liver including theophylline, warfarin, cyclosporine, chloramphenicol, valproate, felbamate, lamotrigine, chlorpromazine, haloperidol, tricyclic antidepressants, enzyme induction level and very variable drug changes in individual patients and related to genetic, enzyme induction it may persist for days to weeks after stopping the drug. The level of carbamazepine may not change or decrease when used with medication phenobarbital. Also, phenobarbital can inhibit the transformation of some drugs as well by vying to capture the enzyme.

The effects of phenobarbital on phenytoin levels are uncertain, drug levels may rise, fall or in most patients, it will not change.

Valproate causes drug levels of phenobarbital to increase which may cause toxic symptoms, effects of phenytoin on phenobarbital levels not predictable but most have no clinical significance.

2.12.5 Phenytoin

Phenytoin is a derivative of hydantoin, has been used to treat epilepsy since 1938. phenytoin is used to treat partial seizure and generalized tonic-clonic seizures but not effective in treatment absence and febrile seizures. The drug works by blocking mechanisms on sodium and calcium channels but the specific mechanism in detail is not yet known.

Phenytoin has many forms including suspension is available in the form of free acid at 30 mg / 5 mL and 125 mg / 5 ml. Chewable tablets are free acid form as well 50 mg, a capsule of 30 mg and 100 mg is in the form of sodium salt, the 50 mg/ml injection form is also in the sodium salt form. The drug is in the form phenytoin sodium salt is 92 % which will affect the drug level. If the drug form is changed which will affect the amount of drug received.

Dosage may begin at a daily dose of 300 mg, maintenance 300-400 mg / d. Dilantin capital is a type of capsule extended-release that can only be administered once a day. Medicine part of other companies and other formats such as suspension and injection must be given in the divided form, the loading dose is 15 mg/kg, oral administration may be given once or divided to 200-400 mg every 2-4 hours, if given IV should not be higher than 50 mg/min, to reduce the risk of hypotension and cardiac arrhythmias caused by propylene glycol 40% that is diluent. In the injection drug when a high-dose injection is administered blood pressure should be measured and heart rate periodically should not be injected into a muscle because there will be crystallization on the muscles, it causes a lot of pain and is poorly absorbed.

Fosphenytoin is a prodrug of phenytoin which soluble well, in injection form propylene glycol is not required. This drug has a less venous irritation effect and can be injected via IM.

Pharmacokinetic

Drug binding to proteins especially albumin and 90 %. Therefore, if the patient has renal failure and in combination with other high protein binding drugs will affect protein binding change and affects drug levels in the blood. Phenytoin is severely damaged by the liver, mainly by the process of para-hydroxylation the main metabolite is 5 - (hydroxyphenyl) -5-phenyl hydantoin which has no anticonvulsant effect, the restless than 5% were excreted in the kidneys original picture. Medicines are eliminated from the body by non-linear pharmacokinetics. Therefore, dose changes a little will cause drastic changes in drug levels.

Adverse drug reactions

Acute adverse reactions associated with the dose, ataxia, diplopia, drowsiness, encephalopathy, and involuntary movements. These symptoms typically occur at drug levels greater than 30 mg/ml and can be cured when stopping the drug or reducing the dose involuntary movement such as dyskinesias of the limbs, torso, the face is similar to prolonged exposure to psychiatric drugs. The toxic dose can also cause seizures but is less found. Also, have nystagmus, is a side effect that is related to the dose as well may be found at drug levels in the range of therapy but do not need to reduce the dose for treatment.

Adverse reactions that occurred with prolonged use of the drug including swollen gums (gingival hyperplasia, facial coarsening, peripheral neuropathy, vitamin deficiencies).

Gingival hyperplasia is a dose-related adverse reaction. It was found in more than 40% of adult patients, usually in the first 3 months and more in the first year of taking the drug. Patients at risk with the following adverse reactions are children and people with poor oral hygiene. Patients must be instructed to brush and floss regularly and see the dentist regularly. If there is still not much swelling, may respond to good oral care or reduction in dose but if it is a lot, surgery may be required or an anticonvulsant drug must be replaced.

Prolonged use of this drug may change the facial contours, hirsutism, and acne, make it a restriction on the use of this drug in children, adolescents, and young women.

Prolonged use of this drug causes peripheral neuropathy with deep tendon reflexes and sensory deficits. It often occurs in patients who take phenytoin and phenobarbital and not reversible. phenytoin caused megaloblastic anemia with folic deficiency less than 1% and treated with folic acid to be substituted but giving folic acid to prevent unnecessary because folic acid, has a disturbing effect on phenytoin metabolism. Medicines affect bone density and mineral content. Although most of them do not have symptoms it may also find osteomalacia and osteoporosis, which may be caused by a change in vitamin D metabolism and interference with calcium absorption with prolonged use of phenytoin, giving vitamin D and calcium replacement is necessary or not, there is no definitive research but patients at high risk such as eat food not getting enough sunlight or exercising should be closely monitored.

Adverse reactions idiosyncratic usually occur within the first 8 weeks such as rash, hepatitis, lymphadenopathy, and effect on the blood system.

Skin rashes occurred less than 10 % occur in the first 14 days and often occurs with hepatitis, lymphadenopathy, and fever, usually a morbilliform rash is found but may develop into a Stevens-Johnson syndrome, erythema multiforme, or TEN, if the rash spreads into the mucous membranes or associated with fever must stop taking the drug. Hepatitis usually occurs with fever, rash, and lymphadenopathy within the first 3 weeks of receiving the drug need to stop taking the drug immediately as well and even after stopping the drug. In some patients, there is still further destruction of the liver and causes encephalopathy, coma, and can die. The effects on the blood system are transient depression of leukocytes and aplastic anemia or agranulocytosis but found very little, the occurrence of idiosyncratic adverse reactions. The severity of these should not be rechallenged and be careful of cross-reactivity with other aromatic AEDs such as phenobarbital or carbamazepine.

Drug interaction

Phenytoin is a potent inducer that will affect the medicine that was eliminated by the same enzyme system causing that drug to be eliminated more including oral contraceptives, warfarin, corticosteroids, cyclosporine, theophylline,

and other anticonvulsants, such as carbamazepine, valproate, felbamate, lamotrigine, and clonazepam, although phenytoin increases warfarin metabolism the results cannot be predicted and may cause the effect of anticoagulant temporarily reduced. Warfarin should be monitored closely when used in combination with phenytoin.

Antacids and nutritional formulas causing phenytoin levels to decrease. This is because phenytoin may bind to (chelate) cation or change the PH or decreased bowel movements reduce the absorption, therefore should give antacid and phenytoin at least 2-3 hours apart. Drug administration rubber strap causing phenytoin levels to drop greatly but the exact mechanism is not yet known, co-administration with Isocal® and Osmolite® resulted in a decrease in phenytoin levels but giving with Ensure® did not reduce the drug level. Therefore, phenytoin levels should be monitored closely when giving through the hose or stop giving way to the hose including when changing the recipes provided by the hose as well.

The medicines heparin, phenylbutazone, tolbutamide, valproate will replace the protein binding of phenytoin. Folic acid, alcohol, rifampin increases the metabolism of phenytoin, valproate, isoniazid, amiodarone, cimetidine, omeprazole, phenylbutazone, disulfiram, sulfonamides, chloramphenicol will reduce the metabolism of phenytoin.

2.12.6 Valproic acid

Valproate is used to treat both partial and generalized seizures including tonic-clonic and absence seizure, effective for treating secondarily generalized tonic-clonic seizures equals carbamazepine valproate short, branched-chain fatty acid. The mechanism of action is not fully known but it may be related to the potentiation of GABA in the CNS.

Valproate is sold in the form of valproic acid (Depakene®) in soft gelatin capsules 250 mg and 250 mg / 5 ml syrup and divalproex sodium (Depakote®) in 125 mg, 250 mg, and 500 mg enteric-coated tablets, divalproex sodium breaks down into valproate. In the digestive tract, dosing with valproic acid should start at 125-250 mg 2-3 times a day and gradually increase the dose to 250 mg every 3-7 days. The usual dose is 750-1,500 mg divided 3-4 times a day.

Pharmacokinetic

Bioactivity of 100% is bound to high protein at blood drug levels below 75 mg / ml bind to protein about 90 %, most of them are albumin but if the drug level is higher than 100 mg / ml will result in saturation of the protein position increased free fraction by more than 50 %. The drug has a half-life of 12-16 hours. The main metabolites of drugs with antiepileptic effect to achieve the maximum effect of the drug takes several weeks.

Adverse drug reactions

The most common side effects were 35% of patients with gastrointestinal tract, nausea, vomiting, anorexia was reported and other abdominal discomforts can reduce symptoms by giving medication that is enteric-coated.

Adverse drug reactions related to neurologic drug dose, common are fine tremor which is reversible. If found to have temporary symptoms during the day may adjust the dose by giving more often but the dose less or may need to be given propranolol. Valproate had fewer behavioral and cognitive effects than phenytoin, phenobarbital, primidone.

Other adverse reactions related to dose were weight gain, more than 50 % alopecia, temporarily during initiation of treatment may be corrected by reducing the dose and changing platelet function causing increased bleeding time which must be careful in patients receiving high-dose or patients who are about to have surgery increased liver enzyme levels by about 40 %, most of them have no symptoms and respond to reducing the dose or discontinuing the drug.

Discontinuation of valproate should be discontinued in the following cases:

- Liver enzyme levels increased by 3 times more than baseline.
- With abnormal liver function for synthesis or metabolism for example having bilirubin levels increased prothrombin time prolonged the albumin decreased.
- Have signs and symptoms of hepatitis (hepatitis).

Therefore, liver enzyme levels and liver function should be measured before starting the drug.

Valproate induces fulminant hepatotoxicity causing coma and can die although the birth rate is very small: 1 in 49,000 but must be careful with use especially at-risk groups including children under 2 years using polytherapy and development delay hepatotoxicity usually during the first 6 months of using the drug, symptoms that can lead to hepatic failure include GI distress, anorexia, sudden loss of seizure control. Therefore, advice on the occurrence of these symptoms or those related to hepatitis must be given. Patients must inform their doctor or pharmacist as soon as possible because if the drug is stopped quickly symptoms may improve. Dreifuss et al. (1987) (41) introduced a guideline to reduce the risk of liver toxicity from valproate as follows.

1. Avoid using valproate with other anticonvulsants in children under 3 years. If using monotherapy does not work. The combined use of antiepileptic drugs should be considered between good and bad.

2. Avoid valproate in patients with liver disease or a family history of liver disease.

3. Give the lowest dose that can control seizures.

4. Avoid using valproate with salicylates in children and avoid fasting children during the illness.

5. Monitor any of these symptoms: nausea, vomiting, headache, lethargy, swelling, jaundice, or seizures especially after a fever.

Drug interaction

Valproate is an enzyme inhibitor specifically CYP2C9 (72), Phenobarbital metabolism inhibitors make the drug level of phenobarbital 80 % higher but it was reported that there was a difference between 0-200 %. Therefore, dosage adjustment is not recommended phenobarbital when used together but may measure drug levels phenobarbital in the blood first and then adjust the dose. The interactions with phenytoin are quite complex both enzyme inhibition and protein binding displacement can occur. Phenytoin levels tended to drop when valproate was administered and with increased valproate, the free fraction of phenytoin may be increased due to the protein binding of valproate.

Phenobarbital, carbamazepine, phenytoin, and primidone causing the valproate level to drop by 30-40 % and the half-life is reduced to 6-9 hours. Aspirin may replace valproate's protein binding and cause competitive inhibit oxidation.

The drug has potential teratogenic effects. Therefore must be careful when using the drug in pregnant women.

2.12.7 Carbamazepine

Carbamazepine is a drug that has a similar structure to imipramine use to treat Generalized tonic-clonic and partial seizures especially complex partial seizures but does not work in a seizure myoclonic or absence seizures. United States Food and Drug Administration approved for use in treating Focal onset seizures, GTC seizures, and mix seizures types. Medicine will make absence seizures worse, induce tonic-clonic seizures. In patients with generalized seizures another kind. The drug works by affecting sodium channels (42,43) by promoting the fast inactivation of voltage-gated Na + channels and may affect voltage-gated Ca2 + and K + channels as well (27).

Carbamazepine (Tegretol®) available in pill form immediate-acting (given 4 times a day) and controlled-release (give twice a day). The dosage should start with 100-200 mg 2 times a day and gradually increase the size at a time of 200 mg every 3-7 days or for adults starting at 400 mg / d, adjusted in a 200 mg increment every week (adjusting the size too quickly, risking a rash). Although the manufacturer advises that the drug should not exceed 1,200 mg / d doses sometimes more than 2,000 mg / d doses are used to be able to control seizures. The loading dose is normally not given to outpatients, due to it affects the gastric disturbance. However, a nasogastric route was given at a dose of 8-10 mg/kg (Some textbooks give 7.4-10.4 mg/kg) once in a critically ill patient if given at high doses, nausea and vomiting may occur and has a depressing effect on the central nervous system. Children may need to be administered more slowly than adults. If there are adverse reactions to the central

nervous system and digestive tract, it may help by giving an increased dose before bed instead keep the tablets must not be exposed to heat and high humidity.

Pharmacokinetic

Medicines there are forms action immediate-release and (controlled-release; Tegretol-XR® and sustained-release Cabatrol®). The absorption of drugs from the digestive tract is often slow and does not follow the first-order kinetics, time at the highest dose level 4-8 hours average (6 hours mean) and may last up to 24 hours, slow absorption may be due to slow dissolution, food does not affect absorption (some textbooks that food increases bioavailability) especially fatty foods (24) no first-pass metabolism early acting drugs have lower maximum drug concentrations and the lowest drug concentration increased, causing an adverse reaction from decreased drug use and improved quality of life. Instructions for using the drug must be given to the patient, is to not crush or chew the drug in such an early-acting form. For Cabatrol® there was a lower bioavailability than Tegretol-XR®. (24)

Since the drug is neutral and lipophilic, it binds to the α1-acid glycoprotein and albumin. Most of the drugs are changed in the liver, most of them will pass through the CYP3A4 system, the major metabolite is carbamazepine 10,11-epoxide which also has an anti-seizure effect. The rest were caught with glucuronide, sulfate or has been altered by other oxidation processes. 2 % of the drug was excreted in the urine in its original form, the half-life when given a single dose is 24-45 hour, long-term dosing (chronic) will have a lower half-life because in the first of receiving the medicine will occur autoinduction of cytochrome P-450, causing the drug level in the blood to be reduced by 50 % but the occurrence of autoinduction. This will be complete in the first 1 month received.

Obtaining drugs are enzyme inducer such as phenytoin, phenobarbital, primidone will add medication changes as well so metabolic clearance and the half-life depends on the duration of treatment and concomitant drugs. Therefore the need for a high dose of the drug and given with a higher frequency than usual such as 3-4 times a day. To reduce the occurrence of seizures during periods of very low drug levels or the occurrence of adverse reactions during periods of very high drug levels but nowadays it is used in the form of CR drugs to solve such problems, due to the absorption of the drug and removal of drugs in individual patients is very different (interindividual variability), medicine has diurnal variation, the drug level in the blood in the evening is lower than in the morning. The drug elimination of women was significantly higher than that of men and the Caucasians were higher than the African Americans. Therefore, a different dose must be prescribed, and measuring blood drug levels to obtain optimal drug levels may be necessary. (24)

Adverse drug reactions

Adverse reactions related to dose-related dosing include dizziness, drowsiness, anorexia, nausea. These symptoms get better in the first few weeks can reduce symptoms or avoid by gradual dose adjustment, disorders of the gastrointestinal tract such as nausea can be alleviated by taking the medicine with food but if nausea occurs from the effect on the brainstem may need to stop the drug, symptoms associated with the drug include diplopia, headache, ataxia, depression, irritability, mental sluggishness, impairment of concentration and short term memory, overdose, unusual movement disorders, and induced seizures.

Hyponatremia and water retention may be caused by increased secretion of antidiuretic hormone is an adverse reaction that is related to the dose as well and will be better when reducing the dose. Hyponatremia (born less than oxcarbazepine) often occurs in the elderly should surveillance and measuring blood sodium levels (24), when the blood sodium level is below 120 mEq/L. There will be a headache, confusion, dizziness, seizures, treatment by limiting water, reducing the dose, or stopping the medication if further medication is needed, treatment may also be performed demeclocycline. Additionally, carbamazepine causes cardiac conduction disturbances which often occurs in elderly patients and is given a high dose. In elderly patients, interviews are required. In elderly patients, interviews are required a thorough history and ECG should be checked before starting to use the drug or measure the drug level in the blood periodically, adverse reactions not related to dose such as rash, about 5-9.9% usually occur during the first 1-2 weeks of drug exposure. The most common is not serious (benign). They are maculopapular, urticaria, and morbilliform but may occur in a serious form including exfoliative dermatitis and Stevens-Johnson syndrome. In some cases, allergic rashes may be accompanied by symptoms including fever, generalized lymphadenopathy, hepatomegaly, splenomegaly, and less common are nephritis and vasculitis, symptoms will disappear when the drug is stopped and administered corticosteroids patients with drug allergy carbamazepine. There may be a drug allergy cross-reactivity with other aromatic anticonvulsants, eg phenytoin, phenobarbital in which case valproate may be given instead.

Reducing the risk of adverse drug reactions persevere blood system do this by educating patients and laboratory monitoring, when starting to use the drug, the patient will have to watch for abnormal symptoms such as high fever, infection, petechiae, or unusual exhaustion if the patient is found to have aplastic anemia must stop the drug and forbidden to be rechallenged.

The laboratory examination section including complete blood counts (CBC), before starting medication and every 2 weeks in the first 2 months, if there is no abnormality check every 3 months or when there are signs or symptoms of the bone marrow, for mild leukopenia, CBC should be checked every 2 weeks until

normal, absolute neutrophil count below 1500/mm^3 or have an infection should stop the drug (some textbooks to discontinue the drug when WBC count < 2,500/mm^3 or absolute neutrophil count < 1,000/mm^3). Also, oftentimes thrombocytopenia and anemia less than 5 % would respond to discontinuation of carbamazepine.

Drug interaction

Carbamazepine is a potent inducer increasing the elimination of drugs such as theophylline, doxycycline, haloperidol, warfarin, corticosteroids, valproate, clonazepam, ethosuximide, lamotrigine, felbamate and various hormones including birth control pills which reduces the effectiveness of these drugs, effect of the drug on phenytoin drug levels, phenobarbital, and primidone, uncertainty may be due to both the induction and inhibition different levels. Therefore, it may be necessary to measure the blood level of the drug when dosing The drugs that inhibit drug destruction carbamazepine, including danazol, dextropropoxyphene, erythromycin, isoniazid, verapamil, diltiazem which these drugs will make carbamazepine have increased blood levels of the drug which can reach toxic levels. Also, cimetidine was found may have an inhibitory effect on drug destruction as well but ranitidine had no effect. The drug increases the destructive drug carbamazepine, Phenytoin, phenobarbital, primidone. Valproate may increase drug levels carbamazepine increased, decreased or unchanged, due to the effect of substituting protein binding carbamazepine, a variety of drugs and may inhibit drug changes carbamazepine but increased levels 10,11- epoxide carbamazepine without affecting drug level carbamazepine.

Carbamazepine dosing in the form of suspension via the NG tube line, resulting in a decreased absorption of the drug which may be caused by the drug binding of the tube, recommended should be diluted before giving the tube.

Original anticonvulsants (First and second generation) is a drug that healthcare professionals are familiar and use frequently for Laos, since as a drug that has been used for a long time. There is information on adverse reactions from drug use and adverse drug reactions were reported to be higher compared to newer drugs. In addition, this class of drugs has complex pharmacokinetic properties both causing a lot of drug interactions. Pharmacists should monitor the results of treatment or the occurrence of adverse reactions from drug use or interaction especially when the drug was used in combination with other drugs. The new group (third generation) of anticonvulsants has the advantage of a new mechanism of action making the choice of antiepileptic drugs more options and anticonvulsants with different mechanisms of action can be used to synergize. However, there are still few adverse reactions and some have severe adverse reactions. They are also expensive. These drugs are used primarily for add-on or adjunctive therapy and still need to monitor for adverse drug use continuously. The selection of anticonvulsants must be correct for the type of seizures and epilepsy is the main.

2.13 Pharmaceutical care for patients with epilepsy

2.13.1 Introduction

Epilepsy patients are the most common neurological disease patients. Treatment is primarily antiepileptic 60-70% can be controlled with monotherapy but some patients need to use polytherapy. The goal of treatment is to control the seizures at least for 2-5 years or some need a lifetime. Therefore, drug use often has problems with drug use such as adherence, and the occurrence of adverse drug reactions because of the antiepileptic properties, especially the first [1] class drugs, they often have complex pharmacokinetic properties and a narrow treatment range and there are many new anticonvulsants. Therefore there may be a problem with adjusting the dose, the occurrence of drug interactions, or choosing the right medication for the many subsequent seizures. Pharmacists play a role in providing pharmaceutical care for epilepsy patients to assist multidisciplinary teams such as finding problems from drug use together with planning to solve, and prevent drug use problems, giving advice and consultation on drugs, monitoring adverse drug reactions, blood drug monitoring service, evaluation of drug use or integrating, up-to-date knowledge such as new antiepileptic drugs. Bioequivalence of drugs or information on pharmaceutical genetics applied in pharmaceutical care to keep patients safe use drugs effectively and have a good quality of life.

2.13.2 The counseling of the drug to patients with epilepsy.

It is pharmaceutical care to find solve and prevent problems from drug use, providing drug counseling to patients and their families with the goal of seizure-free treatment. Therefore, it is recommended that the patient or relative record the number of times and seizure diary to evaluate the efficacy of drugs in seizure control including emphasizing adherence which is very important in symptom control. It should therefore be recommended that the medication be recorded as well. In addition, the observation of adverse drug reactions and management methods must also be suggested during drug consultation giving advice. Pharmacists must find problems from drug use, prevent and modify which may be corrected by educating both the disease about antiepileptic drugs, drug withdrawal, patient behavior modification to enhance drug use co-ordination or coordinating with the treating doctor to modify the dose drug use patterns or change the drug, etc.

Classification of drug use problems, can be divided into several types (41) popular such as the Hepler and Strand (1990) classifications are divided into 8 categories as follows:

1. Untreated indications
2. Improper drug selection
3. Subtherapeutic dosage
4. Failure to receive drugs

5. Overdosage
6. Adverse reactions
7. Drug interactions
8. Drug use without indication

And the European classification of drug use problems is Pharmaceutical Care Network Europe (PCNE). Currently version 8.02 the problem is divided into 3 categories only:

1. Treatment effectiveness
2. Treatment safety
3. Others

Along with the need to identify the cause of the problem from drug use, planning interventions, acceptance of intervention, and the status of the DRP.

Long-term ongoing monitoring needs to consider comorbid conditions, social adjustments such as QOL assessment, drug-drug interaction, drug-food interaction, adherence, and screening periodic depression and anxiety (neuropsychiatric disorders).

Besides find, solved and prevented problems from using drugs, the pharmacist must give advice on other triggers that should be avoided. Triggers include fever, sleep deprivation, sudden stopping of alcohol, certain drugs or drugs, flashing light, noise, severe physical or mental stress, menstruation exercise, avoiding dangerous routine, driving, swimming or being alone near a water source, thermal activities or mechanical lights and high places, etc.

The effects of pharmaceutical care for inpatient epilepsy patients were studied from the hospital totaling 65 cases. The results found that the drug problems were nonadherence 64.6%, insufficient dose 51.9%, adverse reactions from drug use 76.2%, do not use the drug monitoring service in the blood 41.5% and the treatment is unsuitable for patients with liver disease, patients with poor drug co-operation only 19%, only to receive advice on medication and adherence was associated with seizure control (OR 7.06 CI 1.29-38.56, p = 0.019). (42) There were many studies of pharmaceutical care for epilepsy outpatients in Thailand. (14) After the patient received pharmaceutical care, patients had significantly increased control of their seizures (increased from 46.2% to 71.2%), reduced drug use problems from 111 problems to 61 problems where the problem is the interaction of the drug which are potential DRPs must be monitored continuously followed by the failure to receive drug and an adverse reaction from drug use and patients had significantly improved quality of life, especially concerning seizure worry, emotional well-being and about medication effect domain. Another study examines the effects of pharmaceutical care for female patients with epilepsy. (43) A randomized controlled trial was conducted on 182 female epilepsy patients. It was found that after the patients received

pharmaceutical care patients had significantly improved quality of life. It concluded that pharmaceutical care should be provided to patients with epilepsy in the hospital's routine. Pharmacists can find problems with a drug user, and solve and prevent problems from using drugs by giving advice and consultation on drug use with patients and coordinating with the treating doctor to improve the quality of life for patients. In a retrospective study (48), the study was to assess the effect of education by pharmacists on medication adherence and the percentage of valproic acid (VPA) samples reaching the therapeutic reference range in patients with epilepsy conducted at two teaching hospitals in Changsha. China active education by a pharmacist in both oral and written formats was provided at the intervention hospital whereas standard passive pharmacist service. It was found that based on the SMAQ (simplified medication adherence questionnaire) adherence assessment, adherence increased from a minimum of 56.0% to a maximum of 73.9% with stabilization during the last six months of follow-up at the intervention hospital, both the medication adherence rate and the percentage of VPA samples reaching therapeutic range increased as the result of active education by a pharmacist, suggesting that continuous pharmacist intervention had a positive impact in a patient with epilepsy.

2.13.3 Quality of life assessment for patients with epilepsy

Pharmaceutical care for patients with epilepsy aims to improve the quality of life of the patient, assessment of the patient quality of life together with giving advice the drug consultation will make the pharmacist know the patient in all dimensions and can solve and prevent problems from using drugs effectively especially the emotional effects, concerns over disease and the effects of anticonvulsants on the patient's daily life if the pharmacist can assess and understand will make a suggestion effective use of the drug and able to layout solutions for problem-solving to be effective can increase adherence and make it more effective and safe to use drugs.

2.13.4 First aid for patients with epilepsy

In addition to providing drug advice and advice to patients with epilepsy, giving advice about first aid is required to reduce the severity of seizures and other consequences. The first aid advice for patients with epilepsy are as follows:

1. If the patient has convulsive seizures that are unusually long or longer than 5 minutes. They should be brought to the hospital.

2. Provide a safe area where the patient has a seizure such as clearing a wide area, no tables, chairs, solid that will bump or sharp objects.

3. If the victim has a seizure on a raised floor such as a carriage. The area should be secured or supervised not to fall from a height.

4. Find a pillow or soft cloth to support your head, lose the clothes, keep it lying on your side so that your tongue doesn't block your airways.

5. Do not insert solid objects into the patient's mouth so as not to fall to block the trachea or broken teeth falling into the trachea and should not feed water while seizures to prevent choking.

6. Do not squeeze, massage, or stretch limb muscles of the patient during seizures.

7. After the seizures, the patient's resting to regain consciousness as usual.

2.13.5 Therapeutic Drug Monitoring (TDM)

Anticonvulsant drug monitoring service by pharmacists provides advisory services for patients who indicate measuring drug levels, recommend time drilling measuring drug levels in the and service interpret results and give advice on adjusting dose and drug use patterns stopping the drug when drug poisoning occurs to get good clinical results. Patients can control their seizures and has minimal adverse reactions. (44,45) This is one tool that makes it possible to design treatment for a specific patient (personalized pharmacotherapy) because considering variability between individuals and each person taking into account various factors affecting values pharmacokinetic parameters. (46) It is a clinical pharmaceutical activity that can be integrated into the pharmaceutical care for patients with epilepsy to help prevent and resolve problems from the use of anticonvulsants. To make the drug use effective can control seizures and safe with minimal adverse drug reactions at the appropriate dose. The same anticonvulsants (classic) often have a narrow treatment interval. It has complex pharmacokinetic properties including enzyme inducers (phenytoin, phenobarbital, carbamazepine), enzyme inhibitors (valproic acid), autoinducer (carbamazepine), and non-linear pharmacokinetics (phenytoin). However, a new class of anticonvulsants will also require a blood monitoring service such as gabapentin, pregabalin monitoring. (47) There were new guidelines for TDM in neuro-psycho pharmacotherapy in 2017 to be used by many patients and to reduce the cost of treatment. (46) The patients who should take TDM are children and adolescents, pregnant women, elderly patients, intellectual disabilities, drug users, people with abnormal pharmacokinetics. The indications that the blood level of drugs should be measure are people who have not responded to normal dose therapy. There may be problems with drug co-operation an adverse reaction from drug or drug poisoning or drug interactions with pharmacokinetics. (48,49)

Plasma drug concentration monitoring services for patients selected according to appropriate criteria help patients have better clinical outcomes. (50) Currently, blood testing services are available in many countries. (51) Most of them are available only in major hospitals due to a lack of equipment, measuring tools, and cost of service. For Thailand, there is a service for measuring blood levels of drugs in University hospitals and many tertiary hospitals as well. It has been studied for the cost-effectiveness of TDM work by conducting a systematic review of the literature.

However, few studies have been found that providing TDM for group drugs aminoglycosides. It is cost-effective only. However, there is better technology now, highly accurate drug level measurement. However, knowledgeable pharmacists are required to help in interpreting results and giving appropriate advice, benefit the patient. Therefore, should find a way to provide the service that is worth the most and has the most clinical benefit. (51)

2.13.6 ADR Monitoring

Anticonvulsants showed quite some adverse drug reactions. In pharmaceutical care for epilepsy patients, adverse reactions from drug use should be closely monitored and should be monitored systematically (systemic). A prospective observational study followed adverse reactions from anticonvulsant use in 227 children using anticonvulsants in university hospitals in India using the World Health Organization Uppsala Monitoring Center scale, Hartwig's severity scale, and Schumock and Thornton's questionnaire found that the pediatric patients used phenytoin the most (63.5%) and was the drug with the most adverse reactions, found adverse drug reactions were 353 times in 175 (63.2%) children 216 times level probable and 126 times the level possible. The most common adverse reactions to anticonvulsant use are worse in school (19 %) swollen gums (13.3 %), headache (10.2 percent), behavior problems (5.7 %), lethargy (5.7 %) and children over the age of 5 were at greater risk of adverse reactions. (53) Another study is systematic monitoring of adverse reactions from drug use. For new anticonvulsants in clinical practice situations (54) including topiramate, levetiracetam, zonisamide, pregabalin, extended-release oxcarbazepine, lacosamide, and eslicarbazepine. Adverse reactions were categorized according to the WHO-UMC causality assessment found adverse reactions with anticonvulsants in 318 (56.6%) patients. The most common adverse reaction was electrolyte imbalance such as low sodium levels 14.1 %, low potassium levels 4.4 % inferior, it is an adverse reaction to the nervous system, central: dizziness 10.9 %, visual disturbances 8.4 %, tired and exhausted 7.1 %, twitchy eyes 6.4 % and ataxia 5.2 % or the effect on cognitive deficits especially disturbed speech 6.6 %, memory impairment 6.4 % and mental slowing 5.7 %. Factors related to the occurrence of adverse reactions are the number of anticonvulsants and the size of the drug. The drug with minimal adverse reactions and best-tolerated drug toleration is levetiracetam. Another study is an education in Thailand a descriptive study using retrospective data from electronic databases and outpatient medical records found that 382 patients with epilepsy. The more commonly prescribed drugs were phenytoin 46.1 % and sodium valproate 40.44 % found the incidence of adverse reactions in 230 patients 60.2 % is type A, 79.6%, and type B 20.4%. The drug that caused the most adverse reaction type A was phenytoin 49.3%. The most common symptoms are swollen gums 43.9 %. The drug that caused the most adverse reaction type B was

phenytoin as well 55.6 %. The most common symptoms are maculopapular rash 87.8%, risk factors causing type A adverse reaction is to use more than one type of anticonvulsant drug compared to receiving only one antiepileptic drug (4.5 times more likely) and factors causing rashes from phenytoin is that the patient receives a drug that has drug interactions compared to receiving drug without drug interaction (5.39 times more opportunities). (55) Detail of adverse reactions for each anticonvulsant drug (ADRs profile) is one of the important factors that will help in choosing the right medication for the patient.

Knowledge of pharmacogenetics associated with the occurrence of adverse drug reactions is another consideration in providing pharmaceutical care to epilepsy patients to avoid adverse reactions severe desire to the patient such as HLA-B * 1502 gene assay was associated with SJS / TEN incidences from taking the drug carbamazepine (Possibly caused by phenytoin, lamotrigine, oxcarbazepine). The risk of people carrying this gene in Thai people using the drug carbamazepine 54.76 times more likely to have SJS / TEN (OR 95% confidence interval (CI) 14.62-205.13, p = 2.89 × 10-12). The sensitivity and specificity were 88.10% with an incidence of 0.27% positive predictive value (PPV) and negative predictive value (NPV) were 1.92 and 99.96 %. (56) In the future, we may have more information from gene testing which is another important factor involved in choosing safe anticonvulsants for patients.

Conclusion

Currently, pharmacists have a role in providing drug advice for patients with epilepsy by providing knowledge on both the disease and the use of anticonvulsants emphasize adherence medication, adverse drug reaction assessment, provide advice on the management of adverse drug reactions, drug withdrawal or stopping, finding solving, preventing problems associated with the use of drugs. Pharmacists give first aid advice to patients and relatives not being in a risky condition or location and avoid triggers for assessing depression and quality of life assessments in clinical epilepsy patients regularly are few. It is also necessary to advise epilepsy patients, pregnant women, and lactating women on contraception and family planning as for the service for measuring the drug level in the blood. Present have a private company that received a blood test measure and report results quite quickly. Hospitals can receive services and pharmacists can help interpret results and give advice on how to change the medication patterns and follow up for evaluating the new use of anticonvulsants and monitoring. For adverse reactions from anticonvulsant use possible actions can be made to achieve optimal drug use effective and safe. It can be seen that these pharmaceutical activities are interrelated and can be integrated into pharmaceutical care for patients with epilepsy.

2.14 Literature reviews

2.14.1 The multidisciplinary team for epilepsy management

Y. Zheng et al. (2019) investigate the effect of a multidisciplinary program on anxiety, depression, medication adherence, and quality of life in patients with epilepsy in eastern China. A cohort of 184 patients with epilepsy from the epilepsy clinic of a tertiary hospital in eastern China. 12-month multidisciplinary program developed by a group of the epileptologist, pharmacist, psychiatrist, and epilepsy specialist nurse. Patients were assessed both before and after the 12 months. The results of this study was the 12-month multidisciplinary program significantly reduced the number of patients with severe depression (p = 0.013) and anxiety (p = 0.002), increased the number of patients with moderate-to-high AED adherence (p = 0.006), and the overall QOLIE-31 score (p b 0.001) in the intervention group. Both groups demonstrated a significant increase in the number of patients with a low seizure frequency after the 12 months (p b 0.001). This study showed that the 12-month multidisciplinary program offers an effective management strategy in improving psychiatric comorbidities, medication adherence, and quality of life in patients with epilepsy in eastern China. (15)

F. Seyer et al. (2018). Study about the efficacy of a short-term multidisciplinary epilepsy program. To evaluate the efficacy of a short-term program that is based on a biopsychosocial model of health and conceptualized by occupational therapists, physical therapists, neuropsychologists, and social workers. The results showed that at baseline, 80.8% of the patients were rated as impaired according to the total score. A better total score at baseline was significantly related to better neuropsychological functioning and a lower number of concurrent antiepileptic drugs. After the intervention, 50.3% of the patients showed significant improvements regarding the total score. Compliance, activity, and effect were the most responsive domains. This study provides promising results concerning the efficacy of short-term multidisciplinary epilepsy program. (57)

LI et al. (2019) study about the experience of the multidisciplinary team in epilepsy management from a resource-limited country. To summarize their experience and assess the impact of MDT use in managing patients with epilepsy and optimizing their seizure outcomes. MDT is staffed with skilled epileptologists, electroencephalography experts, neurosurgeons, child neurologists, radiologists, and psychiatrists. The detailed clinical characteristics, suggestions, and follow-up data were collected and analyzed. The study showed that epilepsy management can be optimized through MDT discussion to attain accurate diagnosis and favorable seizure outcomes. (58)

2.14.2 Current research of pharmacist managed epilepsy therapy

Adherence managed

AIAjmi et al (2017) evaluate the effectiveness of a pharmacist-led educational interview in terms of adherence to antiepileptic drug administration among adult patients with epilepsy. Antiepileptic drug adherence was measured during clinic visits, and 6 weeks afterwards using the 8-item Morisky Medication Adherence Scale. This study showed that the adherence score average in the intervention group was 5.26±0.98 at baseline and improved to 6.7±0.823 (P<0.0001) after an intervention. In the control group, the adherence score average was 5.76±1.806 at baseline and 5.83±1.627 at 6 weeks (P=0.792). While there was no statistically significant difference in adherence score between intervention and control groups at baseline, the post-intervention difference was significant (P=0.024). The study suggests that pharmacist-led educational interviews had a positive impact on medication adherence in patients with epilepsy. (59)

Israel et al (2018) evaluate the efficacy of pharmaceutical care intervention on patients' adherence to prescribed self-administered antiepileptic medications. The impact of pharmaceutical care intervention was evaluated by using the eight-Item Morisky Medication Adherence Scale. There was a statistically significant difference in medication adherence scores between the control and intervention group over time with as the mean medication adherence score of the intervention group increased from 3.70 (±1.60) at baseline to 4.04 (±1.42) and 6.89 (±0.77) at 3 months and 6 months respectively, indicating a substantial increase in medication adherence among patients in the intervention group compared with the control group where mean medication adherence scores were 3.86 (±1.69), 4.02 (±1.37) and 4.84 (±0.92) at baseline, 3 months and 6 months respectively. Pharmaceutical care services implemented by a clinical pharmacist significantly improved the adherence to antiepileptic drugs in patients with epilepsy. (60)

D. Chandrasekhar et al (2019) evaluate the medication adherence behavior and knowledge of epilepsy patients before patient counseling and monitor and evaluate the outcome of clinical pharmacist mediated patient counseling. The medication adherence was assessed through a medication adherence scale (MMAS-4). This result showed that before the intervention, 40% of patients showed high adherence to antiepileptic drug (AED) therapy followed by 27% patients with a medium level of adherence and 33% of patients exhibited a low level of adherence. After the intervention, 62% of patients showed high adherence followed by 20% of patients with medium adherence and the remaining 18% exhibited a low level of adherence to AED therapy. Medication belief assessment after intervention also showed improving trends ($P \leq 0.05$). The study defined that the overall improvement in medication adherence and knowledge of patients was found to be statistically significant after the intervention. (61)

F. Tang et al.(2014) evaluate the effects of medication education and behavioral intervention on Chinese patients with epilepsy and compare the difference between them. The outcomes that were evaluated both in the beginning and in the end of the study included adherence, which was measured using the four-item Morisky Medication Adherence Scale (MMAS-4). This study showed that after the intervention, the adherence and knowledge of AEDs increased greatly in all patients and the number of patients who had seizures or missed AEDs decreased. However, no significant differences were observed between groups I and II. The observed changes were (group I vs group II, p-value) increased adherence: 62.3% vs 64.3%, 0.827; increased knowledge of AEDs: 88.7% vs 80.4%, 0.231; and improved seizure control: 64.2% vs 64.3%, 0.988. Besides, the percentage of patients who forgot to take their AEDs decreased to 45.0% from more than 70%, and 44.9% of these patients took the missed AEDs as soon as they remembered. (62)

Angela Fogg et al. (2012) determine the feasibility and acceptability of a pharmacist-led epilepsy consultation (PLEC) study. This encompassed estimating the eligibility and consent rate for a PLEC study, plus the acceptability of potential intervention outcome measures and likely effects. Self-reported medication adherence using the MARS. The result showed that the number (percentage 95% confidence interval) of participants reporting adherent behavior pre-PLEC was 22 (44.0 + 13.7%) which increased to 30 (60 + 13.6%) post-PLEC ($P < 0.03$, McNemar test). (63)

Jaiklom C et al. (2022) to study the effect of seizure control and medication adherence after receiving new development of pharmaceutical care for epilepsy patients at Neurological Institute of Thailand. Seizure control and medication adherence data were collected by interviews and self-administered forms before and after received new pharmaceutical care. The result showed After receiving the new epileptic pharmaceutical care, it was found that there was increase in mean scores of medication adherence and statistically significant decrease in seizure frequency ($p<0.05$). There was a negative correlation between increased medication adherence with reduced seizure frequency. (64)

Ruby E Grymonpre et al. (1998) to compare medication adherence calculated from four different data sources including a pill count and self-report obtained during a home medication history, as well as calculations based on refill frequency derived from a provincial prescription claims database (manual and electronic). A pharmacy consultation service located at an interdisciplinary wellness center for the noninstitutionalized elderly. 65 years or older, noninstitutionalized, taking one or more prescribed or nonprescribed medications. Medication adherence was estimated from three sources of data: the pill count and self-report during the HMH, and the province‟s prescription claims database. The pill count was performed on all medications present at the time of a single interview. To verify that all current medications being taken were revealed by the client, the interviewer accompanied the

client to the usual sites for medication storage. Information required for the pill count calculation was recorded from each prescription label and included drug name, strength, and dosage form, instructions for use, quantity dispensed, and dispensing date. Pill count calculations were assessable only for medications prescribed for regular use. The results of this reports showed that mean percent adherence by the drug was high and not statistically different (95.8% ± 17.1%, 107.6% ± 40.3%, and94.6% ± 24.0%, respectively), whereas the pill count adherence was significantly lower at 74.0% ± 41.5% ($p < 0.0001$). An unexpected finding was that the pill count technique used in this study of elderly clients using chronic, repeat medications appeared to underestimate medication adherence. (65)

Singh et al.(2020) to assess compliance with Antiepileptic Drugs. Out of 115 patients enrolled in the study. Compliance was assessed using pill-count and Morisky medication adherence scale (MMAS) during home visits. A pill-count (pills dispensed – pills remaining)/(pills to be consumed between two visits) value of 0.85 to ≤1.15 was recorded as appropriate compliance. Underdose (<0.85) and overdose (>1.15) were labeled as noncompliance. This study showed that both tools complement each other when used in combination, as the use of a single tool was not able to completely detect compliance. (66)

knowledge managed

Theodor W. May et al. (2002) evaluate the efficacy of the educational program MOSES (Modular Service Package Epilepsy). It was developed to improve patients‟ knowledge and understanding of their epilepsy. The result showed that the patients of the educational program improved significantly. Univariate analyses revealed improvement in knowledge ($p<0.001$). Patients of the MOSES program also improved in seizure outcome ($p=0.041$) and became more satisfied with the therapy. (67)

U. Eshiet et al.(2019) evaluate the efficacy of a pharmacist implemented educational treatment program in improving knowledge and perception of epilepsy among people with the condition. There was a statistically significant difference between the control and intervention group overtime on the knowledge of epilepsy, as the knowledge of epilepsy among patients in the intervention group significantly increased; $F(2154) = 150.15$, $p = 0.000$, Partial $\eta 2 = 0.661$. Also, there was a statistically significant difference between the control and intervention group overtime on the perception of epilepsy, as the perception of epilepsy among patients in the intervention group significantly improved. (68)

ADRs and seizure frequency managed

Bansal, D et al.(2013). A Prospective observational study. To investigates the pattern and predictors of treatment-emergent adverse drug reactions (ADRs) in children diagnosed with epilepsy. on 277 epileptic children. Antiepileptic drug (AED)–associated ADRs, demographic and clinical characteristics. The result showed that the pediatric patients used phenytoin the most (63.5%) and was the drug with the most adverse reactions, found adverse drug reactions were 353 times in 175 (63.2%) children 216 times level probable and 126 times the level possible. The most common adverse reactions to anticonvulsant use are worse in school (19 %) swollen gums (13.3 %), headache (10.2 percent), behavior problems (5.7 %), lethargy (5.7 %) and children over the age of 5 were at greater risk of adverse reactions. (69)

A. Hilgers.(2016) To evaluate the tolerability of newer antiepileptic drugs (AEDs), such as topiramate, levetiracetam, zonisamide, pregabalin, extended-release oxcarbazepine, lacosamide, and eslicarbazepine, under real-life conditions by means of an assessment of routine clinical data of inpatients. Adverse reactions were categorized according to the WHO-UMC causality assessment found adverse reactions with anticonvulsants in 318 (56.6%) patients. The most common adverse reaction was electrolyte imbalance such as low sodium levels 14.1 %, low potassium levels 4.4 % inferior, it is an adverse reaction to the nervous system, central: dizziness 10.9 %, visual disturbances 8.4 %, tired and exhausted 7.1 %, twitchy eyes 6.4 % and ataxia 5.2 % or the effect on cognitive deficits especially disturbed speech 6.6 %, memory impairment 6.4 % and mental slowing 5.7 %. Factors related to the occurrence of adverse reactions are the number of anticonvulsants and the size of the drug. The drug with minimal adverse reactions and best-tolerated drug toleration is levetiracetam. (70)

Nathan et al. (2018) A descriptive study using retrospective data from electronic databases and outpatient medical records found that 382 patients with epilepsy. The more commonly prescribed drugs were phenytoin 46.1 % and sodium valproate 40.44 % found the incidence of adverse reactions in 230 patients 60.2 % is type A, 79.6%, and type B 20.4%. The drug that caused the most adverse reaction type A was phenytoin 49.3%. The most common symptoms are swollen gums 43.9 %. The drug that caused the most adverse reaction type B was phenytoin as well 55.6 %. The most common symptoms are maculopapular rash 87.8%, risk factors causing type A adverse reaction is to use more than one type of anticonvulsant drug compared to receiving only one antiepileptic drug (4.5 times more likely) and factors causing rashes from phenytoin is that the patient receives a drug that has drug interactions compared to receiving drug without drug interaction (5.39 times more opportunities). Detail of adverse reactions for each anticonvulsant drug (ADRs profile) is one of the important factors that will help in choosing the right medication for the patient. (55)

Kanjanasilp et al. (2008) determine drug-related problems, clinical outcomes, and humanistic outcomes after the provision of pharmaceutical care to epileptic patients taking phenytoin. Pharmaceutical care was provided to each patient for 6 months. The result of this study showed that before pharmaceutical care, the most frequent groups for seizure frequency were seizure-free (46.15%) and high frequencies (28.85%), while in the period after the provision of pharmaceutical care, the most frequent groups for seizure frequency were seizurefree (71.15%) and high frequencies (13.46%), respectively. That is the seizure frequency reduced after the provision of pharmaceutical care. We found a total of 111 DRPs in the period prior to the provision of pharmaceutical care and 61 DRPs in the period after the provision of pharmaceutical care. The most frequent DRPs were drug interaction, failure to receive the drug, and adverse drug reactions. There were significant differences ($p<0.05$) in seizure worry, emotional well-being, and medication effect domain functions. Pharmaceutical care practice has the potential to increase epileptic patients‟ quality-of-life scores and decrease both the frequency of seizures and the number of drug-related problems. (14)

Losada-Camacho et al.(2014) establish the impact of the application of a pharmaceutical care program on the HRQOL of women with epilepsy. The result showed that the application of a pharmaceutical care program significantly improves HRQOL in WWE. The NNT they found allows a recommendation to implement the PC program for the additional benefit that would be obtained in patients‟ HRQOL. The change (Δ) in the QOLIE-31 score for the IG was 12.45 points (p-value=0.001) and for the control group, it was 2.61 (p-value=0.072). The mean of the change (Δ) (after-before) in the QOLIE-31 scores in the final group was 12.45 points in the IG and 2.61 points for the CG. The study demonstrated that the application of a pharmaceutical care programme significantly improves HRQOL in WWE. The NNT we found allows a recommendation to implement the PC programme for the additional benefit that would be obtained in patients' HRQOL. (71)

D. Campos-Fernández, E. Fonseca, M. Olivé-Gadea et al. (2020) to analyze the relationship between seizure frequency, irritability, and depression and describe how they mediate each other's effect on QoL in epilepsy. Psychiatric symptoms were evaluated using scales to quantify irritability (State–Trait Anger Expression Inventory–2 [STAXI-2]), anxiety and depression (Hospital Anxiety and Depression Scale [HADS]), and QoL (Quality of Life in Epilepsy Inventory-10 [QOLIE-10]). The result of this study was Seizure frequency ($R = -0.193$, $P = .053$), irritability ($R = 0.216$, $P = .039$), and depression ($R = -0.598$, $P < .001$) had all a negative effect on QoL. In the adjusted linear regression model, depression was the only independent predictor of impaired QoL ($B = -2.453$ [95% confidence interval (CI): −3.161, −1.744], $P < .001$). The Sobel test showed that depression exerted a significant mediating effect on seizure frequency ($Z = -1.984$; $P = .047$) and

irritability (Z = −3.669; P < .001) in their influence on QoL. Depression is an independent predictor of worse QoL and significantly mediated the effects of irritability and poor seizure control on QoL impairment in patients with epilepsy. (72)

Pham et al . (2021) to assess the efectiveness of pharmacist interventions in epilepsy treatment at a Vietnamese general hospital. A before-and-after study . All patients with a diagno- sis of epilepsy and being treated at the investigated hospital were recruited and screened for eligibility and exclusion criteria. The primary outcome was the proportion of patients in good control of their epilepsy (with two seizures or less in a year). The secondary outcome was the number of patients maintaining optimized concentrations within the therapeutic range of carbamazepine (4–12 mg/L), phenytoin (10–20 mg/L), or valproic acid (50–100 mg/L). The result showed that over 56% of the participants still experienced adverse drug efects. More than half of the patients received at least one pharmacists' intervention, which increased by 25.0% the efectiveness of the therapy ($p<0.001$) and by 14.6% the number of patients with optimized drug con- centrations ($p=0.018$). Epilepsy management requires a multiple-stepped and comprehensive approach, with a focus on the health and safety of the patients. As part of the healthcare team, pharmacists need to engage at every stage to moni- tor the patient's response and determine the most efective treatment with the fewest adverse drug reactions. (73)

CHAPTER III
METHODOLOGY

This study was mixed-method research including qualitative and quasi-experimental study to multidisciplinary team-managed epilepsy at Setthathirat Hospital, as well as to assess its outcomes on patients using antiepileptic drugs. There were two phases of this study:

Phase 1: Qualitative interviews

The processes of phase 1 included individual and focus group interviews:

- Individual interviews

+ Individual interviews were conducted to investigate the views of healthcare professionals such as doctors, pharmacists, and nurse.

+ Focus group interviews were undertaken to gain views of healthcare professionals involved in the provision of healthcare services for patients using antiepileptic drugs and develop the practical intervention called multidisciplinary team-managed epilepsy at Setthathirat Hospital based on the evidence-based intervention model.

Phase 2: A quasi-experimental study

It was conducted to evaluate the effects of multidisciplinary team-manage epilepsy at Setthathirath Hospital

3.1 Phase 1: Qualitative interviews

3.1.1 Research design

Qualitative interviews were conducted to develop a multidisciplinary team-managed epilepsy as a practical intervention model. The interviews included individual and focus group interviews.

3.1.2 Research setting

The interview was undertaken in the outpatient clinic at the Department of Neurology, Setthathirat Hospital, LAOS PDR. Healthcare service is only morning on Wednesday. The healthcare team in charge of providing care for patients using antiepileptic drugs included 2 doctors, 2 nurses, and 2 pharmacists. Each day, there are two doctors conducting a diagnosis, prescribing and following up with patients with epilepsy, two nurses providing the first screening and information, and two pharmacists dispensing drugs to patients.

3.1.3. Sample of study

3.1.3.1 The individual interviews.

+ The inclusion criteria of participants were healthcare professionals having at least one year of work experience with patients using antiepileptic drugs.

+ Purposive sampling was used to recruit participants for the interviews.

+ Six healthcare professionals providing care for patients using antiepileptic drugs from the outpatient department were selected including 2 doctors, 2 nurses, and 2 pharmacists.

3.1.3.2 The focus group interviews

+ Inclusion criteria of participants were healthcare professionals having at least one year of work experience with patients using antiepileptic drugs.

+ The sampling was used to recruit doctors, pharmacists, and nurses. Two doctors, two pharmacists, and two nurses were recruited.

3.1.4 Research tool

One interview guide was made for face-to-face semi-structured interviews.

3.1.4.1 The individual interviews

The interview guide was created based on the purpose of the research. The main topic guides were as follows (see Appendix A):

+ Doctors' and nurses' interview guide

Q1. Have you ever experienced the problems of a patient with epilepsy? If yes. What were the problems?

Q2. From question 1. What would you like to improve? Who do you think that they would be able to contribute to improvement?

Q3. Currently, how do patients with epilepsy receive the usual care?

Q4. Apart from the question, do you think a patient with epilepsy should receive special care from other health care professionals? And what or how should they receive?

Q5. What do you think if pharmacists managed epilepsy is provided?

Q6. If all health care professional is involved in the care of the patient with epilepsy, do you think the policy, the system, the manpower, and the budget are sufficient or not?

+ Pharmacists" interview guide questions 1 to 6 are the same as a doctor and nurse interview guide. Extra interview guide for pharmacists is:

Q1. Have you ever advised a patient with epilepsy? What advice do you give?

Q2. Do you think the advice you give is sufficient or not? If no, what could be the best for you to give sufficient advice to patients?

- Focus group interviews:

During the interview, a practical intervention model is proposed and the main topic guides are established as follows:

1. The process of care for patients with epilepsy
2. The pharmacists‟ roles for the patient with epilepsy
3. The education tool by pharmacists for the patient with epilepsy.

To develop the practical intervention called multidisciplinary team-managed epilepsy at Setthathirat Hospital based on an evidence-based intervention model. The main topic guides are established as follows:

Q1. What do you think about the process of care for patients using antiepileptic drugs, is there any part of the proposed intervention that should be improved?

Q2. What should be the roles of pharmacists involved in the practical process at the outpatient clinic at the Department of Neurology, Setthathirat Hospital, LAOS PDR?

3.1.5 Validation of interview guides

- The interview guide was created based on the purpose of the research. The interview guides for individual and focus group interviews was validated by two research supervisors.
- The interview guides were translated into Lao languages by a researcher
- An interview guide version Lao language was validated by two experts working in the healthcare field (one expert is working at Setthathirat Hospital and one is working at the University of Health Science, Lao PDR).

3.1.6 Recording tool

- In the interviews, the participants' voice was recorded by using digital voice recording machine.

3.1.7 Data collection procedures

- The researcher coordinate with the hospital to inform the purpose of the research and to confirm for the interview dates and times. The dates of an interview were in September 2021.
- After that, selected the interviewees from the healthcare professionals, and allowed to participate in the individual interviews.

+ Face-to-face semi-structured interviews were processed as follows:

- The researcher described the purpose of the study.
- The face-to-face interviews lasted about 20 minutes per person.
- The interviews were conducted following the interview guides (see Appendix A).

+ Focus group interviews processed as follow:

- The researcher described the purpose of the study Intervention model developed by the researcher and based on the literature review of multidisciplinary team-managed epilepsy (systematic review and meta-analysis) was proposed.

- A researcher presented the problems of pharmacist-managed antiepileptic therapy by healthcare professionals' views from the results of face-to-face interviews. Major themes derived from the face-to-face semi-structured interview were explained.

- The researcher presented three main topics to the interviewee: the process of care for patients using antiepileptic drugs, the pharmacists' roles for patients using antiepileptic drugs, and the education tool by a pharmacist for a patient using antiepileptic drugs.

- The pharmacist intervention model called "multidisciplinary team-managed epilepsy" is finally developed and is to be used for the experimental study.

- The researcher stressed that all information would be kept anonymous and that the audiotaped were secretly kept and only the research team can access them.

3.2 Phase 2: A quasi-experimental study

3.2.1 Research design

A quasi-experimental study using developed methods from phase 1, a study of multidisciplinary team-managed antiepileptic drug therapy to access efficacy and safety of the ways compared before and after receiving the multidisciplinary team intervention for a patient with epilepsy at Setthathirath hospital.

3.2.2 Research setting

This study was set in the outpatient clinic at the Department of Neurology, Setthathirat Hospital, LAOS PDR. This department is available one day per week (Wednesday morning). Patients who receive antiepileptic therapy is about 10 cases per day. The duration of the study is six months and it was carried out between November 2021 to August 2022.

3.2.3 Population and sample

Patients with epilepsy were recruited consecutively in the outpatient clinic at the Department of Neurology, Setthathirath Hospital, LAOS PDR. Recruitment period: November 2021-August 2022.

3.2.4 Inclusion criteria

Patients included in this study met the following requirements:

3.2.4.1 Aged 18 years or older and had a physician's diagnosis of epilepsy

3.2.4.2 Patients with a definite diagnosis of epilepsy according to the 2014 International League Against Epilepsy (ILAE) classification by physician.

3.2.4.3 Patient who had been receiving antiepileptic drugs for at least 1 month and were expected to continue antiepileptic drugs for a minimum of 6 months.

3.2.4.4 Patient had the ability to read and wrote the Lao language.

3.2.4.5 Patient were agreeable to be the participant and be willing to provide a written informed consent form.

3.2.5 Exclusion criteria

Patients having the following conditions were excluded from this study:

3.2.5.1 Patient who has co-morbid: cancer, psychiatric or neurological diseases

3.2.5.2 Pregnancy patients

3.2.5.3 Mentally retarded patients who cannot give information

3.2.6 Sample size estimate

Sample size estimation has used a calculation of comparing the mean between groups before and after receiving. The calculation was based on previously published data

$$n = \frac{(z_{\frac{\alpha}{2}} + z_{\beta})^2 \, \pi(1-\pi)}{(\pi - \pi_0)^2}$$

There was an estimate from a doctor responsible for the treatment of epilepsy in Setthathirath Hospital (LAO) about adherence to medication in a patient with epilepsy was about 60 %. Singh et al. (2020) conducted a prospective observational study to the assessment of compliance with AED, using pill count and Morisky medication adherence scale (MMAS) during home visits. A pill count (pills dispensed– pills remaining)/(pills to be consumed between two visits) value of 0.85 to ≤1.15 was recorded as appropriate compliance. Underdoses (1.15) were labeled as non-compliance. (72)

Before the intervention, 40% of patients showed high adherence to antiepileptic drug (AED) therapy, after the intervention, 62% of patients showed high adherence increase.

A confidence level of 95 %, α is 0.05. A power of 80 %, β is 0.20. 1 and 2 are the proportion of the group.

N = number of sample size

$\alpha = 0.05$ $Z_{\alpha/2} = 1.96$

$\beta = 0.02$ $Z_{\beta} = 0.84$

$\pi = 0.85$

π_0 = Proportion of patient before the intervention 60%

π = Proportion of patient after the intervention 85%

$$N = \frac{(1.96+0.94)^2\ 0.85(1-0.85)}{(0.60-0.85)^2} = \frac{(2.9)^2\ 0.425}{(-0.25)^2} = \frac{8.41\ x\ 0.1275}{0.0625} = 57 \text{ patients}$$

Dropout rate 30 %, $n = \frac{(57)x(20\%)}{(100)} =$ 11 patient

Our study will be conducted in 68 patients

All patients received the multidisciplinary team management at an outpatient clinic at the Department of Neurology, Setthathirat Hospital, LAOS PDR between November 2021 to August 2022 and will be selected using the inclusion and exclusion criteria.

3.2.7 Research outcome

The primary outcome was the adherence

The secondary outcomes were:

+ The knowledge score
+ The seizure frequency
+ DRPs: consequences of problem-solving
+ The quality of life

3.2.8 Measurements and data collection tool

Measurements and data collection tools were used by the review of literature from a previous study. This research collected data using the following tools:

3.2.8.1 The research data collection form consists of 6 parts:

1.The patients' data collecting form

Part 1: General information:

- Gender,
- Age
- Education
- Occupation
- Marital status
- Residence of patient
- Monthly income of patients
- Family history of epilepsy

- Seizure frequency
- Number of AEDs
- Type of epilepsy
- Type of AEDs
- Comorbiditie

Part 2: Patients adherence assessment tool was used pill-count and self-report of how to take medicine. Patients who had good adherence were those who got scores more or equal to 85 percent.

% adherence:

$$= \frac{(quantity\ dispensed) - (quantity\ remaining)}{(prescribed\ number\ of\ \frac{tablets}{d})\ X\ (number\ of\ days\ between\ dispensing\ date\ and\ interview)}\ X\ 100$$

(The number of drugs delivered in advance = The number of drugs taken per day – The number of days are administered orally).

+ In some cases of the patient receiving poly therapy, the method for calculating the drug was to add the number of pills of both drugs together and calculate according to the formula.

Part 3: Patients' knowledge assessment tool was used the tool that following the test by using question adapt from Siriporn Tiamkao (2007). (19) The patient's knowledge was assessed by the mean score of 11 questions in the questionnaire. There were 6 items about epilepsy and 5 items about antiepileptic drugs. The answer type is yes and no. The scores from the scale ranged from 0-63 points. In this study, the researchers divided the scores into 3 levels: high, medium, and low from the stratification calculation as follows.

$$\text{Class Interval} = \frac{\text{highest score} - lowest\ score}{number\ of\ class}$$

$$x = \frac{63 \pm 0}{3} = 21$$

We can be determined according to the following criteria:

A score of 0 – 21 indicates a low level of knowledge.
A score of 22 – 41 means moderate knowledge.
A score of 42 – 63 means having a high level of knowledge.

Part 4: Seizure frequency was measured by using the base on the mean of seizure in 3 months (Devinsky et al.,1995). (21) Seizure frequency groups were divided into four groups including a seizure-free group, a low-frequency group, a moderate-frequency group, and a high-frequency group. In the seizure-free group, patients did not have a seizure. In the low-frequency group, there were 1-20 simple partial seizures or absence seizures or 1-4 complex partial seizures, or 1 general tonic-clonic seizure. In the moderate frequency group, there are 21-100 simple partial seizures or absence seizures or 5-12 complex partial seizures, or 2-4 general tonic-clonic seizures. In the high-frequency group, there were 101-200 simple partial seizures or absence seizures or 13-24 complex partial seizures, or 5-12 general tonic-clonic seizures.

Part 5: Drug-related problems were classified according to Hepler and Strand classification (1990) DRPs focus on the consequences of problem-solving of DRP. (20)

Part 6: Patient's quality of life assessment tools were measured by a test modified from the test by using questions adapted from Joyce. Cramer (1996). (22) The self-administered 10-item questionnaire covers different epilepsy- and treatment-related issues, including energy, mood, mobility, work limitations, social limitations memory problems, physical treatment effects, cognitive treatment effects, seizure worries, and general QOL.

3.2.9 Research tools

3.2.9.1 Medical record

3.2.9.2 Patient books

3.2.9.3 Participant information form

3.2.9.4 Prescription

3.2.9.5 Informed consent form.

3.2.9.6 Guide to epilepsy

3.2.9.7 Home medication calendar

3.2.10 Quality of measurement instruments

To determine the quality of measurement instrument need to be access based on standardized criteria the most important are validity and reliability.

3.2.10.1 Validity

Validity is one of the most important properties of research tools. It is an instrument that can measure exactly as you want to measure. There are several ways to check for straightness.

Content validity will demonstrate the level of instrument accuracy in measuring what it is intended to measure and provides information on representativeness. The patients' data collecting form assessment will validate by three experts. Three supervisors will be requested to evaluate each item by giving the item a rating of +1 = yes, -1 = no, or 0 = don't know for each objective. The formula to evaluate Item Objective Congruence (IOC). IOC scores are ≥ 0.5 on representativeness. language version form will validate by three experts working in the healthcare field (two experts are working at Setthathirat Hospital and one is working at the University of Health and Sciences, Lao PDR). The final results of the IOC score were 0.6 scores for all questions.

3.2.10.2 Reliability

Reliability or otherwise known as confidence is another important feature of a good tool. The fact is that any tool is very accurate. It means that the instrument has a high degree of measurement stability.

If the instrument is re-measured, the difference is less repeated showing that the tool has high precision. Cronbach's alpha will use for reliability. of the translated patients' knowledge assessment tool. The experiment with 20 patients of Mahosot Hospital using antiepileptic therapy used about a week for test reliability. The questionnaire for patients' knowledge assessment was 0.765 for Cronbach's alpha calculation means the internal consistency was good.

3.2.11 Research ethics

- Study participants were informed description of the research participants (Information Sheet for Research Participant) and received a signed letter of consent to participate in the research project (Inform Consent Form) voluntarily.

- Study participants if in doubt can ask for information from the researcher at any time.

- Confidentiality concealed the patient's name, and surname in presenting the study data.

- Respecting the rights of study participants during the study, participants can request to cancel their participation in the study without any effect on the treatment.

- Memorandum to the Chairman of the Human Research Ethics Committee Mahasarakham University presents a research project. To be considered for the ethics of human research. Mahasarakham University and a request form for ethics consideration in human research. (For Human Research Ethics Subcommittee's consideration).

- Memorandum to the Ministry of health national ethics committee for health research Laos presents a research project to be considered for the ethics of research.

3.2.12 Data collection procedure

3.2.12.1 Preparatory stage

- The researcher conducted face-to-face interviews and focus group activities in a multidisciplinary team. It consists of doctors, nurses, and pharmacists who take care of patients in an outpatient clinic in Seththathirat Hospital to find patterns and guidelines for additional care that are appropriate among patients in assessing patients' adherence, assessing patient knowledge, assessing the seizures-frequency, monitoring problems arising from drugs to prevent and resolve the problem that arises, and assessing the patient quality of life of a patient with epilepsy.

- Design tools used to collect research data, part 1 general information, part 2 patients adherence assessment, part 3 Patients' knowledge assessment, seizure-frequency assessment, part 4 drug-related problems monitoring assessment, and part 5 patients' quality of life assessment.

- Verify all data collection tools according to the instrument verification procedure.

- Set the pattern and guidelines for care

- To increase understanding of continuity and regularity in taking more medications and monitoring problems arising from every time the patient comes to get service give a home medication calendar and the self-report book for ease when taking medication and what happens.

- Motivate encouragement by counseling nurses every time you come to get service health care advice practices to increase your immunity both physically and mentally, smiling, laughing, meditation, and exercising.

3.2.12.2 Research process

After approval by the Ministry of Health's national ethics committee for health research Laos and the Human Research Ethics Committee at Mahasarakham University, the researcher proceeded with the following steps:

- The researcher was a pharmacist at an outpatient clinic, which is a care clinic for epilepsy patients clarifies the purpose data collection procedure, and asks for cooperation Multidisciplinary team that works full-time in the outpatient clinic consists of a doctor and a nurse.

- Conducted a sample selection according to qualifications for inclusion criteria and exclusion criteria in a research project from November 2021-August 2022.+ Pharmacist intervention:

1: The interview involves a 30-min structured verbal face-to-face interview conducted by a pharmacist researcher who is a clinical pharmacy individually and privately, in the counseling room.

2: Obtaining medication history

3: Reviewing current drug therapy for appropriateness

4: Assessing the patient adherence

5: Assessing the patient's knowledge

6: Assessing the patients' DRPs

7: Assessing the patient seizure frequency

8: Assessing the patient's QOL

9: Consulted with the patient and recommended relevant changes in drug therapy to physicians

10: Provided patient education and consultation regarding the disease, its management, and drug therapy.

11: Gave a self-report book and the time and date of an appointment following each visit.

12: The self-report book had a table for the patients to record the time that they took their antiepileptic drugs and the time that they had a seizure or experience unusual symptoms.

+ All participants received:

- Patient registration by a queue card.

- A nurse interviewed them about some patient characteristics. To measure blood pressure, record it in the patient's book, and will advise on health education including exercises, daily behavior, how to take medicine, and adherence to medication.

- The doctor (neurology specialist) diagnosed, recommend to continues or changing antiepileptic drugs, and provides short counseling about the disease and the medication used by the patient. So, the next follow-up is up to the doctor's appointment.

+ Research period:

The trial period for each patient took a total of 6 months as follows:

1. Visit 1 (month 0):

+ The interview involves a 30-min structured verbal face-to-face interview individually and privately, in the counseling room.

+ The patient was asked for patients data

+ + Patients' adherence assessment tool used pill count and, self-report of how to take medicine.

+ The patient was assessed with the baseline knowledge (pre-test) of epilepsy and asked a question following the test by using a question adapt from Siriporn Tiamkao (2007).

+ Patient was assessed the seizures-frequency of 3 months ago.

+ Patient was asked a question following the QOLIE-10 for the baseline quality of life assessment test by using a question adapted from Joyce. Cramer (1996).

+ Gave the self-report book to each patient to take a short note every day.

+ During this visit, the researcher gave individual education about the medical aspects of the patient's disease including the definition, causes, and types of epilepsy by pharmacotherapy, give them an epilepsy patient guide, pharmacotherapy of antiepileptic drugs, and therapeutic drug monitoring, and medication advice.

+ The patient has assessed the knowledge after education (Post-test1)

+ In the case of DRP arising, the pharmacist notified the doctor and record the change in the DRP assessment form. Pharmacists were advised on how to solve or prevent problems for doctors, searching for problems, and then gave suggestions on how to solve or prevent problems for patients.

Motivate, and encourage patients.

2. Visit 2 (month 3):

+ The interview involves a 30-min structured verbal face-to-face interview individually and privately, in the counseling room.

+ Patients' adherence assessment tool was used pill count and, self-report of how to take medicine.

+ Patient has assessed the knowledge of epilepsy at 3 months after intervention with the same test (Post-test 2).

+ Monitor problems arising from drugs to prevent and resolve problems that arise.

+ Monitor problems with seizure frequency in the last 3 months

+ During this visit, the researcher was an education about medication use, and the result of adherence, non- adherence, and pharmacotherapy of antiepileptic drugs.

+ Give the individual short note to each patient to take short notes every day.

+ Motivate, and encourage patients.

3. Visit 3 (month 6):

+ The interview involves a 30-min structured verbal face-to-face interview individually and privately, in the counseling room.

+ Patients' adherence was assessed tool using pill count and, self-report of how to take medicine.

+ Patient has assessed the knowledge of epilepsy 6 months after intervention with the same test (Post-test 3).

+ Monitor problems arising from drug-using to prevent and resolve problems that arise.

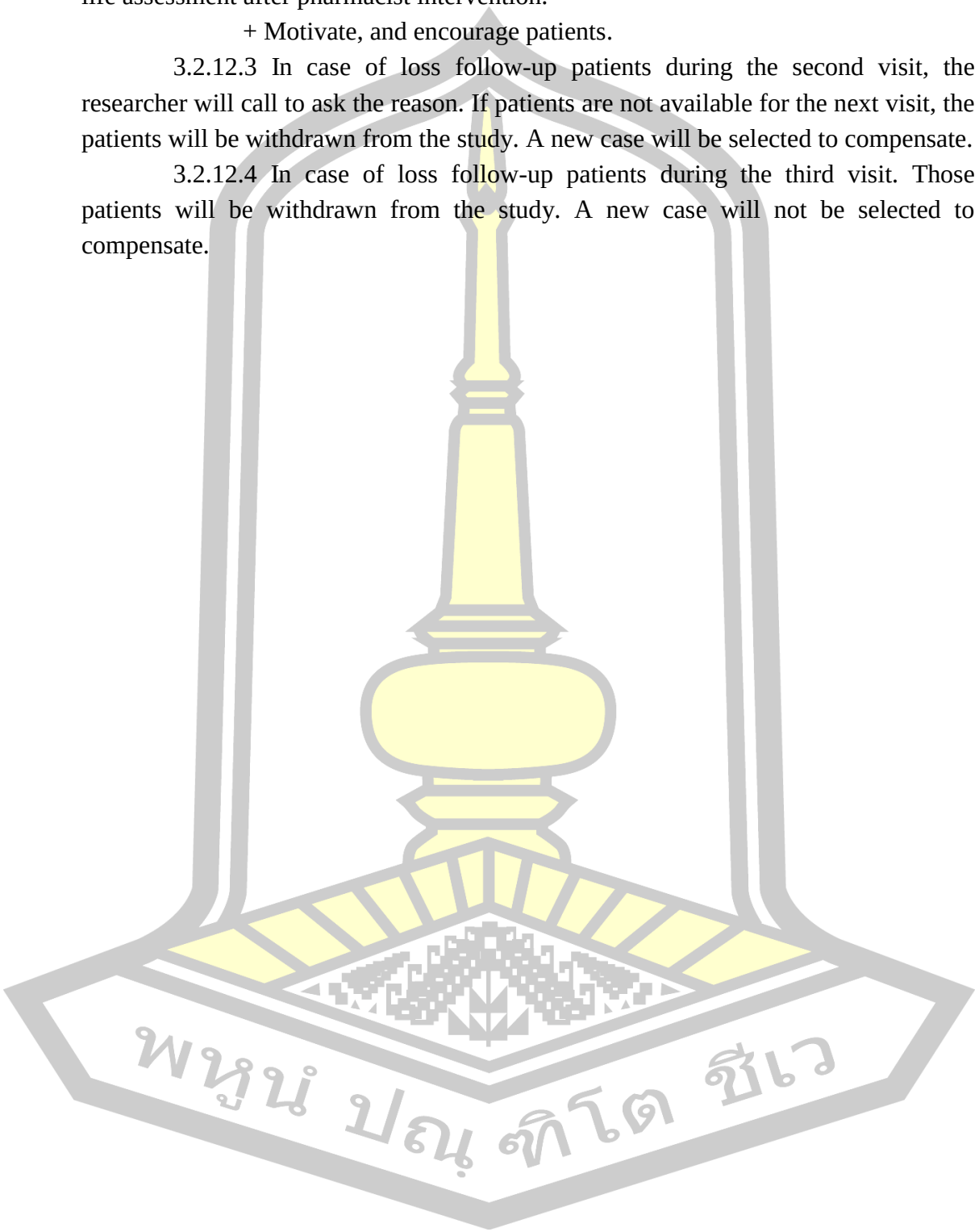
+ Monitor problems with seizure frequency in the last 3 months.

+ Patient was asked a question following the QOLIE-10 for quality of life assessment after pharmacist intervention.

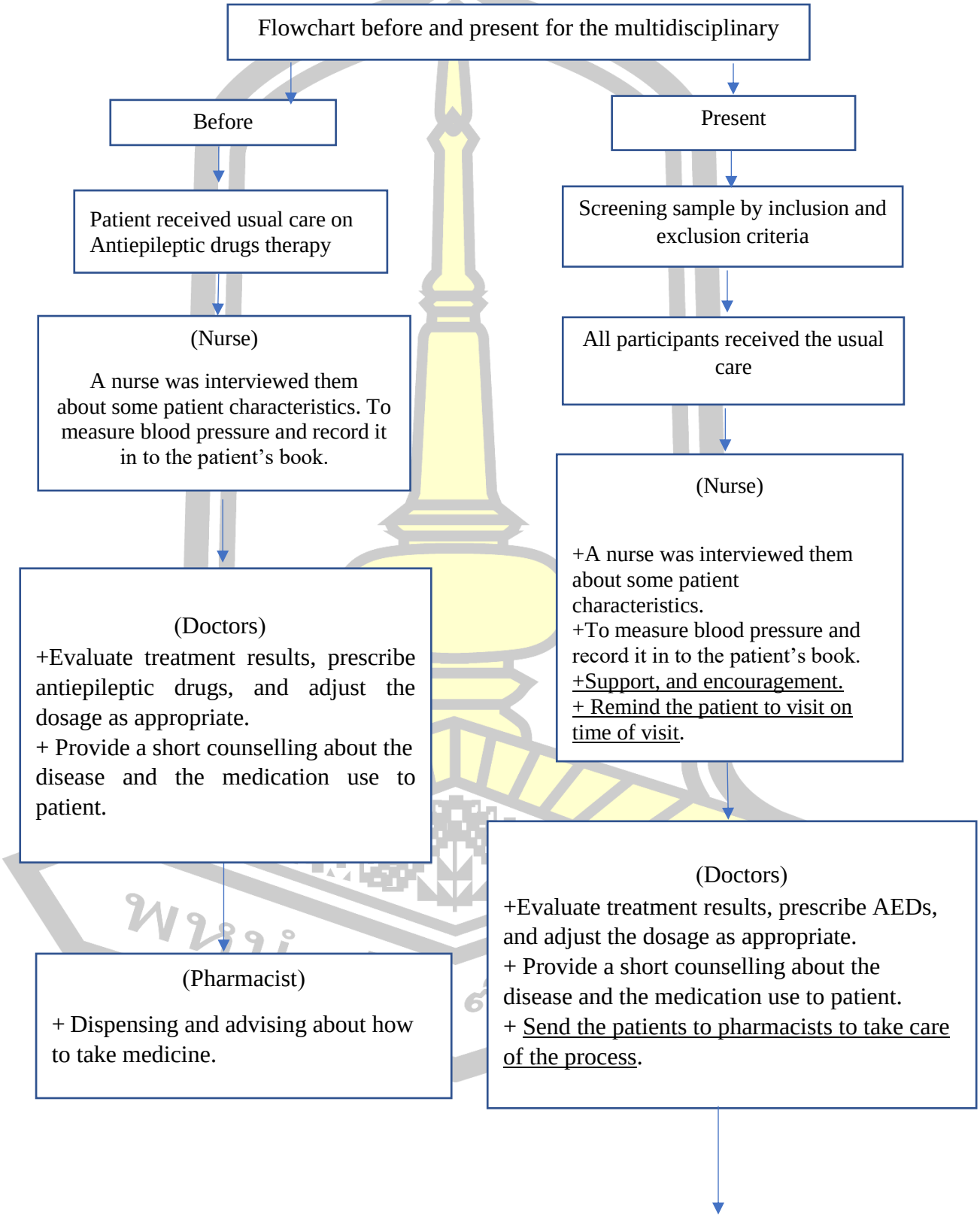
+ Motivate, and encourage patients.

3.2.12.3 In case of loss follow-up patients during the second visit, the researcher will call to ask the reason. If patients are not available for the next visit, the patients will be withdrawn from the study. A new case will be selected to compensate.

3.2.12.4 In case of loss follow-up patients during the third visit. Those patients will be withdrawn from the study. A new case will not be selected to compensate.



❖ Flowchart before and now for the multidisciplinary team for epilepsy management at Setthathirat hospital in LAO PD



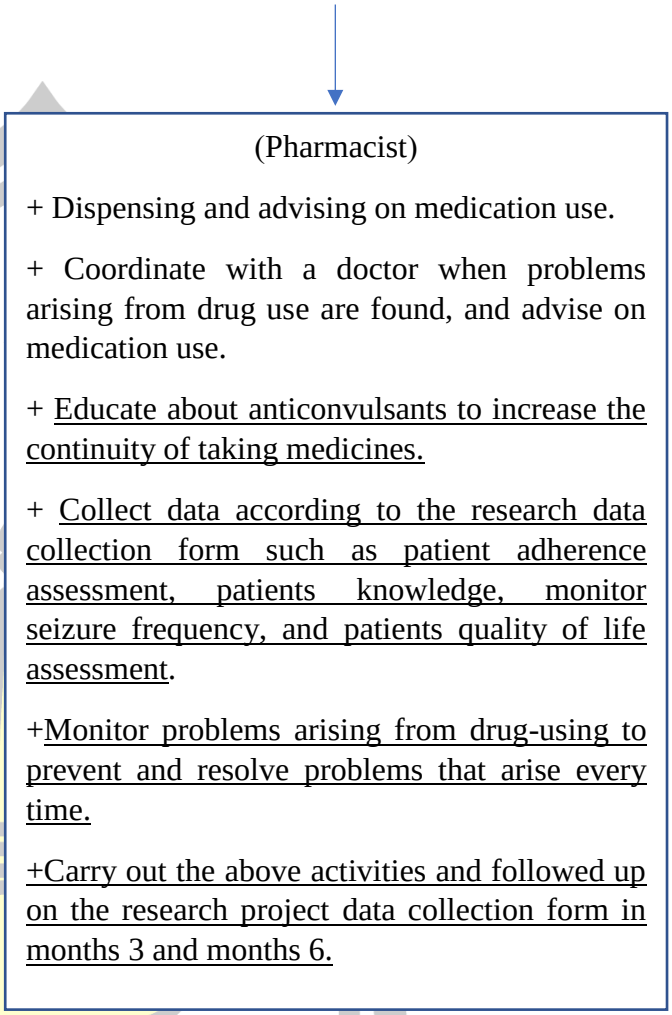


Figure 3 Flowchart before and present for the multidisciplinary team

3.2.13. Data analysis

All data was used in a computer program analysis, statistical analysis was performed using IBM SPSS Statistics Version 21. The statistical significance was considered as $p<0.05$.

3.2.13.1 The statistics were shown as means with standard deviations for continuous variables and frequencies with percent for categorical variables.

3.2.13.2 Categorical variables were presented as numbers and percentages. Patients' gender, age, education, marital status, the residence of the patient monthly income of patients, family history of epilepsy, and number of AEDs were presented by group variables. Type of AEDs, comorbidities, seizure type, patient knowledge, and patient adherence were presented by categorical variables.

3.2.13.3 The Kolmogorov-Smirnov test uses to test the null hypothesis that a set of data comes from a Normal distribution.

3.2.13.4 Comparison of differences in the percentage of medication adherence score, percentage of knowledge score, percentage seizure frequency score, and percentage of quality of life scores of the samples between before and after receiving intervention from the multidisciplinary team if found the distribution curves are normal using the dependent t-test or Chi-square at the statistical significance level of 0.05. If the distribution is not normal, use Wilcoxon Signed Rank Test.

3.3 Protection of human participants

The human research ethics board at the Lao PDR National Ethics Committee for Health Research and Division of Research Facilitation and Dissemination Mahasarakham University was established for this study. All data were kept in a secure place by the researcher.

CHAPTER IV

RESULTS

The objectives of this study were aimed to establish and develop a multidisciplinary team for epilepsy management at an outpatient clinic at the Department of Neurology, Setthathirath Hospital, LAOS PDR. The general objective was to evaluate the outcome of the multidisciplinary team for epilepsy management at the outpatient clinic, Setthathirath Hospital. The specific objective was to compare the adherence to medication, the knowledge, the consequences of problem-solving of DRP, seizure frequency, and quality of life of patients with epilepsy before and after receiving the multidisciplinary team intervention.

Phase 1: Qualitative interviews. In this phase, there were individual and focus group interviews.

Phase II: A quasi-experimental study was to evaluate the effects of multidisciplinary team-managed antiepileptic therapy on patient clinical outcomes at Setthathirath Hospital

4.1 The individual interviews

The individual interviews were conducted to investigate healthcare professionals including doctors, nurses, and pharmacists.

4.1.1: Roles of healthcare professionals in current practice.

4.1.2: Views of service and antiepileptic drug problems.

4.1.3: Views of pharmacists' roles in the epilepsy clinic.

4.1.4: Ways to improve services.

4.2 Focus group interviews

Focus group interviews were undertaken to gain views on collaborations among healthcare professionals involved in the provision of health care services for patients using antiepileptic drugs to develop the practical intervention model called multidisciplinary team-managed antiepileptic drugs therapy at Setthathirat Hospital based on an evidence-based intervention model.

The key concepts of pharmacists' roles in providing pharmaceutical care services for patients using antiepileptic drugs extracted from systematic reviews studies were integrated into the intervention model. Expectations of pharmacists' roles by healthcare professionals focus on medication adherence, knowledge, seizures-frequency, quality of life, how to manage when receiving DRP (Drug-Related Problem), and the importance of following up on doctors' appointments.

Phase II: A quasi-experimental study

This phase was conducted to evaluate the effects of multidisciplinary team-managed antiepileptic therapy on patient clinical outcomes at Setthathirath Hospital.

The results of the analysis are presented in a tabular form for the lecture, divided into 6 parts as follows:

4.3 Patient characteristics

4.3.1 Patients' adherence
4.3.2 Patients' knowledge
4.3.3 The Drug-related problems
4.3.4 Patients' quality of life
4.3.5 Seizure-frequency

Phase 1: Qualitative interviews. In this phase, there were individual and focus group interviews.

4.1 Individual interviews

The Individual interviews were conducted to investigate the views of healthcare professionals including doctors, nurses, and pharmacists. This individual interview presented healthcare professionals' experiences of current practice problems with antiepileptic therapy; views of service and antiepileptic drug problems, and views of pharmacists' roles in the epilepsy clinic.

4.1.1 Roles of healthcare professionals in current practice.

At Setthathirath Hospital, currently, doctors and nurses worked together. Doctors gave general counseling on antiepileptic use and provided regular monitoring for individual patients. Nurses provided antiepileptic counseling on how to safely use the drug as prescribed and followed up on doctors' appointments. However, pharmacists said that they just only dispensed antiepileptic drugs to patients. They did not give proper counseling to individuals due to workloads and time constraints.

4.1.2: Views of service and antiepileptic drug problems.

Doctors, nurses, and pharmacists had the same views of antiepileptic problems that needed more attention from the healthcare team. In addition, the other important problems found were not following up with doctors' appointments, lack of medication, and buying antiepileptic drugs by themselves at the drug store. Antiepileptic drug is not legally allowed to sell in drugstores. Purchasing antiepileptic drugs from these stores was commonly found in practice because it was very convenient for patients. It could cause patients problems not coming for a regular follow-up, resulting in a not controlled seizure. Patients were also lack of knowledge

about how to take the antiepileptic drugs properly. These problems then led to the patient can not control seizures and poor quality of life.

Patients need to adjust the dose of medicine depending on their seizure frequency. One more important thing that could be seen is the lacking of antiepileptic drugs in the clinic, Lack of medication information lack of drug use tracking. This problem has made some difficulties for healthcare professionals since antiepileptic therapy are depending on the doctor's decision. The pharmacist is only responsible for distributing medicines to patients. Other than that, some pharmacists pointed out that there was still a mistake in dispensing antiepileptic drugs which is a mistake by a pharmacist. All of that is proposed to improve the drug dispensing process because there are effects on DRPs.

4.1.3 Views of pharmacists' roles in the epilepsy clinic.

All healthcare professionals agreed with pharmacist counseling for patients using antiepileptic therapy. Doctors said that their roles are to prescribe drugs, give some important information to patients and keep up monitoring patients as necessary. Doctors and nurses had the same suggestions about pharmacists' roles; for instance, providing key information on how to take antiepileptic safety and agreed on the role of pharmacists in informing patients about common ADRs and how to manage them, their side effects, important things to be aware of, not buying antiepileptic at the drug store, and following up doctors' appointments. Doctors agreed that the importance and benefits of having pharmacist counseling were not just directly for the patients but also to help save time for doctors.

4.1.4: Ways to improve services

All healthcare professionals agreed on Pharmacists should be a part of epilepsy management. the benefits pharmacist are involved in the team, which could help to improve overall patients' health outcomes as well as reduce antiepileptic drug problems, give knowledge on disease and medication, support adherence, follow up seizure frequency, and take care of the quality of life. This clinic would then be beneficial for epilepsy patients using the antiepileptic drug.

4.2 Focus group interviews

Focus group interviews were undertaken to gain views on healthcare professionals involved in the provision of healthcare services for patients using the antiepileptic drug. This was to develop the practical intervention model called a multidisciplinary team for epilepsy management at Setthathirat Hospital based on an evidence-based intervention model. The key concepts of pharmacists' roles in providing pharmaceutical care services for patients using antiepileptic drugs extracted from systematic review studies were integrated into the intervention model. Then the process of care delivering "a multidisciplinary team for management antiepileptic therapy", was drafted and discussed in the focus group interviews.

Results from the literature review of systematic review studies presented a multidisciplinary team and the pharmacist activities below:

1: The multidisciplinary team for epilepsy management

2: Pharmacist-led educational interview in terms of adherence to antiepileptic drugs.

3: Pharmaceutical care Intervention improves adherence to antiepileptic medication

4: Pharmacist care Improves quality of life in with epilepsy

5: Improve patients‟ knowledge and understanding of their epilepsy.

6: Pharmaceutical care practice ADRs and seizure frequency

7: Pharmaceutical care Intervention improves adherence to antiepileptic medication

8: The impact of clinical pharmacists on drug-related problems and clinical outcomes

In addition, the summaries of a face-to-face interview of healthcare professionals at Setthathirath Hospital presented the main theme: healthcare professionals' experiences of current practice problems with antiepileptic therapy. Views of service and antiepileptic drug problems, roles of healthcare professionals in current practice, the ways for improving services, and views of pharmacists' roles. The researcher created the practical intervention model to present at the focus group interview. The main topics discussed were as follows:

- The process of care for patients using antiepileptic drugs was established from the real practice at Setthathirath Hospital and the researcher added one step of pharmacists' intervention at the end of the process.

- The pharmacists' roles for patients taking the antiepileptic drug, it was created by using the results of a literature review of systematic review studies by pharmacist activities for epilepsy patients. Expectations of pharmacists' roles by healthcare professionals focus on medication adherence, knowledge, seizures-frequency, quality of life, DRP management, and the importance of following up on doctors' appointments.

- The education tool for pharmacists was recognized by using the results of face-to-face interviews, especially from the sub-themes of views of pharmacists' roles that can be done at Setthathirath Hospital. During the interview, a practical intervention model was proposed, discussed, and summarized key points of the interviews based on the main topics guide. A multidisciplinary team intervention model called "A multidisciplinary team for epilepsy management" was finally developed after finishing focus group interviews.

Major themes that emerged during the focus group interviews included: collaborations among healthcare professionals and expectations of pharmacists' role as healthcare professionals. Because this is a good opportunity for pharmacists to help patients' knowledge and understanding of the proper and safe use of antiepileptic drugs for the maximum benefit of the individual patient.

After interviews and focus groups, the generated interventions will be used in the next phase.

Phase II: A quasi-experimental study

This phase was conducted to evaluate the effects of a multidisciplinary team for epilepsy management on patients' clinical outcomes at Setthathirat Hospital. The intervention was conducted from phase I, interview determines the protocol of multidisciplinary team management. A multidisciplinary team-managed antiepileptic drug therapy focuses on pharmacist educated included adherence assessment, knowledge assessment, Seizure-frequency assessment, quality of life assessment, medication review, DRPs assessment, and in case of any DRPs found, the pharmacist has notified the doctor and records the response of management in DRPs assessment form.

Multidisciplinary team interventions were the result of interviews including collaborations among healthcare professionals that needed pharmacists to be a part of antiepileptic therapy at Setthathirat Hospital. The expectations of pharmacists' roles as healthcare professionals include recommending to the patient how to take the antiepileptic drug properly, patients can control seizures, increase adherence, increase knowledge, adverse drug reaction monitoring, and management, how to manage when occurring receiving problems, the importance of following up with doctor appointment. The practical intervention model was discussed and accepted by all healthcare professionals from the focus group interviews.

4.3 Patient characteristics

A total of 68 patients diagnosed cases of epilepsy patients were found eligible for the inclusion and exclusion criteria of the study (Table 8)summarizes the characteristics of all patients enrolled in this study. The study included 64.7 % of female patients and 35.3% of male patients. The majority of patients were between 18-39 years (67.6%). The education of patients in the primary was 10.3%, in the secondary was 30.9%, and in university was 29.4%. For marital status found that 54.4 % of the patients were single, 42.6% were married, and 2.9% were widows. Almost the patients who live out-town 72.1%, and 27.9% live in town. Of the occupations of patients, 36.8% were selling a product, 17.6% were government officers, 16.2% were unemployed, 13.2% were students, 11.8% were farmers, 2.9% were workers, and 1.5% were retired. The monthly income of patients with more than > 5.000 .000 kip

was 2.9%. Most of the patients have an income in the range of 2.000.000 kip (44.1%). There were 86.8% of patients without comorbidity, 7.4% with hypertension, 1.5% with diabetes mellitus, and 2.9% with depression. The type of antiepileptic drugs were phenobarbital 38 (55.9%), carbamazepine 11 (16.2%), valproic acid 13 (19.1%), phenytoin 5 (7.4%) In addition, the study found that 95.6% of the patients was treated epilepsy with monotherapy, and only 4.4% were treated with poly therapy. (Table 11)

Table 11 Demographics and clinical characteristics of the study population

Characteristics	N	%
Gender		
Male	24	35.3
Female	44	64.7
Age		
18-39	46	67.6
40-59	19	27.9
>=60	3	4.4
Education		
Primary	7	10.3
Secondary	21	30.9
High school	20	29.4
University	20	29.4
Marital status		
Single	37	54.4
Married	29	42.6
Widow	2	2.9
Residence		
In town	19	27.9
Out of town	49	72.1
Occupation		
Farmer	8	11.8
Worker	2	2.9
Sell product	25	36.8
Government officer	12	17.6
Unemployed	11	16.2
Retirement	1	1.5
Student	9	13.2

Table 11 (continue)		
Characteristics	N	%
Income		
No income	27	39.7
1.000.000-2.000.000 kip	30	44.1
2.000.000-5.000.000 kip	9	13.2
> 5.000.000 kip	2	2.9

Table 12 Demographics and clinical characteristics of the study population (next)

Family history of epilepsy		
Positive family history	12	17.6
Negative family history	56	82.4
Comorbidities		
Patients without comorbidity	59	86.8
Patients with Hypertension	5	7.4
Patients with lipid	1	1.5
Patients with diabetes mellitus	1	1.5
Patients with depression	2	2.9
Type of AEDs		
Phenobarbital	38	55.9
Carbamazepine	11	16.2
Valproic acid	13	19.1
Phenytoin	5	7.4
Type of therapy		
Monotherapy	65	95.6
Poly therapy	3	4.4

4.4 Efficacy outcomes

Patients' efficacy outcomes included patient adherence, patients' knowledge, seizure-frequency, drug-related problems, and patients'quality of life. The researcher met the sample patients 3 visits, each visit was 3 months after the doctor's appointment.

4.4.1 Patients' adherences

Patients' adherence was assessed by using pill count and self-report of how to take medicine. Patients who had good adherence were those who got scores ≥85%.

Table 13 Patients' adherences. (N=68)

% Adherence	Visit 1		Visit 2		Visit 3	
	N	%	N	%	N	%
Appropriate compliance	1	1.5 %	63	92.6 %	68	100 %
Noncompliance	67	98,5 %	5	7.4%	0	0

Table 14 Outcome of patients' adherences assess by using pill-count. (N=68)

Adherence	Mean ± SD	Z	P-value
Before receiving the intervention visit 1 (month 0)	58.15±27.3	-7.168	0.0001
Post the intervention visit 2 (month 3)	90.17±4.5		
Post the intervention visit 2 (month 3)	90.17±4.5	-6.471	0.0001
Post the intervention visit 3 (month 6)	95.24±2.03		

(* Statistic test by Wilcoxon Signed Ranks Test)

Patients who had good adherence were those who got scores more or equal to 85 percent. The number of patients with noncompliance was 67 patients (98.50 %) on the first visit before receiving the intervention visit 1 (month 0). After receiving the intervention, the number of patients with appropriate adherence was 63 (92.6%) and 68 patients (100%) on the visit 2 (month 3), and visits 3 (month 6), respectively. (as shown in table 10)

The mean percentage of pill count in the post-intervention visit 2 (month 3) was 90.17±4.5 higher than 58.15±27.3 before receiving the intervention visit 1 (month 0), with a significant difference between before and after intervention p-value = 0.0001 (as shown in Table 11)

4.4.2 Patients' knowledge

The patient's knowledge was assessed by the mean score of 11 questions in the questionnaire. There were 6 items about epilepsy and 5 items about antiepileptic drugs. The total score about epilepsy was 39. The mean baseline score (pre-test month 0) was 29.72±3.6. After post-counseling in (month 0), the patients' knowledge was reassessed and the mean score increased to 37.63±1.1. The outcome showed a statistically significant difference between the pre-test (month 0) and post-test (month 0)score (p-value = 0.001)

There were 5 items of antiepileptic drug knowledge. There was divided into assessments of 5 out of 11 items in the questionnaires. The total score about antiepileptic drug was 23. The mean score in the pre-test (month 0) and the post-test (month 0) were 6.00 ± .45 and 9.58 ± 1.12 (p-value = 0.000). The outcome showed a statistical difference after receiving an intervention. But our study found the mean score of the antiepileptic drug's knowledge in post-visit 1 (month 0) similar to visit 2 (months 3) (as shown in table 15)

Table 15 Comparing patients' knowledge between before receiving the intervention and after receiving the intervention. (N=68)

Outcomes	(Mean ± SD)	Z	p-value*
All questionnaires (Total score =39)			
Pre-knowledge visit 1(month 0)	29.72±3.6	-7.176	.0001
Post-knowledge visit 1 (month 0)	37.63±1.1		
Post-knowledge visit 2 (month 3)	37.57±1.2	1.941	0.05
Post-knowledge visit 3 (month 6)	37.10±1.6		
Antiepilsptic's knowledge (Total score = 23)			
Pre-knowledge (month 0)	6.00±0.45	-7.265	.0001
Post-knowledge (month 0)	9.58±1.12		
Post-knowledge (month 3)	9.89±1.46	-3.103	.002
Post-knowledge (month 6)	9.45±1.21		

(* Statistic test by Wilcoxon Signed Ranks Test)

4.4.3 Drug-related problems

The DRPs assessment was modified from Hepler and Strand criteria. The focus categories of DRPs were to identify actual or potential DRPs by pharmacists' roles management as follows drug interaction, the side effect of drugs, over dosage, and changes the antiepileptic drug, lacking of phenobarbital 100mg.

The focus categories of DRPs were to identify actual or potential DRPs as following 3 items:

1: Drug interactions are drug-drug interactions that can increase or decrease the antiepileptic drug effect that cited the side effect of drugs Wong & Lhatoo 2000. (8)

2: Adverse reaction (the side effect of drugs) is an assessment of actual patients for each visit that cited the side effect of drugs Wong & Lhatoo 2000. (8)

3: Over dosage is an assessment of a doctor's prescription (looking for patient's dose of antiepileptic drugs over the therapeutic range for each visit).

The study assessed DRPs on each of the 3 visits for patients. Twenty-four DRPs were found at visit 1(month 0). Also, the result showed DRPs decreased from visit 1 (month 0) to visit 2 (month 3) and visit 3 (month 6) (24 DRPs to 11 DRPs and to 15 DRPs). The most type of DRP from the 3 visits was drug interaction which consist of 14 cases for patients (10, 4 cases at visit 1 (month 0) and visit 2 (month 3) and visit 3 (month 6) respectively). Followed by overdosage 2 cases (in visit 1 (month 0) failure to receive drugs 9 cases in visit 3 (month 6) and adverse reactions in visit 1(month 0) such as weight gain in 4 cases, alopecia 2 cases, behavior change in 1 case, sedation in 1case, and headache 2 cases, dizziness in 1 case, and allergy, in 1 case. Overdosage found, a researcher consulted with doctors to adjust the dose of the antiepileptic drug by decreasing the dose using international guidelines. however, some cases were not accepted by doctors and patients had to keep taking the same dose and then monitoring their symptoms of seizure. There were 7 patients who had DRP more than one time in visit 1 (month 0) and 4 patients in visit 2 (month 3). DRPs were accepted by multidisciplinary team and managed together at visit 1 (month 0) to visit 3 (month 6) at 29.9 %, 10.3 and 14.7 % respectively. More information on DRPs assessment was shown in (appendix D). For drug interaction with antiepileptic drugs, 10 cases were found at visit 1 (month 0), and 4 cases at visit 2 (month 3). A drug-drug interaction found at the baseline visit was the interaction of carbamazepine and amlodipine, phenobarbital and simvastatin, phenobarbital and carbamazepine, carbamazepine and valproic acid, valproic acid, and phenobarbital, phenobarbital and metformin/pioglitazone as same as the second visit but it was from different patients. When a drug interaction was found, a researcher was counseling patients on taking antiepileptic drugs not over by doctor's advice. For adverse reaction found weight gain 4 cases, sedation 1 case, behavior change 1 case, alopecia 1 case, dizziness 1 case, headache 1 case, allergy 1 case at visit 1 (month 0). The researcher was counseling patients focusing on food, alcohol, sleep, exercise, relax which could lead to decrease adverse reactions. At the next follow-up, the study did not find any cases of sedation, dizziness, and headache after patients got counseling from pharmacists. Only one case of allergy from phenobarbital at visit 1 (month 0). A

researcher consulted with doctors and changed other antiepileptic drugs which were not allergies and monitored drug allergy for this patient. At the next follow-up, the study did not find any cases of drug allergy.

During the data collection. there was a problem with the lack of anticonvulsants in the hospital Phenobarbital 100 mg is not available in the hospital and is absent everywhere, 9 patients did not have medication to take for the next month. A researcher consulted with the team to change a new antiepileptic drugs for seizure control. The team resolved this problem by replacing phenobarbital 100 mg with Valproic acid 200 mg. A researcher counsel patients on taking antiepileptic drugs not over by prescription and closely monitoring (as shown in Table 16)

Table 16 Number of drug-related problems in the 6 months before and after the provision of a multidisciplinary team for 6 months. (N=68)

Outcomes	Visit 1(month 0) (N%)	Visit 2(month3) (N%)	Visit3(month6) (N%)
Drug interaction	10 (14.7)	4 (5.9)	0 (0.00)
Over dosage	2 (2.9)	0 (0.00)	0 (0.00)
Failure to receive drugs			9 (13.2)
Adverse reaction:			
Weight gain	4 (5.9)	4 (5.9)	4 (5.9)
Sedation	1 (1.5)	0 (0.00)	0 (0.00)
Behavior change	1 (1.5)	1 (1.5)	0 (0.00)
Alopecia	2 (2.9)	2 (2.9)	2 (2.9)
Dizzeness	1 (1.5)	0 (0.00)	0 (0.00)
Headach	2 (2.9)	0 (0.00)	0 (0.00)
Allergy	1 (1.5)	0 (0.00)	0 (0.00)
Number of patients had >1 DRP	7 (10.3)	4 (5.9)	0 (0.00)
MDT managed together	19 (27.9)	7 (10.3)	10 (14.7)
Total DRPs (cases)	24	11	15

4.4.4 Frequency of Seizures

The seizure frequency for each patient was collected for 3 months before and after the provision multidisciplinary team. Seizure-frequency groups were based on the number of seizures in 3 months (Devinsky et al., 1995).

Before the provision of a multidisciplinary team, there were 9 patients in seizure-free group (13.2%) and patients had 3 times seizures per 3 months 20 patients (29.4%). After the provision of a multidisciplinary team, groups that were

seizure-free in (month 3) were 48 (70.6%), seizure-frequency decrease by 7(10.3%), and in (month 6) seizure-free were 61 (89.7%). There were statistically significant differences (p <0.01) between seizure-frequency groups in the periods before and after the provision of a multidisciplinary team shown in Table 15.

Table 17 Frequency of Seizures per 3 months before and after the provision of a multidisciplinary team in months 3, and month 6. (N=68)

Frequency of Seizures	(Mean ± SD	Z	p-value
Frequency of Seizures before the provision of intervention	2.85 ± 1.37	-6.447	.0001[a]
Frequency of Seizures in month 3	0.75 ± 1.38		
Frequency of Seizures in month 6	0.10 ± 0.30	-3.955	.0001[b]

Frequency of Seizures	Before month 0 N (%)	Month 3 N (%)	Month 6 N (%)
0 time	9 (13.2%)	48 (70.6%)	61 (89%)
1 time	4 (5.9%)	7 (10.3%)	7 (10%)
2 time	18 (26.5%)	2 (2.9%)	
3 time	20 (29.4%)	6 (8.8%)	
4 time	7 (10.3%)	3 (4.4%)	
5 time	6 (8.8%)	2 (2.9%)	
6 time	4 (5.9%)		

[a] Statistic test by Wilcoxon Signed Ranks Test compared between before and after provision of multidisciplinary team on month 3

[b] Statistic test by Wilcoxon Signed Ranks Test compared between before and after provision of multidisciplinary team on month 6

4.4.5 Quality of Life

Patient-weighted QOL in epilepsy was assessed by the QOLIE-10-P, an adapted and extended version of the brief questionnaire QOLIE-10 (Cramer et al., 1996). The self-administered 10-item questionnaire covers different epilepsy- and treatment-related issues, including energy, mood, mobility, work limitations, social limitations memory problems, physical treatment effects, cognitive treatment effects, seizure worries, and general QOL.

Accordingly, for the QOLIE-10 total score, a minimum of 10 and a maximum of 51 points could be achieved, with higher scores indicating greater impairment.

There were significant differences ($p<0.01$) in overall scores of QOLIE-10 between before and after the 6 months of the provision of a multidisciplinary team. There were significant differences ($p<0.05$) in these 7 domain functions: mood, work limitations, social limitations, memory problems, physical treatment effects, cognitive treatment effects, and seizure worries. There were no statistically significant differences ($p \geq 0.05$) in 3 domain functions: energy, mobility, and general QOL (Table 18)

Table 18 of Quality of Life (N=68 patients)

QOLIE-10	Scores (pre-month 0) (Mean ± SD)	Scores (post-month 6) (Mean ± SD)	Z	p-value
QOLIE-10 total score	30.23 ± 4.4	24.48 ± 3.48	-6.031	.0001
Energy	1.78 ± 0.96	1.62 ± 0.69	-1.980	0.048
Mood	3.04 ± 0.63	2.57 ± 0.65	-4.088	.0001
Mobility	1.91 ± 0.95	1.74 ± 0.90	-1.91	0.05
Work limitations	3.32 ± 0.88	2.66 ± 0.53	-4.40	.0001
Social limitations	3.00 ± 0.57	2.74 ± 0.44	-2.87	0.04
Memory problems	3.26 ± 0.63	2.82 ± 0.51	-4.40	.0001
Physical treatment effects	2.99 ± 0.53	2.62 ± 0.51	-3.87	.0001
Cognitive treatment effects	4.46 ± 0.85	2.93 ± 0.55	-6.74	.0001
Seizure worries	4.22 ± 1.07	2.91 ± 0.56	-6.27	.0001
General QOL	2.01 ± 0.90	1.72 ±0.64	-2.35	0.019

(Statistic test by Wilcoxon Signed Ranks Test compared between before and after provision of multidisciplinary team on (month 0) and (month 6)

CHAPTER V
CONCLUSION, DISCUSSION and LIMITATION

Individual interviews were conducted to find out the views of healthcare professionals toward the multidisciplinary team's roles and process of care for patients with epilepsy. The present study was based on interviewing 6 healthcare professionals: 2 doctors, 2 pharmacists, and 2 nurses. This could help in having different views and broad ideas.

The major themes that emerged from the individual interviews consisted of 1: Roles of healthcare professionals in current practice, 2: Views of service and antiepileptic drug problems, 3: Views of pharmacists' roles in the epilepsy clinic, 4: Ways to improve services.

The results from the face-to-face interviews were used to develop the intervention of this study is called "Outcome of a multidisciplinary team for epilepsy management"

The focus group interviews were conducted among healthcare professionals. There were 2 doctors, 2 nurses, and 2 pharmacists, who were on the healthcare team and, working at the outpatient clinic at Setthathirat hospital, LAOS PDR.

The major themes that emerged during the focus group interviews included collaborations among healthcare professionals, expectations of pharmacists' roles by healthcare professionals, and showing to team know about the key concepts of pharmacists' roles in providing pharmaceutical care services for patients using antiepileptic drugs.

The results of the focus group interviews were used to conduct a quasi-experimental study and evaluated the effect of the multidisciplinary team intervention for the management of antiepileptic drugs on patients' clinical outcomes. The key concept of a quasi-experimental study was to assess the efficacy and safety outcomes. The efficacy outcomes were the percent of adherence, the knowledge score, the seizure frequency, and the quality of life. The safety outcomes was drug-related problems with antiepileptic drug therapy (DRPs).

All patients were followed up for 6 months including visit 1 (month 0), visit 2 (month 3), and visit 3 (month 6). Most patients were aged 18-39 years old. The patients have education at the level of secondary, followed by high school and university levels. Most of them are single and lived in town. The main occupation of the patient was selling the product, followed by a career government officer. The comorbidities of the patient were hypertension and depression. The most favored regimen was monotherapy. The type of antiepileptic drug was phenobarbital. Patients' adherence was assessed by using pill count and self-report of how to take medicine. Patients who had good adherence were those who got scores ≥ 85%. By analyzing the

patients' adherence 68 patients enrolled in our study found the number of patients with noncompliance was 67 patients (98.50 %) on the first visit before receiving the intervention visit 1 (month 0). The results of patients' adherence were 58.15±27.3 for patients before receiving the intervention visit 1 (month 0), and 90.17±4.5 post the intervention visit 2 (month 3) with a significant difference between before and after intervention p-value= 0.0001. For patients' knowledge scores, there were statistically significant increases from the first 1 (month 0) to visit 2 (month 3) (29.72±3.6 and 37.63±1.1 p-value = 0.001), as well as antiepileptic drug knowledge was increased too from 1 (month 0) to visit 2 (month 3) (6.00±0.45 and 9.58±1.12 p-value = 0.001). Before the provision of an MDT visit 1 (month 0), there were 9 patients in the seizure-free group (13.2%) and patients had 3 times seizures per 3 months 20 patients (29.4%). After the provision of an MDT, groups that were seizure-free in visit 2 (month 3) were 48 (70.6%), seizure frequency decreased by 7(10.3%), and in visit 3 (month 6) seizure-free were 61 (89.7%). There were statistically significant differences ($p < 0.01$) between seizure-frequency groups in the periods before and after the provision of an MDT shown in (Table 15). The most type of DRPs from 3 visits was a drug interaction which consist of 10 cases in visit 1 (months 0), and failure to receive drugs 9 cases in visit 3 (months 6). Patient-weighted QOL in epilepsy was assessed by the QOLIE-10. There were significant differences ($p<0.01$) in overall scores of QOLIE-10 between before and after the 6 months of the provision of a multidisciplinary team.

5.1 DISCUSSION

5.1.1 Qualitative study

The results of the face-to-face interviews were consistent with the previous study (74) conducted Developing Regional Guidelines of Epilepsy for Multidisciplinary Teams. with regards to the acceptance of doctors and nurses in pharmacists' roles of providing pharmaceutical care services for patients using antiepileptic drugs. The health professional team consisting of doctors, pharmacists, and nurses who have the roles to provide health care to epileptic patients in northeastern hospitals agreed with the practicability of the Regional CPG for Epilepsy.

The important problem found in the interview with healthcare professionals was patients were not following up with doctors' appointments. This could be caused by inconvenient transportation, continuous absence from work or school, inadequate knowledge and understanding of diseases, the side effect of medication, forgetting to take medication, and how to take antiepileptic drugs properly. These reasons cause patients problems resulting in can not control seizures and non-adherence. This finding was consistent with the study by

Amudhan and colleagues (75), identified many factors associated with loss of follow-up; for example, their expectations of management, side effects, and lifestyle choice. AED treatment fails often due to the inadequacy of patients to stick with their prescribed regimen. Scanty medication adherence is one of the keystone reasons for poor epilepsy management and negative outcome.

This study helped identify the importance of clinical pharmacy services in the pharmaceutical care and overall quality of life of epilepsy patients since clinical pharmacy services are in the infancy stage at the Lao health care system. This study outcome will assist with showing the benefit of executing a clinical pharmacist-led educational intervention in neurology department settings to improve self-care practices and clinical outcomes among Lao epileptic patients.

5.1.2 A quasi-experimental study.

The study assessed the effects of multidisciplinary team-managed antiepileptic therapy counseling on patients' adherence, patients' knowledge, frequency of seizures, drug-related problems, and quality of life of patients with epilepsy. A total of 68 diagnosed cases of epilepsy patients were included in this study. Among 35,3% of epilepsy patients were male and 64.7% of epilepsy patients were female. Most of the epilepsy patients in this study (95.6%) were on AED monotherapy, while 4.4% of patients were on AED poly therapy there was consistent with those of (D. Chandrasekhar and colleagues (61) the epilepsy patients (64%) were on AED monotherapy, and 36% of patients were on AED poly therapy.

In this study among 68 patients, about 98,5 % of patients showed noncompliance before the intervention. Only 1.5 % showed appropriate compliance. These results are compared with similar studies by Singh et al where they used a pill count and MMAS were two different tools used to assess compliance during home visits. Over a period of 6 months, an equal number of patients was found to be noncompliant with both pill count and MMAS (n = 64). After a comparison of data from pill count and MMAS, a significant difference between noncompliant patients was found (p = 0.000).

Our study’s findings suggest that a multidisciplinary team by the use of clinical pharmacist intervention can improve the utilization of treatment by educating patients with epilepsy. Similar research albeit limited in number shows similar directions. There was consistent with D. Chandrasekhar and colleagues. (61) In a before-after study conducted on adults with epilepsy. by a pharmacist counseling on the knowledge and adherence to antiepileptic drug therapy. The study concluded that low adherence to the medications and lack of knowledge about the disease was the major reasons for the unsuccessful drug treatment which can be cleared up to a satisfying extent by the use of clinical pharmacist intervention.

There was consistent with Jaiklom and colleagues (64) to study the effect of seizure control and medication adherence after receiving new development of pharmaceutical care for epilepsy patients. Seizure control and medication adherence data were collected by interviews and self-administered forms before and after received new pharmaceutical care. The study shown After receiving the new epileptic pharmaceutical care, it was found that there was increase in mean scores of medication adherence and statistically significant decrease in seizure frequency ($p<0.05$). There was a negative correlation between increased medication adherence with reduced seizure frequency.

There was consistent with those of (Angela Fogg and colleagues. (63) A before-and-after study used the Medication Adherence Report Scale (MARS). The intervention was a 30 min consultation to provide participants with an opportunity to ask questions related to their epilepsy therapy. Baseline data collection was repeated after 2 months by a pharmacist. The result shows The proportion of participants reporting adherent behavior significantly increased post-PLEC. Pre-PLEC, 22 (44.0 ± 13.7%) respondents reported never deviating, which increased to 30 (60 ± 13.6%) post-PLEC ($P < 0.03$). Our results show the mean percentage of pill count in month 3 (90.17 ± 4.55) was statistically significantly higher than the first visit 0 (58.15 ± 27.31), ($p <0.0001$). Our results suggest that multidisciplinary team intervention could positively impact the medication adherence of patients with epilepsy.

Compared with previous studies AlAjmi and colleagues. (59) A before-and-after study. In this study, self-reported adherence was assessed using the 8-item Morisky Medication Adherence Scale (MMAS-8) to measure medication adherence in patients with epilepsy who completed the 6 weeks post-intervention adherence measurement. The adherence score average in the intervention group was 5.26±0.98 at baseline and improved to 6.7±0.823 (P,0.0001) after the intervention. In the control group, the adherence score average was 5.76±1.806 at baseline and 5.83±1.627 at 6 weeks (P=0.792). While there was no statistically significant difference in adherence score between intervention and control groups at baseline, the post-intervention difference was significant (P=0.024).

However, it has been reported that the self-report approach to estimating adherence is a basic, modest, and valuable method for distinguishing non-adherence in the clinical setting.

Reported by Singh and colleagues (66) (compliance was assessed using pill count and Morisky medication adherence scale (MMAS) during home visits. A pill count (pills dispensed–pills remaining)/(pills to be consumed between two visits) value of 0.85 to ≤1.15 was recorded as appropriate compliance. Underdose (<0.85) and overdose (>1.15) were labeled as non-compliance. The result shown out of 105 patients, 54 patients were noncompliant with both pill count and MMAS. 10 patients were noncompliant with pill count only, while 10 were noncompliant with MMAS.

Both tools complement each other when used in combination, as the use of a single tool was not able to completely detect compliance. which is consistent with our study.

Although our study found a statistically significant difference in adherence score between baseline and 3 months. Our results suggest that multidisciplinary team intervention could positively impact the medication adherence of patients with epilepsy.

For patients' knowledge, results obtained from our study suggest that the pharmacist's educational interventions significantly improved patients' knowledge of epilepsy as well as their perception of the condition. Patient's knowledge score showed significant increases, from pre-knowledge (month 0) 29.72±3.6 to 37.63±1.1 post-knowledge (month 0) after multidisciplinary-managed antiepileptic drugs therapy. Due to the pharmacist's education during each visit and assessment of the knowledge from the questionnaire, the result of the post-intervention showed that there was a significant difference between patients' knowledge scores. The obvious reason of what makes the different results is that each patient was educated by the pharmacist on every visit. When pharmacists participated the routine care on antiepileptic drugs knowledge, and patients' behavior, the patients would have better quality use of antiepileptic drugs, proving by the seizure frequency reduce and a patient can control seizures. Several studies reported that patients' knowledge outcomes improved after patients' education through pharmacist intervention. Theodor W. May and colleagues (67), U. Eshiet and colleagues. (68)

The results not only showed significant differences between the pre and post-intervention epilepsy knowledge scores among the patients but also showed significant differences between the epilepsy knowledge scores of patients before and after intervention over time of the intervention, indicating that the patients significantly improved in their knowledge of epilepsy following the multidisciplinary team intervention. Patients' knowledge and understanding of their condition is a major determinant of their ability to cope with the condition. There was consistent with Theodor W. May and colleagues. (67) The significant improvement in the patient's knowledge as noted in this study is an indication of the efficacy of the educational treatment program. This result clearly shows the potential impact of educational interventions for people with epilepsy irrespective of their age, educational status, or duration of epilepsy.

Before providing the multidisciplinary team intervention. There were 9 patients in the seizure-free group (13.2%), and patients had 3 times seizures per 3 months 20 patients (29.4%), had 2 times seizures 18 patients(16.5%), 4 times seizures 7 patients (10.3%), and had 5 times seizures 6 patients (8.8%). After receiving the multidisciplinary team intervention There were 48 patients in the seizure-free group (70.6%), and patients had 3 times seizures per 3 months 6 patients (8.8%). These results indicate that patients could control their seizures after receiving

the multidisciplinary team intervention. There was consistent with a previous study, by Kanjanasilp et al. 2008 (14) has shown a significant difference before and after a received intervention. Before providing pharmaceutical care, the most frequent seizure-frequency groups were seizure-free (46.15%), and high-frequency (28.85%). While in the period after the provision of pharmaceutical care, the most frequent seizure frequency groups were seizure-free (71.15%), and high-frequency (13.46%). These results indicate that a majority of patients could control their seizures after the pharmacist had provided pharmaceutical care.

DRPs in our study were reduced after the multidisciplinary team provided intervention. All adverse drug reactions (ADRs) were actual DRPs. DRPs focus on the consequences of problem-solving DRPs including drug interactions, side effects, and improper drug selection for epileptic patients for 6 months. The total DRPs before receiving the intervention were 33 cases, and after receiving the intervention DRPs reduce to 14 cases. The finding that the most frequent DRPs were drug interactions 10 cases (14.7%), over dosage (2 cases) change AEDs 9 cases, and adverse reactions such as weight gain (4 cases), Alopecia (2 cases), headache (2 cases) , and found one case allergy phenobarbital. There was consistent with a previous study, by Kanjanasilp and colleagues (14) found a total of 111 DRPs in the 6 months before the provision of pharmaceutical care and 61 DRPs in the 6 months after the provision of pharmaceutical care. There were significant differences ($p<0.01$) between the number of DRPs in the periods before and after the provision of pharmaceutical care.

QOLIE-10 is a disease-specific measure of the quality of life for epileptic patients. There were significant differences ($p<0.05$) in overall scores of QOLIE-10 between the 6 months before and after the provision of multidisciplinary team management. The multidisciplinary team had a positive impact on the patient's quality of life with epilepsy. There was consistent with a previous study by, U.I. Eshiet and colleagues (68) evaluated the impact of pharmacist-led education and counseling interventions on the health-related quality of life of patients living with epilepsy BY using the QOLIE-10P questionnaire. There was a statistically significant difference between the usual care (UC) and the pharmaceutical care (PC) group on the quality of life in epilepsy scores post-intervention. Comparisons between groups (UC versus PC) revealed that patients in the PC group had a significantly higher QOLIE score than those in the UC group at 3 months and 6 months. And there was consistent with a study by Kanjanasilp and colleagues (14) there were significant differences ($p<0.01$) in overall scores of QOLIE-31 between the 6 months before and after the 6 months of the provision of pharmaceutical care. There were significant differences ($p<0.05$) in these 3 domain functions: seizure worry, emotional well-being, and medication effects. There were no statistically significant differences ($p \geq 0.05$) in 4 domain functions: overall QOL, energy fatigue, cognitive functioning, and social function.

This study helped identify the importance of multidisciplinary team services in the care and overall quality of life of epilepsy patients since multidisciplinary team services are in the infancy stage in the Laos health care system. This study outcome will assist with showing the benefit of executing a clinical pharmacist-led educational intervention in neurology department settings to improve self-care practices and clinical outcomes among Laos epileptic patients.

5.2 Limitation of study

limitations of our study need to be addressed. Firstly, there was no electronic medical record in Setthathirat hospital. The only way to check or know the patients' records was through the patients' books. There was not any record of the ADR or DRPs of antiepileptic drugs so we recommended future studies continue collecting these data for baseline. Secondly limitation was the epilepsy clinic is open only in the morning on Wednesdays, and not enough time for the patient comes to visit. The third limitation is the lack of medication in the hospital (there are 9 cases of change from phenobarbital to Valproic acid) at the visit in month 6. The fourth limitation is the relatively small number of epileptic patients studied.

5.3 Future research

Our study demonstrated an effective intervention to improve epilepsy such as medication adherence, knowledge, seizure frequency, problem-solving of DRPs as well as the quality of life. Prospective studies in other areas, with different sample populations and a longer follow-up, are expected to further validate the efficacy and utility of the multidisciplinary management program.

5.4 Application

In summary, the result of antiepileptic therapy by a multidisciplinary team managed by pharmacists was better than usual care with no pharmacists involved. The pharmacists' role was the main point of this study which needed to be enhanced to meet the expectation of all parties in the hospital. Pharmaceutical care in this study could help to assess DRP, educate patients, be a benefit for patients, and develop a pharmacist role in this hospital.

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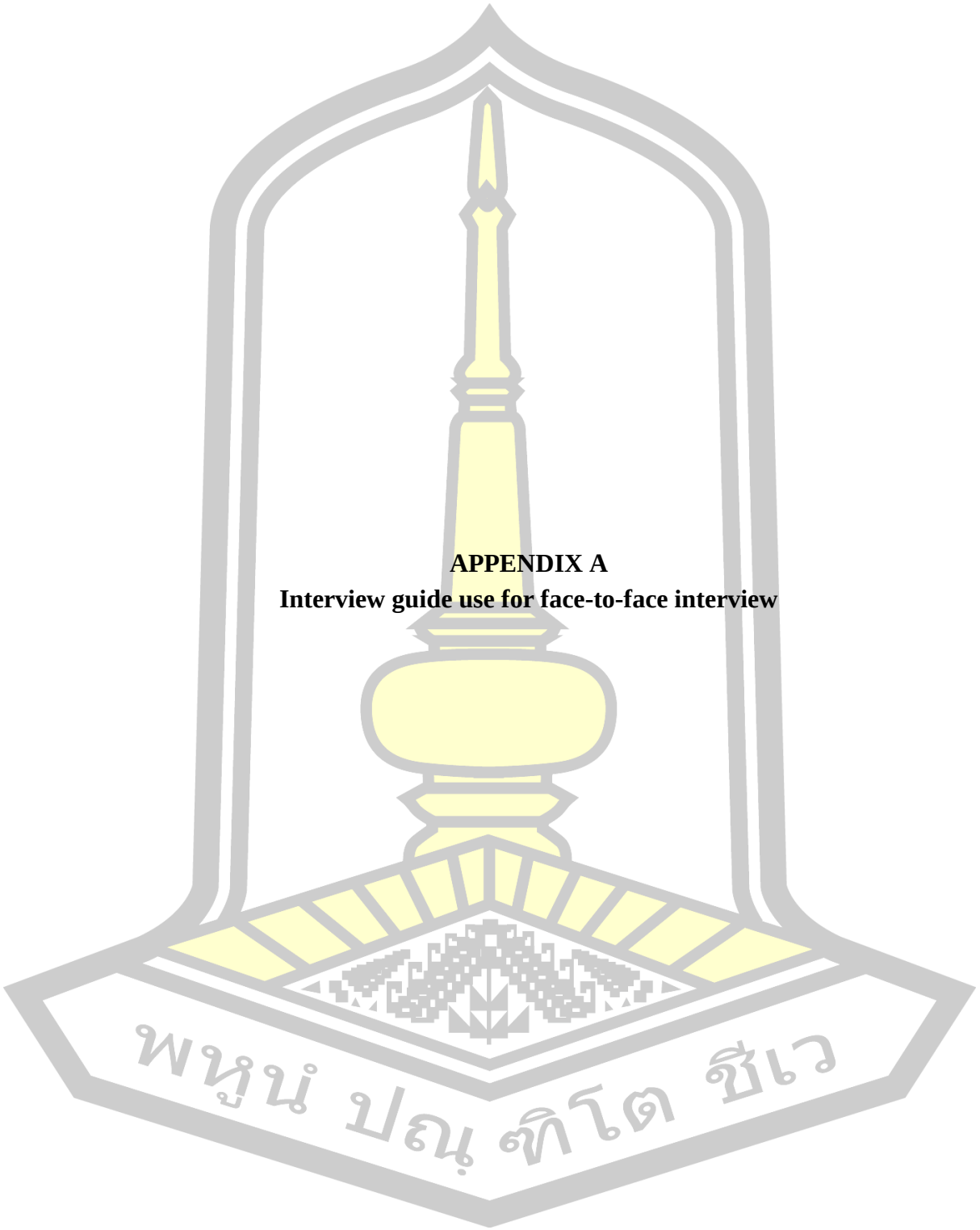
APPENDIX



APPENDIX A
Interview guide use for face-to-face interview

Interview guide use for face-to-face interview

Age…… Year of work experience on patients using anti-epileptic drug …….
Q1. Have you ever experienced the problems of patients taking the anti-epileptic drug? If yes. What are the problems?
Q2. Currently, how do patients with antiepileptic drugs receive the usual care?
Q3. Apart from the question, do you think patients taking antiepileptics drugs should receive special care from another healthcare professional? And what or how should they receive?
Q4. From question 1. What would you like to improve? Who do you think would be able to contribute to improvement?
Q5. What do you think if pharmacists-managed antiepileptics drug therapy is provided?
Q6. If all healthcare professional is involved in the care of patients taking antiepileptics drug, do you think the policy, the system, the manpower, and the budget are sufficient or not?

Additional interview guide for pharmacists is:
Q1. Have you ever advised antiepileptics drug patients? What advice do you give?
Q2. Do you think the advice you give is sufficient or not? If not, what could be the best for you to give sufficient advice to patients?

APPENDIX B

The pharmacists' roles for patient using antiepileptic drugs

The pharmacists' roles for patient using antiepileptics drug

The literature review of pharmacist-managed antiepileptics drug therapy showed the pharmacist's role for patients using antiepileptics drugs as follows:

Pharmacists' roles	Participants	Tools
Dosage adjustment	Doctor Pharmacist	Schedule for dosage adjustment
Appointment and follow-up visit	Doctor Pharmacist	Schedule for dosage adjustment
Education provision to patients	Pharmacist Nurse	Education tool
Assess compliance with the regimen	Pharmacis	pill-count and self-report
Review medications, comorbidities, and drug interactions	Pharmacis	Data collection form
Screen for side effects, seizure frequency	Doctor Pharmacis	Data collection form

APPENDIX C

The education tool by pharmacists for the patient using antiepileptic drugs

The education tool by pharmacists for patient with epilepsy using antiepileptic drugs

The following detail is an education provided by pharmacist:

1. Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.
2. Risk factors :
   - The onset of epilepsy is most common in children and older adults, but the condition can occur at any age.
   - Family history.
   - Head injuries. ...
   - Stroke and other vascular diseases. ...
   - Dementia. ...
   - Brain infections. ...
   - Seizures in childhood

3. There are many possible causes of epilepsy, including an imbalance of nerve-signaling chemicals called neurotransmitters, tumors, strokes, and brain damage from illness or injury, or some combination of these. In the majority of cases, there may be no detectable cause for epilepsy.
4. Symptoms and Signs:
   - Temporary confusion
   - A staring spell.
   - Stiff muscles.
   - Uncontrollable jerking movements of the arms and legs.
   - Loss of consciousness or awareness.
   - Psychological symptoms such as fear, anxiety or dejavu.
5. Treatment goals:
   - The most important part of controlling seizures in patients with epilepsy is compliance.
6. Here are things you can do to help someone who is having this type of seizure (caregiver):
   - Ease the person to the floor.
   - Turn the person gently onto one side. This will help the person breathe.
   - Clear the area around the person of anything hard or sharp. This can prevent injury.
   - Put something soft and flat, like a folded jacket, under his or her head.
   - Remove eyeglasses.

- Loosen ties or anything around the neck that may make it hard to breathe.
- Time the seizure. Call hospital if the seizure lasts longer than 5 minutes.

7. Side effects of antiepileptic drugs:

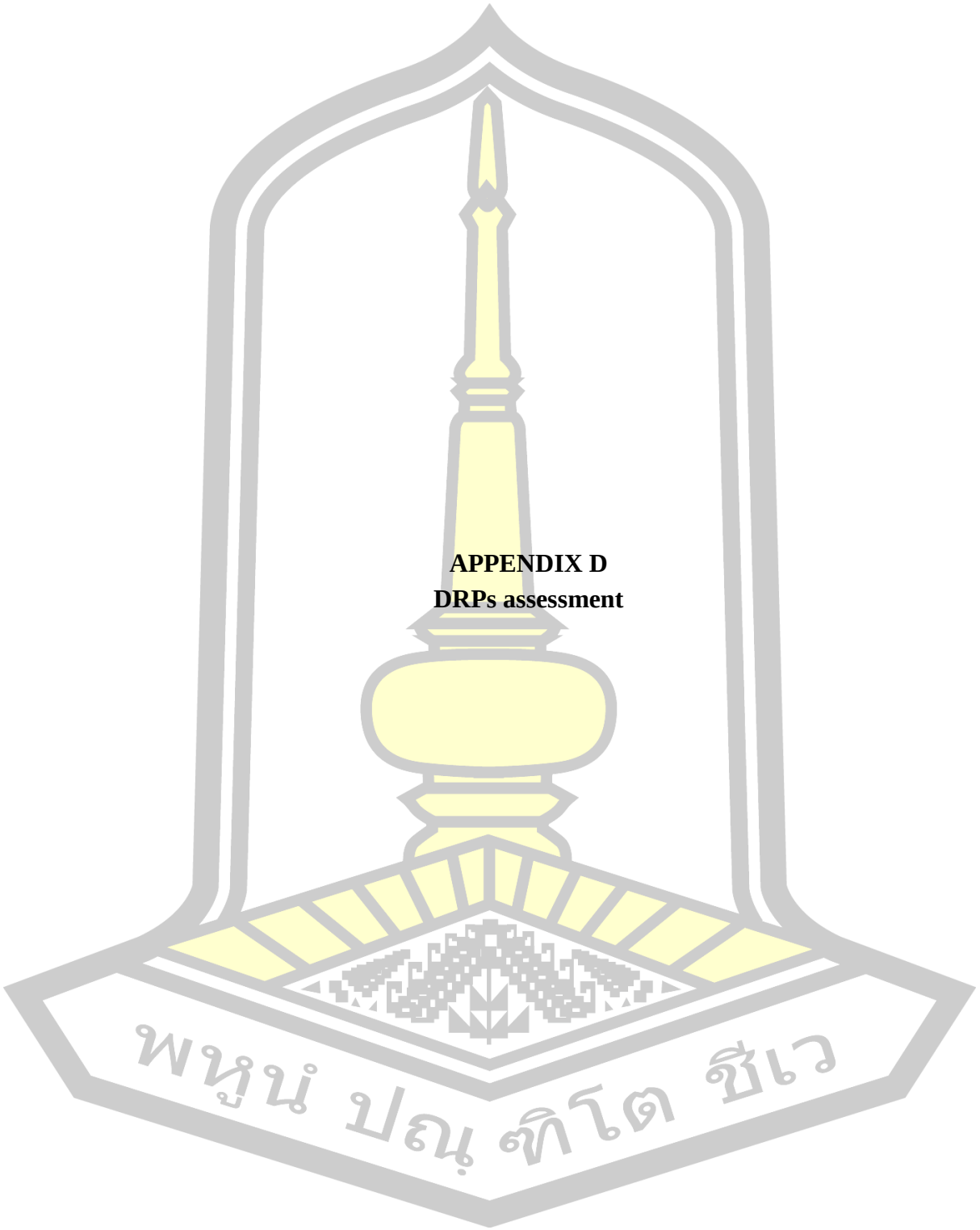
These include nausea, drowsiness, abdominal pain, dizziness, irritability, anxiety or mood changes, uncontrollable shaking (tremor), hair loss or unwanted hair growth, and swollen gums. These are usually not serious, but if rashes please contact with the doctor as it might mean you're having a serious reaction to your medicine.

8. While traveling or working abroad, carry your medications with you at all times.

9. What epilepsy should not eat: stimulants such as tea, coffee, alcohol, chocolate, sugar, sweets, soft drinks, excess salt, spices and animal proteins may trigger seizures and patient can eat pork.

10. What do people with epilepsy need to avoid:

- Do not miss doses of your medications
- Get plenty of sleep.
- Drink plenty of water.
- Eat a healthy balanced diet and do not skip meals.
- Try to reduce stress and control anxiety.
- Avoid alcohol and recreational drugs.
- Certain people with epilepsy should avoid flashing lights.



APPENDIX D
DRPs assessment

			Visit1	Visit2			Visit3		
no	sex	age	Medication		Adverse event	Management with doctors or patients		Adverse event	
2	M	26	Phenobarbital 100mg foilic acide 5 mg		allergy phenolbarbital change to new depakin 200mg bid pc	Consult with team and team agree			
5	F	31	Phenobarbital 100mg foilic acide 5 mg	Metformin/pioglitazone 500mg/15mg	DI phenol will decrease the level or effect of pioglitazone , minor/significance unknow	Consult with team and follow-up			
7	M	84	Carbamazepine200mg+ foilic acide5mg	Amlodepine 10mg	Carba will decrease the level or effect of amlodipine by hepatic/intestinal enzyme CYP3A4	Consult with team and follow-up			
11	F	32	Carbamazepine200mg+ foilic acide 5mg				Add new Phenobarbital 100mg	Phenol will decrease the level or effect of carbamazepine by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/monitor	
12	F	66	Phenobarbital100mg+foilic acide 5mg	Enarapril 20 mg					
19	F	48	Valproic acid500mg+foilic acide5mg	Enarapril 20 mg+			add new carbamazepine 200mg	Valproic acid will increase the level or effect of carbamazepine by mechanism:decreasing metabolism.usecaution/mornitor	

22	F	59	Valproic acid500mg+folic acide5mg	Amlodepine 1o mg, Deanxit, methylcobal	Carba will decrease the level or effect of amlodipine by hepatic/intestinal enzyme CYP3A4				
23	F	20	Phenobarbital100mg+folic acide5mg				Add new Cabamazepine 200mg	Phenol will decrease the level or effect of carbamazepine by affecting hepatic/intestinal enzyme CYP3A4 metabolism. Use Caution/monitor	
27	F	70	Phenobarbital100mg+folic acide5mg	simvastatin 20 mg	Phenobarbital will decrease the level or effect of simvastatin by affect hepatic/intestinal enzyme CYP3A4 metabolism. Avoid or use alternative drug.	Consult with team and follow-up			
36	F	33	Valproic acid500mg+folic acide5mg				add new cabamazepine	Valproic acid will increase the level or effect of carbamazepine by mechanism:decreasing metabolism usecaution/monitor	
38	M	38	Phenobarbital100mg+folic acide5mg				add new depakine 500mg	Valproic acid will increase the level of phenobarbital by unspecified interaction mechanism. Minor/significance Unknown.	
40	F	52	Phenobarbital100mg+fo	Tryptanol10			depakin 500 mg	Valproic acid will	

APPENDIX E
Informed consent form 1

Mahasarakham University Institutional Review Board	(Informed Consent Form)

Research title: Outcome of multidisciplinary team for epilepsy management at Setthathirat hospital in LAO PDR.

Consent day-Date ..... Month …….....
Year…….. Health cares professional's
ID:……

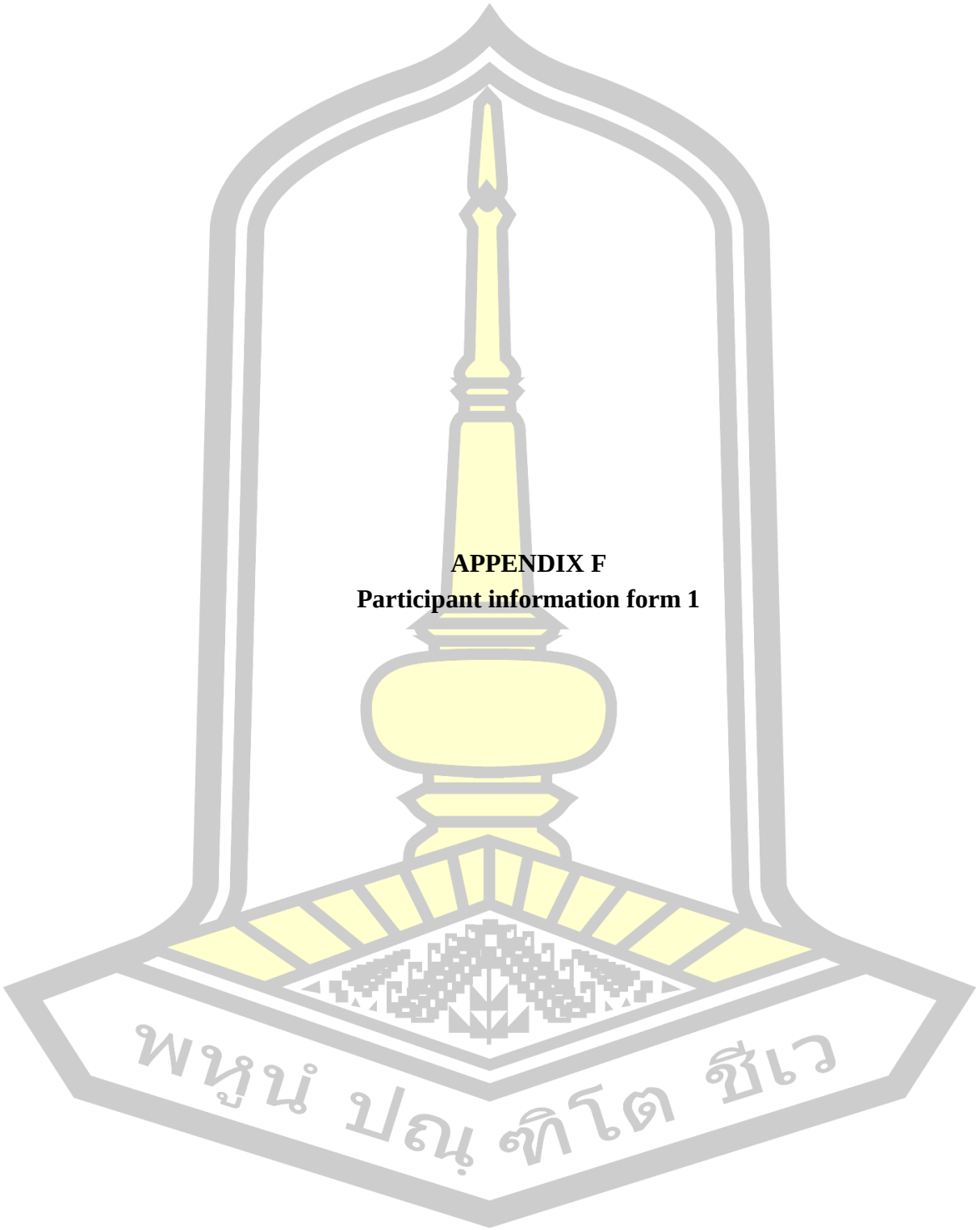
Willingness to participate in the research of outcome of multidisciplinary team for epilepsy management at Setthathirat hospital, Lao PDR. I have been informed about the source and purpose of the research, detailed steps, to be interviewed, expected benefits of research, and the risk that may arise from participating in this research. Including the prevention and corrective measures if any. Also, I had received an explanation about the question from the researcher of the research project.

I volunteered to participate in this project: If I have been interviewed incorrectly, as stated in the participant's explanation. I will be able to contact the human research ethics board at the Lao PDR National Ethics Committee for Health Research, call +856-21-250670-207 or 208.

If I have a question about the research process during the project, I will be able to contact the researcher Mrs. Saysamooth Phanouvong throughout 24 hours on-call: +856-20- 59409294.

The foregoing information has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Sign……...Contributor and consent message
(……) Date……
Sign……Researche
(Saysamooth Phanouvong) Date.....
Sign..... Witness
(……) Date.....



APPENDIX F
Participant information form 1

Participant information form 1

AF 04-10/3.0

Mahasarakham University Institutional Review Board	(Information Sheet for Research Participant)

Research projects: Outcomes of the multidisciplinary team for epilepsy management at Setthathirat hospital in LAO PDR.
Sponsor Research: Faculty of Pharmacy, Mahasarakham University
Researcher: Mrs. Saysamooth Phanouvong
Address: Master student, Faculty of Pharmacy, Mahasarakham University
Telephone: 0647052737, E-mail moothphanouvong@gmail.com
Co-Researcher 1: Assist. Prof. Dr. Peeraya Sriphong
Address: Faculty of Pharmacy, Mahasarakham University
Telephone: 089-710-5987 e-mail: peeraya.s@msu.ac.th
Co-Researcher 2: Assist. Prof. Dr. Juntip Kanjanasilp
Address: Faculty of Pharmacy, Mahasarakham University
Telephone: 089-205-1878 e-mail: Junthip.k@msu.ac.th

Dear all participation,

You are invited to participate in this research project before you decide to join or not. Please, carefully read all the text in this document or listen to the researcher to know why were you invited to participate in this project. This document may contain some unclear words, please ask the researcher to explain until you understand. To participate in this research project must be voluntary. No compulsion on who does not participate or withdrawing from this research project, it will not affect you anyhow. Please, do not sign the document until you are sure that you wish to participate in this research project.

Background and important of the research

Epilepsy is a chronic brain disorder that affects millions of people worldwide. Only 10-20% of all people living with epilepsy (PWEs) receive appropriate treatment. Pharmacotherapy is the primary choice for the treatment of epileptic disorders and antiepileptic drugs, either alone or combined with other antiepileptics. Pharmacists are important health professionals in counseling and monitoring patients with epilepsy (PWE) because they are easily accessible and know about pharmacotherapy, health education, and management of chronic diseases. There

was evidence proved that when the epilepsy was managed by the multidisciplinary team, patients produced better clinical outcome.

Research objective

The objective of the study to develop the multidisciplinary team for epilepsy management at Setthathirat hospital in LAO PDR. The aim to evaluate the outcome of the multidisciplinary team for epilepsy management, and the process of care for patients with antiepileptic drug use. To explore views of health care professionals including doctors, nurses, and pharmacists on managed Antiepileptic drugs Therapy. To conduct a quasi-experimental study to evaluate the multidisciplinary team for epilepsy management at the outpatient clinic, Setthathirath hospital.

Method related to research

After you consent to participate in this research project, a researcher will request to interview you follow the interview guides. For the individual interviews, it will be used about 20-30 minutes.

Responsibilities of the volunteers participating in the research project

To make this research successful. The researcher would like to cooperate with you to answer the questions. In case of any unusual questions that occur to you during the interview, please report to the researcher

Risks that may be received

You might be getting minimal risks such as wasting time and inconvenience. Please inform the researcher in case of your inconvenience.

The benefit from this study

You will not get any benefit from participating in this research. But the study results will be implementing the multidisciplinary team model for epilepsy management at the outpatient department. It does not guarantee that the study will improve the multidisciplinary team for epilepsy management.

The practice while participating in the research project

Please do the following:
- Please provide your information to do with the truth.
- Please inform the researcher immediately if you don't want to continue the interview.

Possible risks of participating in the research project and the responsibilities of the researche

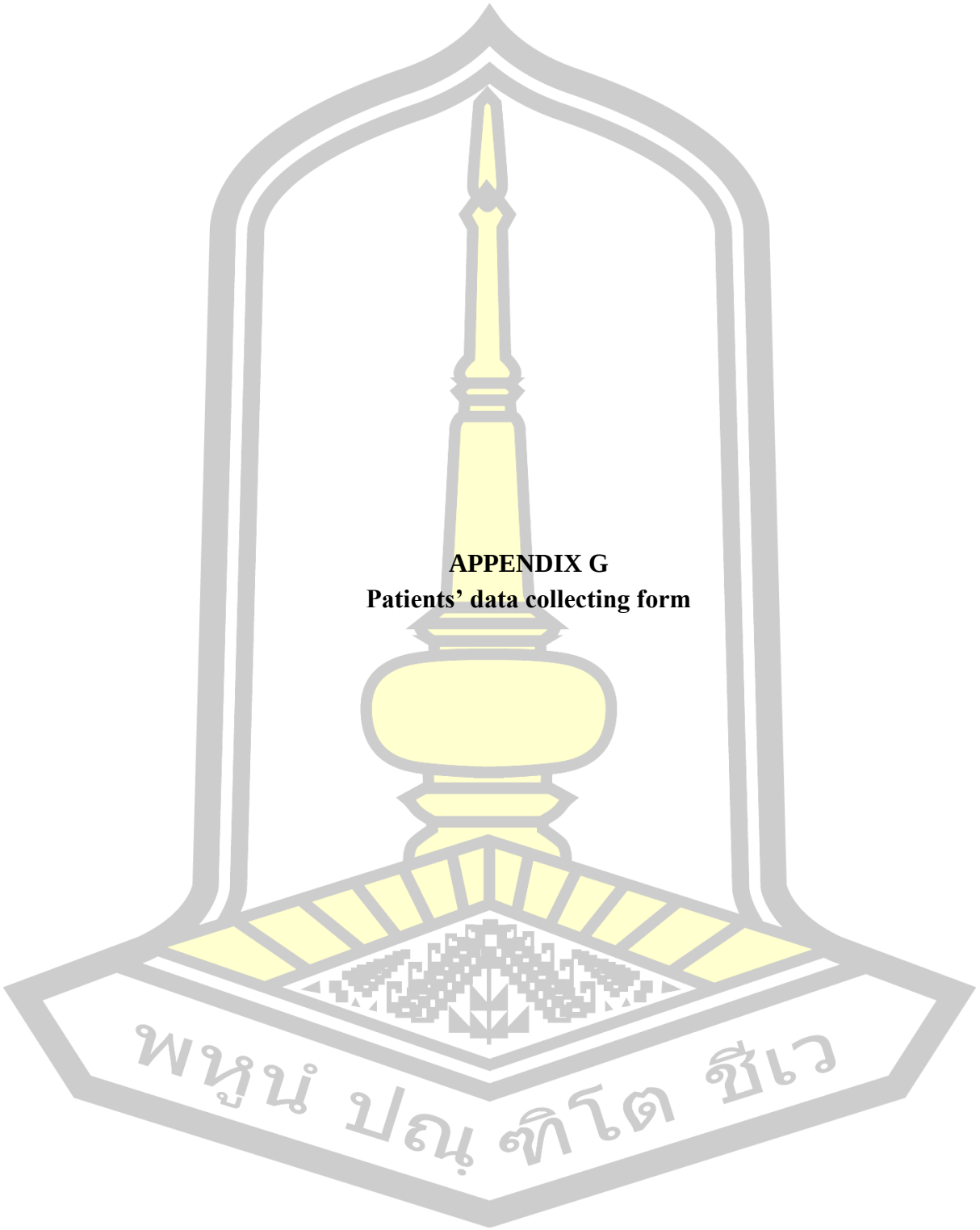
This study is an interview face to face. However, if any problems arise during the study, the participant can stop the interview immediately.

Protecting confidential information of participants.

Information that may lead to your disclosure will be covered and will not be disclosed to the public. The researcher will be stressed that all information would be kept anonymous and that the audiotaped, videotaped interviews will be stored in a locked cupboard that only the research team can access it by using the password.

If you are not protected as shown in the data explanations for the participant's information sheet in the research. You can complain at the Lao PDR National Ethics Committee for Health Research, call +856-21-250670-207 or 208.

Thank you for your cooperation



APPENDIX G
Patients' data collecting form

Patients data collection form

Patient‟s ID code: …….. Address: ……

Part 1: General information:

- Gender: □ Female □ Male
- Age: Years
- Caregiver: □ Yes □ No
- Education: □ Primary □ Secondary □ High school □ College graduate □ etc…..
- Marital status: □ Single □ Married □ Widowed □ Divorced □ etc…..
- Occupation: □ Working □ Housewife □ Student □ Retired □ Unemployed □etc……
- Residence of patient: …….
- Monthly income of patients (kip) : □ no income □ < 1.000.000 kip □ 1.000.000 -2.000.000 kip □ 2.000.000 – 5.000.000 kip □ > 5.000.000 kip □…….
- Family history of epilepsy: □ Yes □ No
- Seizure frequency: □ One per week □ One per □ etc…….
- Number of AEDs: □ One □ More than one
- Type of AEDs: □ Phenobarbital □ Phenytoin □ Valproic acid □ Carbamazepine □ etc……..
- Comorbidities: □ No □ Yes ……. …….

Medication used and comorbidities

Medication	Comorbidities	Each visit		
		Visit 1 (month 0)	Visit 2 (month 3)	visit 3 (month 6)

Part 2: Patient adherences

- Calculate adherence to medication using how to pill count (70).

% adherence:

$$= \frac{(quantity\ dispensed) - (quantity\ remaining)}{(prescribed\ number\ of\ \frac{tablets}{d})\ X\ (number\ of\ days\ between\ dispensing\ date\ and\ interview)}\ X\ 100$$

Note:

The number of drugs delivered in advance = The number of drugs taken per day – The number of days are administered orally.

- Home medication calendar and the self-report book for the patient with epilepsy. The self-report adherence was determined during the medication history.

Patient code:……

Home medication calendar to record the time that they took their antiepileptic drugs

November/2021						
Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday
10 () not taking medicine () not taking medicine on time () take medicine on time	11 () not taking medicine () not taking medicine on time () take medicine on time	12 () not taking medicine () not taking medicine on time () take medicine on time	13 () not taking medicine () not taking medicine on time () take medicine on time	14 () not taking medicine () not taking medicine on time () take medicine on time	15 () not taking medicine () not taking medicine on time () take medicine on time	16 () not taking medicine () not taking medicine on time () take medicine on time
17 () not taking medicine () not taking medicine on time () take medicine on	18 () not taking medicine () not taking medicine on time () take medicine on	19 () not taking medicine () not taking medicine on time () take medicine on	20 () not taking medicine () not taking medicine on time	21 () not taking medicine () not taking medicine on time	22 () not taking medicine () not taking medicine on time () take medicine on	23 () not taking medicine () not taking medicine on time () take medicine on

November/2021						
Wednesday	Thursday	Friday	Saturday	Sunday	Monday	Tuesday
time	time	time	() take medicine on time	() take medicine on time	time	time
24 () not taking medicine () not taking medicine on time () take medicine on time	25 () not taking medicine () not taking medicine on time () take medicine on time	26 () not taking medicine () not taking medicine on time () take medicine on time	27 () not taking medicine () not taking medicine on time () take medicine on time	28 () not taking medicine () not taking medicine on time () take medicine on time	29 () not taking medicine () not taking medicine on time () take medicine on time	30 () not taking medicine () not taking medicine on time () take medicine on time
December/2021						
1 () not taking medicine () not taking medicine on time () take medicine on time	2 () not taking medicine () not taking medicine on time () take medicine on time	3 () not taking medicine () not taking medicine on time () take medicine on time	4 () not taking medicine () not taking medicine on time () take medicine on time	5 () not taking medicine () not taking medicine on time () take medicine on time	6 () not taking medicine () not taking medicine on time () take medicine on time	7 () not taking medicine () not taking medicine on time () take medicine on time

The time that they had a seizure or unusual symptoms

Visit 1 (month 0)	
The date and the time	Had a seizure or unusual symptoms
Visit 2 (month 3)	
The date and the time	Had a seizure or unusual symptoms
Visit 3 (month 6)	
The date and the time	Had a seizure or unusual symptoms

	Visit 1(month 0)	visit 2(month 3)	visit 3(month 6)
% adherence			

Part 3: Seizure-frequency

	Visit 1 (month 0)	visit 2 (month 3)	visit 3(month 6
Number of Seizure-frequency			

Part 4: Patients' quality of life (for visit 1 month 0)

These questions are about how you have been FEELING during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling							
How much of the time during the past 4 weeks… (Circle one number on each line							
No		All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
		1	2	3	4	5	6
1	Did you have a lot of energy?						
2	Have you felt downhearted and low?						
		A great deal	A lot	Somewhat	Only a little	Not at all	
		1	2	3	4	5	
3	Driving (or other transport)						
		Not at all bothersome	A little	Somewhat	A lot	Extremely bothersome	
		1	2	3	4	5	
4	How much do your work limitations bother you?						
5	How much do your						

	social limitations bother you?						
6	How much do your memory difficulties bother you?						
7	How much do physical effects of antiepileptic drugs bother you?						
8	How much do psychological effects of antiepileptic drugs bother you?						
		Very afraid	Somewhat afraid	Not very afraid	Not afraid at all		
		1	2	3	4		
9	How afraid are you of having a fit during the next 4 weeks?						
		Very good: could hardly have been better	Pretty good	Good & bad about equa	Pretty bad	Very bad: could hardly have been worse	
		1	2	3	4	5	
10	How has your quality of life been during the past 4 weeks (that is, how have things been going for you)						

Part 4: Patients' quality of life (visit 3 month 6)

These questions are about how you have been FEELING during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling							
How much of the time during the past 4 weeks… (Circle one number on each line							
No		All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
		1	2	3	4	5	6
1	Did you have a lot of energy?						
2	Have you felt downhearted and low?						
		A great deal	A lot	Somewhat	Only a little	Not at all	
		1	2	3	4	5	
3	Driving (or other transport)						
		Not at all bothersome	A little	Somewhat	A lot	Extremely bothersome	
		1	2	3	4	5	
4	How much do your work limitations bother you?						
5	How much do your social limitations bother you?						
6	How much do your memory difficulties bother you?						
7	How much do physical effects of antiepileptic drugs bother you?						
8	How much do psychological effects of antiepileptic drugs bother you?						

		Very afraid	Somewhat afraid	Not very afraid	Not afraid at all		
		1	2	3	4		
9	How afraid are you of having a fit during the next 4 weeks?						
		Very good: could hardly have been better	Pretty good	Good & bad about equa	Pretty bad	Very bad: could hardly have been worse	
		1	2	3	4	5	
10	How has your quality of life been during the past 4 weeks (that is, how have things been going for you)						

Part 5: DRPs assessment form

ID	DRPs	Yes or No	Management	Result of management
Visit 1 (month 0)				
1	Drug interaction			
2	Improper drug selection			
3	Adverse reactions: side effect			
visit 2 (month 3)				
1	Drug interaction			

ID	DRPs	Yes or No	Management	Result of management
2	Improper drug selection			
3	Adverse reactions: side effect			
visit 3 (month 6)				
1	Drug interaction			
2	Improper drug selection			
3	Adverse reactions: side effect			

Part 6: Question for patients‟ knowledge assessment (for visit 1month 0)

Patient‟s ID code:……

No	Questions	Visit 1 (month 0)		Visit 2 (month 3)		Visit 3 (month 6)	
		Yes	No	Yes	No	Yes	No
1	What do you think the cause of a seizure is? (Check all that you think apply) 1. [ ] an abnormal electrical discharge in the brain 2. [ ] demonic possession 3. divine punishment 4. an abnormal movement						
2	What do you think causes epilepsy? (Check all that you think apply) 1. an evil spirit 2. a head injury 3. brain tumor 4. divine punishment for reneging on a vow 5. sleep deprivation 6. alcohol withdrawal or heavy drinking 7. stroke 8. genetic disease 9. high fever 10. eating pork						
3	What types of seizures exist? (Check all that you think apply) 1. physical stiffness followed by jerking movements (tonic-clonic seizure) 2. unusual sensations or abnormal jerking with preserved awareness (simple partial seizure) 3. lost awareness and physical immobility, repetitive involuntary movements (complex partial seizure) 4. loss of muscle strength and tone: the person collapses (atonic seizure) 5. staring spell, sudden mental						

No	Questions	Visit 1 (month 0)		Visit 2 (month 3)		Visit 3 (month 6)	
		Yes	No	Yes	No	Yes	No
	absence, loss of awareness (absence seizure)						
4	Do you think epilepsy can be cured? 1. Yes 2. No						
5	How often should anti-epileptic drugs be taken? 1 for life 2 2-5 years 3 only at the full moon 4 only during an episode 5 for 3-6 months						
6	What limitations do persons with epilepsy face? (Check all that you think apply) 1. not allowed to drive a motor vehicle 2. no sexual intercourse 3. cannot get married 4. should not work with machinery 5. cannot get pregnant 6. abruptly stop anti -epileptic drugs during pregnancy 7. not able to lactate 8. should not eat pork 9. must quit work 10. should not drink alcoholic beverages						
7	What should be done during a seizure? (Check all that you think apply) 1. place the person in a semi -prone position to prevent choking 2. place something in the mouth to prevent biting the tongue 3. administer an anti -epileptic drug during the episode 4. restrain the person and perform chest compressions (CPR) 5. take actions to prevent injury						

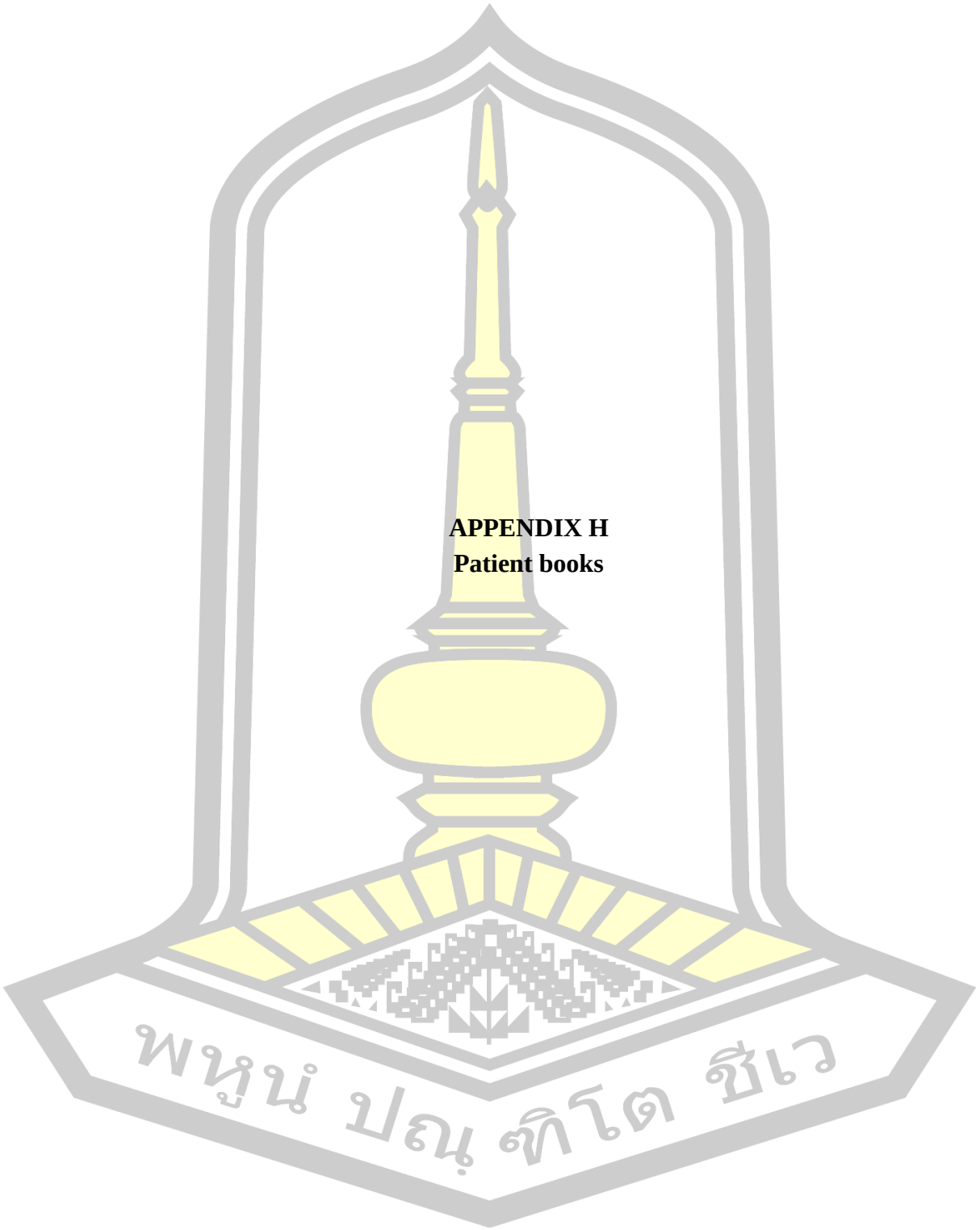
No	Questions	Visit 1 (month 0)		Visit 2 (month 3)		Visit 3 (month 6)	
		Yes	No	Yes	No	Yes	No
	during the episode						
8	What do you think which the adverse reactions related to phenobarbital but it will get better in 2 -3 weeks. : (Check all that you think to apply) 1. sedation 2. nystagmus 3. dizziness 4. ataxia 5. mild drowsiness						
9	What do you think which the adverse reactions related to carbamazepine but it will get better in the first few weeks : (Check all that you think to apply) 1. dizziness 2. drowsiness 3. anorexia 4. nausea 5. urticaria 6. exfoliative dermatitis						
10	What do you think which the adverse reactions related to valproic acid but it will get better in 2 -3 weeks. : (Check all that you think to apply) 1. gastrointestinal tract 2. weight gain (use long term) 3. anorexia 4. nausea 5. vomiting 6. alopecia (use long term)						
11	What do you think which the adverse reactions related to phenytoin acid but it will get better in 2 -3 weeks. 1. nystagmus 2. dizzniess 3. sedation 4. fatique 5. behavior change 6. ataxia						

Part 6: Question for patients' knowledge assessment visit 3 (month 6)

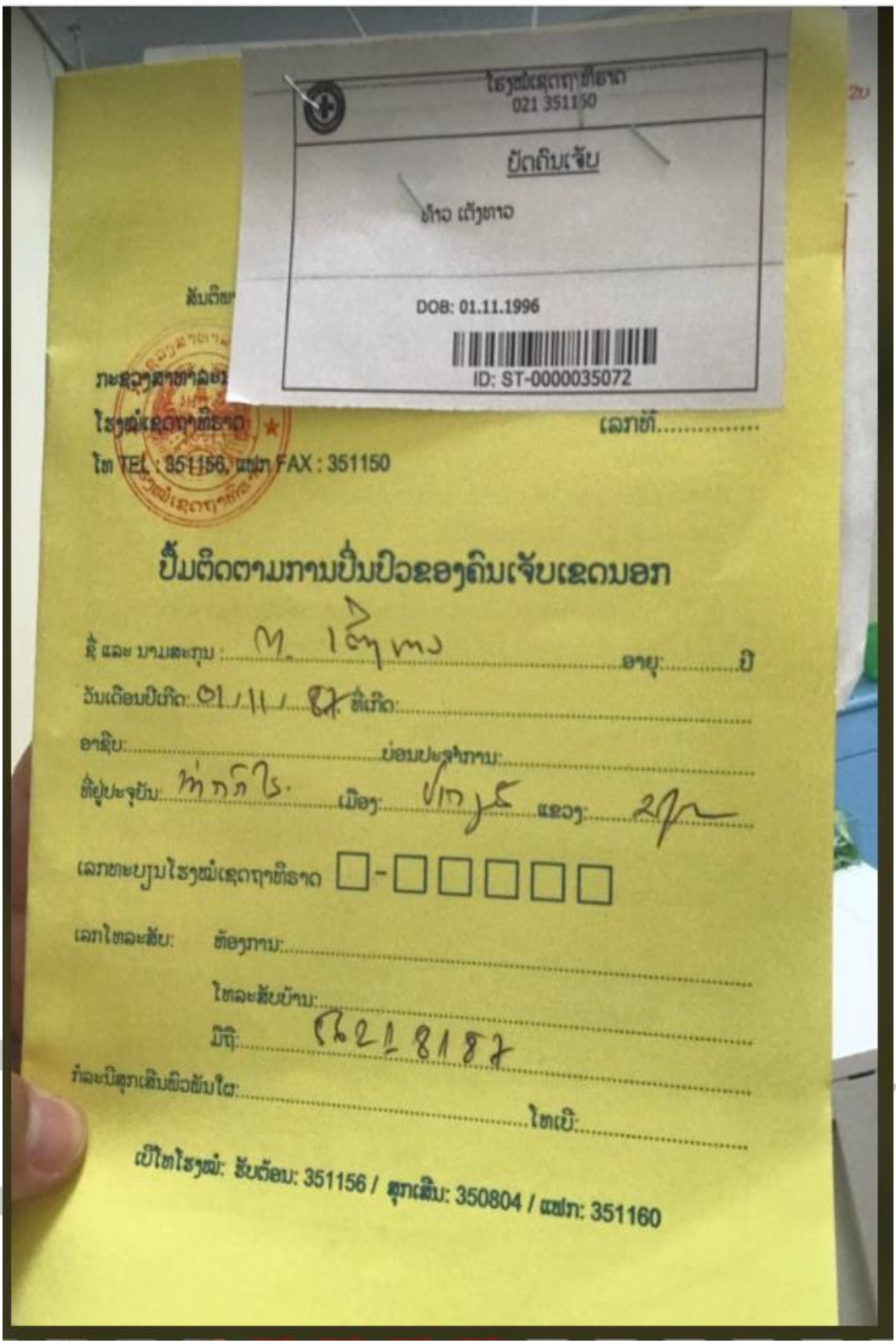
No	Questions	Visit 1 (month 0)		2 visit 2(month 3)		visit 3(month 6)	
		Yes	No	Yes	No	Yes	No
1	What do you think the cause of a seizure is? (Check all that you think apply) 1. an abnormal electrical discharge in the brain 2. demonic possession 3. divine punishment 4. an abnormal movement						
2	What do you think causes epilepsy? (Check all that you think apply) 1. an evil spirit 2. a head injury 3. brain tumor 4. divine punishment for reneging on a vow 5. sleep deprivation 6. alcohol withdrawal or heavy drinking 7. stroke 8. genetic disease 9. high fever 10. eating pork						
3	What types of seizures exist? (Check all that you think apply) 1. physical stiffness followed by jerking movements (tonic-clonic seizure) 2. unusual sensations or abnormal jerking with preserved awareness (simple partial seizure) 3. lost awareness and physical immobility, repetitive involuntary movements (complex partial seizure) 4. loss of muscle strength and tone: the person collapses (atonic seizure) 5. staring spell, sudden mental						

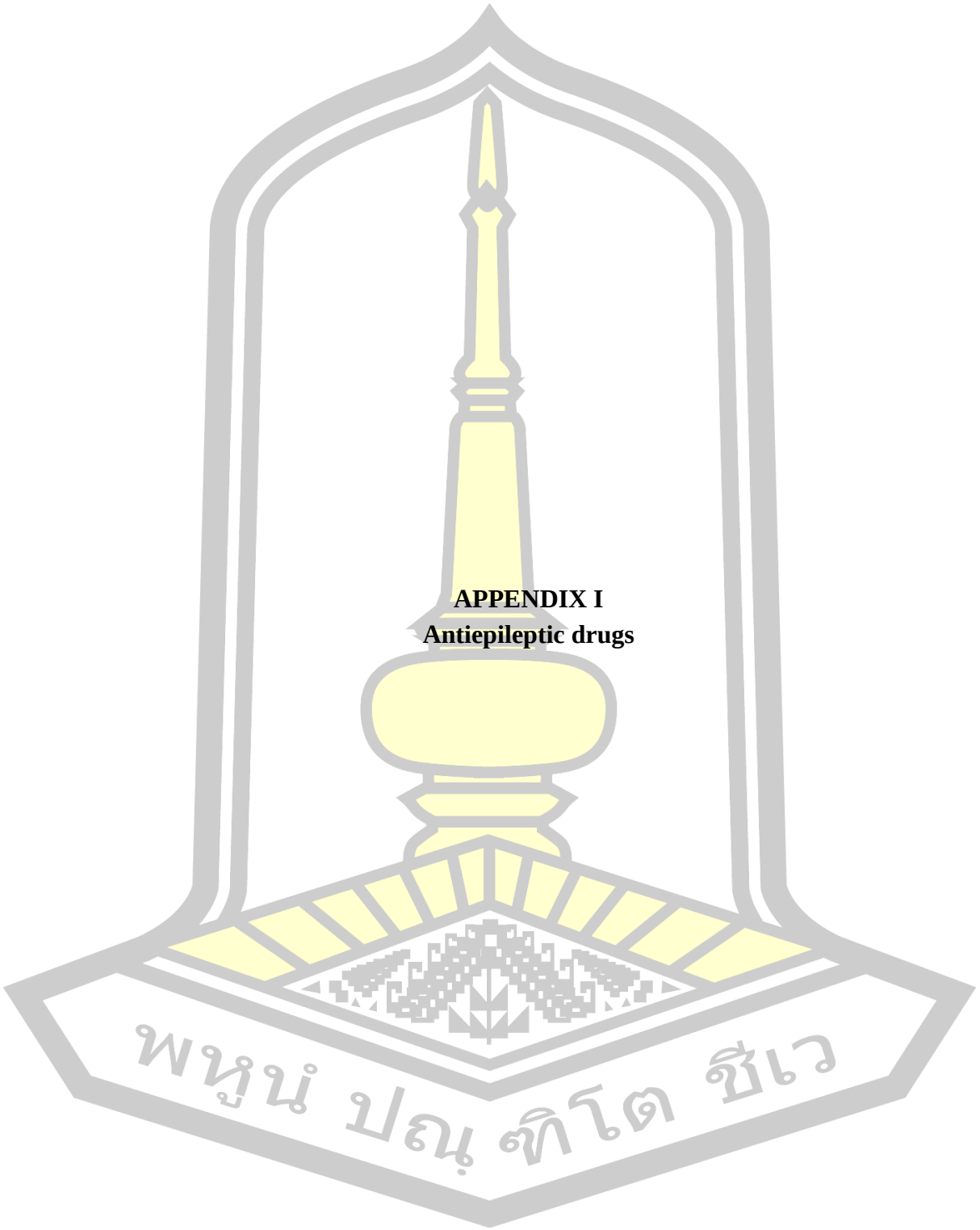
No	Questions	Visit 1 (month 0)		2 visit 2(month 3)		visit 3(month 6)	
		Yes	No	Yes	No	Yes	No
	absence, loss of awareness (absence seizure)						
4	Do you think epilepsy can be cured? 1. Yes 2. No						
5	1. How often should anti-epileptic drugs be taken? 2. for life 2-5 years 3. only at the full moon 4. only during an episode 5. for 3-6 months						
6	What limitations do persons with epilepsy face? (Check all that you think apply) 1. not allowed to drive a motor vehicle 2. no sexual intercourse 3. cannot get married 4. should not work with machinery 5. cannot get pregnant 6. abruptly stop anti -epileptic drugs during pregnancy 7. not able to lactate 8. should not eat pork 9. Must quit work 10. Should not drink alcoholic beverages						
7	What should be done during a seizure? (Check all that you think apply) 1. place the person in a semi -prone position to prevent choking 2. place something in the mouth to prevent biting the tongue 3. administer an anti -epileptic drug during the episode 4. restrain the person and perform chest compressions (CPR) 5. take actions to prevent injury during the episode						

No	Questions	Visit 1 (month 0)		2 visit 2(month 3)		visit 3(month 6)	
		Yes	No	Yes	No	Yes	No
8	What do you think which the adverse reactions related to phenobarbital but it will get better in 2 -3 weeks: (Check all that you think to apply) 1. sedation 2. nystagmus 3. dizziness 4. ataxia 5. mild drowsiness						
9	What do you think which the adverse reactions related to carbamazepine but it will get better in the first few weeks: (Check all that you think to apply) 1. dizziness 2. drowsiness 3. anorexia 4. nausea 5. urticaria 6. exfoliative dermatitis						
10	What do you think which the adverse reactions related to valproic acid but it will get better in 2 -3 weeks. : (Check all that you think to apply) 1. gastrointestinal tract 2. weight gain (use long term) 3. anorexia 4. nausea 5. vomiting 6. alopecia (use long term)						
11	What do you think which the adverse reactions related to valproic acid but it will get better in 2 -3 weeks. 1. nystagmus 2. dizzniess 3. sedation 4. fatique 5. behavior change 6. ataxia						

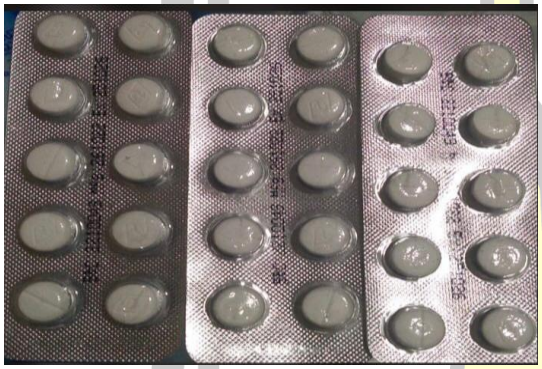


APPENDIX H
Patient books


ໂຮງໝໍເຊດຖາທິຣາດ
021 351150
ບັດຄົນເຈັບ
ທ້າວ ເຕັງຫາວ
DOB: 01.11.1996
ID: ST-0000035072
ໂຮງໝໍເຊດຖາທິຣາດ
ໂທ TEL : 351156, ແຟກ FAX : 351150
ເລກທີ.....
ປຶ້ມຕິດຕາມການປິ່ນປົວຂອງຄົນເຈັບເຂດນອກ
ຊື່ ແລະ ນາມສະກຸນ : ..... ອາຍຸ: ..... ປີ
ວັນເດືອນປີເກີດ: ..... ທີ່ເກີດ: .....
ອາຊີບ: ..... ບ່ອນປະຈຳການ: .....
ທີ່ຢູ່ປະຈຸບັນ: ..... ເມືອງ: ..... ແຂວງ: .....
ເລກທະບຽນໂຮງໝໍເຊດຖາທິຣາດ □-□□□□□
ເລກໂທລະສັບ: ຫ້ອງການ: .....
ໂທລະສັບບ້ານ: .....
ມື້ຖື: .....
ກໍລະນີສຸກເສີນພິວພັນໃສ: ..... ໂທເບີ: .....
ເບີໂທໂຮງໝໍ: ຮັບຕ້ອນ: 351156 / ສຸກເສີນ: 350804 / ແຟກ: 351160



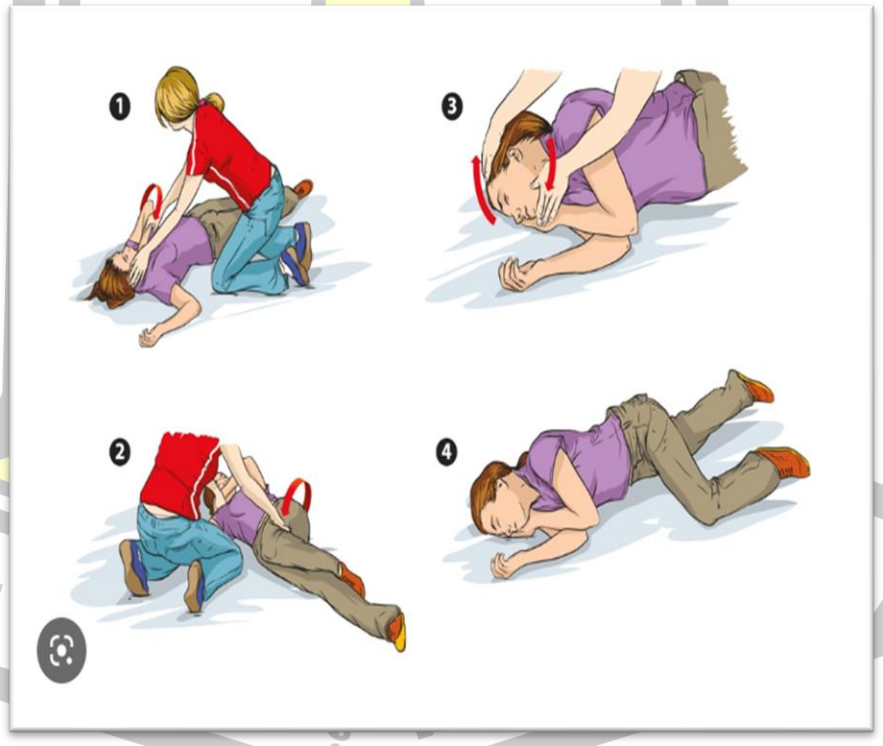
APPENDIX I
Antiepileptic drugs

Antiepileptic drugs	
  	Phenobarbital 100mg
 	(Pantol) Cabamazepine 200 mg
 	(Depakine) Valproic acid 200 mg Valproic acid 500 mg

Antiepileptic drugs	
 	(Dilantin) Phenytoin 100 mg

APPENDIX J
The education tool by pharmacists for patient with epilepsy


Know what to do
and what NOT to do


1
3
2
4

ພະຍາດລົມຊັກທີ່ຄວນຮູ້

1. ພະຍາດລົມຊັກແມ່ນຫັຍງ ?

ພະຍາດລົມຊັກຄືພະຍາດທີ່ເກີດຈາກຄວາມຜິດປົກກະຕິຂອງກະແສໄຟຟ້າໃນສະໝອງ ສິ່ງຜົນໃຫ້ຄົນເຈັບມີອາການຜິດປົກະຕິໄດ້ຫລາຍແບບເຊັ່ນ: ການຊັກເກັ່ງກະຕຸກທັ້ງໂຕ ແລະ ຫມົດສະຕິ ຫລື ທີ່ຮູ້ຈັກກັນທົ່ວໄປວ່າ ລົມຊັກບ້າໝູ. ການຊັກເກັ່ງຫລືກະຕຸກສະເພາະສ່ວນຂອງຮ່າງກາຍ ເຊັ່ນ ແຂນ ຂາ ໃບຫນ້າ ການນັ່ງນິ້ງນິ້ງ ເບິ່ລອຍ ເປັນໄລຍະ ຮ່ວມທັ້ງພຶດຕິກຳແປກແປກ ອາການດັ່ງກ່າວຈະເປັນເປັນ ຫາຍຫາຍ ໃນໄລຍະເວລາອັນສັ້ນສັ້ນ ເຊັ່ນ 1–3 ນາທີ ແລະມີອາການຊ່ຳຄ້າຍອາການເດີມ.

2. ພະຍາດລົມຊັກ ເກີດມາຈາກສາເຫດຫຍັງ?

ສາເຫດຂອງພະຍາດລົມຊັກທີ່ພົບຫລາຍໃນແຕ່ລະຊ່ວງອາຍຸແຕກຕ່າງກັນເຊັ່ນ: ທຳອິດເກີດສາເຫດຈາກພະອະຂາດອົກຊີເຈນ, ການຕິດເຊື້ອລະຫວ່າງການເກີພາ, ເດັກນ້ອຍເກີດຈາກພາວະຕິດເຊື້ອໃນສະໝອງ, ໄຂ້ສູງ, ໄວລຸ້ນເກີດຈາກອຸປະຕິເຫດຕໍ່ຫົວ ເຊັ່ນ: ລົດຈັກລົ້ມ ຫລື ບໍ່ຮູ້ສາເຫດ. ໄວຫນຸ່ມ ກາງຄົນເກີດຈາກພະອະເນື້ອງອກສະໝອງ, ໄວສູງອາຍຸເກີດຈາກພະຍາດອຳມະພາດຫລອດເລືອດສະໝອງ ແລະ ເນື້ອງອກສະໝອງ.

3. ພະຍາດລົມຊັກຮັກສາຫາຍ ຫລື ບໍ ?

ພະຍາດລົມຊັກເປັນພະຍາດທີ່ມີການປິ່ງມະຕິພະຍາດ ທີ່ດີພະຍາດຫນຶ່ງ ເຊິ່ງ 2 ໃນ 3 ຂອງຄົນເຈັບສາມາດຮັກສາໃຫ້ຫາຍຂາດໄດ້ . ຄົນເຈັບທີ່ເຫລືອເຄິ່ງຫນຶ່ງສາມາດຮັກສາໃຫ້ບໍ່ມີອາການຊັກໄດ້ ແຕ່ຕ້ອງກິນຢາກັນຊັກຢ່າງຕໍ່ເນື່ອງ ມີພຽງສ່ວນຫນ້ອຍເທົ່ານັ້ນທີ່ບໍ່ສາມາດຢຸດອາການຊັກໄດ້ດ້ວຍຢາ ແລະ ຕ້ອງຮັກສາດ້ວຍການຜ່າຕັດ.

4. **ພະຍາດລົມຊັກມີການປິ່ນປົວຈັກວິທີ ?**

ການປິ່ນປົວພະຍາດລົມຊັກມີ 2 ວິທີ ຫລັກ:

- ວິທີທີ່ 1 ຄື: ການກິນຢາກັນຊັກເຊິ່ງຄົນເຈັບຫລາຍກ່ວາ 95% ກິນຢາກັນຊັກ.
- ວິທີທີ່ 2 ຄື: ການຜ່າຕັດສະໝອງໃນກໍລະນີຄົນເຈັບມີສາເຫດການຊັກຈາກສະໝອງມີຄວາມມີຄວາມຜິດປົກກະຕິເຊັ່ນ:ພະຍາດເນື້ອງອກສະໝອງ ເລືອດອອກໃນສະໝອງເປັນຕົ້ນ ຫລື ໃນກໍລະນີຄົນເຈັບບໍ່ຕອບສະໜອງຕໍ່ຢາກັນຊັກ ການຜ່າຕັດກໍ່ເປັນວິທີໜຶ່ງທີ່ໄດ້ຜົນດີ. ນອກຈາກນີ້ຍັງມີວິທີການກະຕຸ້ນເສັ້ນປະສາດ ເວກັດຣ ເຊິ່ງເປັນວິທີທີ່ຍັງບໍ່ທັນນິຍົມກັນໃຊ້ຢ່າງກວ້າງຂວາງ ເພາະໄດ້ຜົນບໍ່ຄ່ອຍດີ ແລະ ມີຄ່າໃຊ້ຈ່າຍຢ່າງກວ້າງຂວາງ.

5. **ຕ້ອງກິນຢາກັນຊັກດົນປານໃດ ?**

ໂດຍທົ່ວໄປຕ້ອງກິນຢາກັນຊັກຕິດຕໍ່ກັນດົນປະມານ 2 ປີ ນັບຈາກຄວບຄຸມອາການຊັກໄດ້ ຫລັງຈາກນັ້ນຈະຄ່ອຍຄ່ອຍ ຫລຸດຜ່ອນຂະໜາດຢາລົງຢ່າງຊ້າຊ້າ ພາຍໃນໄລຍະເວລາ 6 – 12 ເດືອນ. ສະຫລຸບແລ້ວຄົນເຈັບຕ້ອງກິນຢາກັນຊັກດົນປະມານ 2 ປີ ເຄິ່ງ ຫາ 3 ປີ.

6. **ຈຳເປັນຕ້ອງກິນຢາກັນຊັກທຸກຄົນ ຫລືບໍ່?**

ຄົນເຈັບລົມຊັກບໍ່ຈຳເປັນຕ້ອງກິນຢາກັນຊັກທຸກຄົນ ເຊັ່ນ ໃນຄົນເຈັບທີ່ມີອາການຊັກພຽງຄັ້ງດຽວ. ການຊັກຫລາຍໆ ຄັ້ງ (ໜ້ອຍກວ່າ 1 ຄັ້ງຕໍ່ປີ) ຫລືໃນຄົນເຈັບທີ່ມີອາການຊັກຊະນິດບໍ່ຮຸນແຮງ ແລະ ເປັນສະເພາະຊ່ວງທີ່ນອນຫລັບເທົ່ານັ້ນຄົນເຈັບເຫລົ່ານີ້ອາດບໍ່ຈຳເປັນຕ້ອງກິນຢາກັນຊັກ. ຄົນເຈັບທີ່ມີອາການຊັກຕັ້ງແຕ່ 2 ຄັ້ງ ຂຶ້ນໄປ ແລະ ເປັນການຊັກທັງໃຕ ໜ້ົດສະຕິ ມັກຈຳເປັນຕ້ອງກິນຢາກັນຊັກ. ແຕ່ຢ່າງໃດກໍຕາມຄວາມຈຳເປັນຕ້ອງກິນຢາກັນຊັກ ຫລືບໍ່ ຕ້ອງພິຈາລະນາລາຍລະອຽດກ່ຽວກັບ ຂໍ້ດີ – ຂໍ້ເສຍ ຂອງການກິນຢາກັນຊັກ ຫລື ບໍ່ກິນຢາໃນຄົນເຈັບແຕ່ລະກໍລະນີໄປ.

7. **ຄຳຖາມທີ່ 7 ຄົນພະຍາດລົມຊັກ ມີໂອກາດເສຍຊີວິດ ສູງກວ່າຄົນທົ່ວໄປ ຫລື ບໍ່?**

ໂດຍທົ່ວໄປແລ້ວໂອກາດເສຍຊີວິດໃນຄົນເຈັບ ບໍ່ໄດ້ແຕກຕ່າງຈາກຄົນທົ່ວໄປ. ໂອກາດການເສຍຊີວິດຂຶ້ນຢູ່ກັບສາເຫດຂອງພະຍາດລົມຊັກຫລາຍ

ກວ່າ ເຊັ່ນ ພະຍາດເນື້ອງອກສະໝອງ, ພະຍາດ ອຳມະພາດເສັ້ນເລືອດສະໝອງ. ຢ່າງໃດກໍຕາມຄົນ ເຈັບອາດເສຍຊີວິດຈາກອຸບັດຕິເຫດທີ່ເກີດຂຶ້ນຈາກ ການຊັກ ເຊັ່ນ: ຊັກຄະນະຂັບລົດ ສິ່ງຜົນໃຫ້ເກີດ ອຸບັດຕິເຫດ. ນອກຈາກນີ້ໃນຕ່າງປະເທດມີລາຍ ງານກ່ຽວກັບການເສຍຊີວິດກະທັນຫັນໃນຄົນເຈັບ ລົມຊັກ.

8. **<u>ການປະຕິບັດໃຕ້ທີ່ເໝາະສົມເປັນແນວໃດ ?</u>**

ການປະຕິບັດໃຕ້ເປັນສິ່ງທີ່ສຳຄັນໃນການຮັກສາ ພະຍາດລົມຊັກ ຄົນເຈັບຕ້ອງກິນຢາກັນຊັກຢ່າງ ສະໝ່ຳສະເໝີ ຫ້າມຢຸດຢາກັນຊັກເອງທັນທີ ຄວນຫ້າມ ຄວນຢຸດ ຫລື ຫລຸດຜ່ອນຄວາມທີ່ຂອງ ການຂັບລົດເພາະອາດຈະເກີດອຸບັດຕິເຫດໄດ້ຖ້າ ເກີດອາການຊັກຄະນະຂັບລົດ. ກໍລະນີເຈັບໄຂ້ຕ້ອ ໄປພົບທ່ານໝໍ ຕ້ອງແຈ້ງໃຫ້ທ່ານໝໍຮູ້ວ່າ ເປັນ ພະຍາດລົມຊັກ ແລະ ກິນຢາກັນຊັກຊະນິດໃດ. ບໍ່ ຄວນດື່ມເຫລົ້າ, ບໍ່ຄວນນອນເດິກ ພັກຜ່ອນໃຫ້ ພຽງພໍ. ຫລີກລ້ຽງການຫລິ້ນກິລາທີ່ບໍ່ຕ້ອງປະທະ ກັນ ຮຸນແຮງ ຫລື ກິລາທາງນ້ຳ. ການປະຕິບັດໃຕ້ທີ່ ດີ ຈະນຳໄປສູ່ການຄອບຄຸມອາການຊັກທີ່ດີ.

9. **<u>ອາຫານທີ່ຫ້າມກິນໃນຄົນເຈັບລົມຊັກມີຫລືບໍ່ ?</u>**

ຄົນເຈັບພະຍາດລົມຊັກສາມາດກິນອາຫານໄດ້ທຸກ ຊະນິດທີ່ຖືກສຸຂະອານາໄມທາງໂພສະນາການ, ບໍ່ມີ ອາຫານຕ້ອງຫ້າມໃດໆ ຮ່ວມທັງຊີ້ນໝູກໍສາມາດ ກິນໄດ້.

10. **<u>ຄົນເຈັບຍິງ ທີ່ເປັນພະຍາດລົມຊັກ ສາມາດແຕ່ງງານ ແລະ ມີລູກໄດ້ ຫລື ບໍ່?</u>**

ຜູ້ຍິງທີ່ເປັນພະຍາດລົມຊັກ ສາມາດແຕ່ງງານ ແລະ ມີລູກໄດ້ຄືກັບຄົນທົ່ວໄປ ພຽງແຕ່ມີຂໍ້ແນະນຳວ່າຖ້າ ຕ້ອງການມີລູກນັ້ນຕ້ອງຄອບຄຸມການຊັກໄດ້ເປັນ ຢ່າງດີ ແລະ ຢຸດຢາກັນຊັກໄດ້ແລ້ວຈະດີທີ່ສຸດ. ແຕ່ ຖ້າຕ້ອງກິນຢາກັນຊັກກໍຄວນເປັນໃນຂະໜາດຢາ ຕ່ຳໆ ເພື່ອຫລຸດໂອກາດການເກີດຄວາມຜິດປົກະຕິ ຂອງເດັກໃນທ້ອງ.

11. **<u>ການກິນຢາກັນຊັກໃຫ້ຖືກຕ້ອງຄວນເຮັດແນວໃດ?</u>**

1. ຕ້ອງກິນຢາສະໝ່ຳສະເໝີຢ່າງຕໍ່ເນື່ອງ.
2. ບໍ່ຄວນຢຸດຢາກັນຊັກໂດຍທ່ານໝໍບໍ່ໄດ້ສັ່ງ ໃຫ້ຢຸດຢາ ຍົກເວັ້ນເມື່ອມີອາການແພ້ຢາ ເກີດຂຶ້ນ.
3. ບໍ່ຄວນປະສົມຢາກັນຊັກ ກັບອາຫານ ຫລື ນ້ຳ ຍົກເວັ້ນຊະນິດທີ່ທ່ານໝໍແນະນຳເທົ່າ ນັ້ນ ເນື່ອງຈາກຢາກັນຊັກບາງຊະນິດອາດ ດູດຊຶມບໍ່ໄດ້ດີ ຖ້າກິນພ້ອມອາຫານ ຫລື ນ້ຳ.

4. ຖ້າລືມກິນຢາໃນມື້ໃດມື້ຫນຶ່ງ ຄວນຝ້າວກິນທັນທີ ທີ່ຄິດອອກໄດ້ ແລ້ວກິນມື້ຕໍ່ໄປຕາມປົກະຕິ.
5. ກໍລະນີກິນຢາກັນຊັກແລ້ວຮາກ ຖ້າຮາກພາຍໃນເຄິ່ງຊົ່ວໂມງຫລັງກິນຢາ ໃຫ້ກິນຢາຊ້ຳໃນຂະຫນາດເກົ່າໄດ້ ແຕ່ຖ້າຮາກ ຫລັງກິນດົນເກີນກວ່າ ເຄິ່ງຊົ່ວໂມງບໍ່ຕ້ອງກິນຢາຊ້ຳ ໃຫ້ກິນຢາມື້ຕໍ່ໄປຕາມປົກະຕິ.
6. ຄວນພົບທ່ານຫມໍຢ່າງສະຫມ່ຳສະເຫມີ ເພື່ອຕິດຕາມຜົນການຮັກສາ ແລະ ຜົນຂ້າງຄຽງຂອງຢາທີ່ອາດຈະເກີດຂຶ້ນ. ບາງຄັ້ງ ທ່ານຫມໍອາດປັບປ່ຽນຂະຫນາດຢາ ຫລື ຊະນິດຢາ ເພື່ອຄວາມເຫມາະສົມຄວນແຈ້ງໃຫ້ທ່ານຫມໍຮັບຮູ້ວ່າມີອາການຊັກເກີດຂຶ້ນລະຫວ່າງການປິ່ນປົວ.

12. <u>ຢາກັນຊັກມີອາການຂ້າງຄຽງຫ້ຍງແດ່ ?</u>

ຜົນຂ້າງຄຽງຂອງຢາກັນຊັກທີ່ອາດຈະພົບມີດັ່ງນີ້:

1. ເຮັດໃຫ້ມີອາການງ່ວງຊຶມ ຊຶ່ງອາດເປັນເພາະ 1 ຫລື 2 ອາທິດທຳອິດ ແລ້ວຈະປັບໂຕໄດ້. ໃນກໍລະນີທີ່ປັບໂຕບໍ່ໄດ້ ຄວນປຶກສາກັບທ່ານຫມໍທີ່ປິ່ນປົວເພື່ອພິຈາລະນາປ່ຽນຢາ.
2. ອາການຂ້າງຄຽງອັນອື່ນໄດ້ແກ່ ອາການເຫງືອກບວມ, ຜົມຫລົ່ນ, ນ້ຳຫນັກເພີ່ມຂຶ້ນ ຫລື ເບື່ອອາຫານ ຂຶ້ນກັບຊະນິດຂອງຢາກັນຊັກ ແລະ ຂະຫນາດຂອງຢາກິນ.
3. ອາການແພ້ຢາຮຸນແຮງຈະເກີດຂຶ້ນພາຍໃນ 1–2 ອາທິດ ຫລັງຈາກໄດ້ຮັບຢາ ໄດ້ແກ່ ອາການຜື່ນ ຕຸ່ມຂຶ້ນຕາມຕົ້ນໂຕ ແຜ່ໃນປາກ ຕາແດງ ມີໄຂ້ ຖ້າມີອາການເຫລົ່ານີ້ເກີດຂຶ້ນຕ້ອງຢຸດຢາ ແລະ ໄປພົບທ່ານຫມໍທັນທີ.

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ຈັດທຳໂດຍ

ໂດຍ ນາງ ສາຍສະມຸດ ພານຸວົງ ນັກສຶກສາປະລິນຍາໂທ ການຢາປິ່ນປົວ (Clinical Pharmacy) ຮ່ວມກັບທີມ ສາຂາວິຊີບ ພະແນກລະບົບປະສາດ ໂຮງຫມໍເຊດຖາທິຣາດ

ໃນຫົວຂໍ້ ວິໃຈ

Outcomes of multidisciplinary team for epilepsy management at Setthathirat hospital in LAO PDR

IOC score

+1 = yes, 0 = don‟t know, and -1 = No

Patients' data collecting form

	Content	+1	0	–1	Comment
Part 1: General information					
1	Gender				
2	Age				
3	Education				
4	Occupation				
5	Marital status				
6	Residence of patient				
7	Monthly income of patients				
8	Family history of epilepsy				
9	Seizure frequency				
10	Number of AEDs				
11	Type of epilepsy				
12	Type of AEDs				
13	Comorbidities				
Part 2: Patient adherences					
14	Patients‟ adherence assessment tool will be using pill-count and self-report of how to take medicine. **% adherence:** $= \frac{(quantity\ dispensed) - (quantity\ remaining)}{(prescribed\ number\ of\ \frac{tablets}{d})\ X\ (number\ of\ days\ between\ dispensing\ date\ and\ i}$				
Part 3; Seizure-frequency					
15	Number of Seizure-frequency in 3 months				
Part 4: ADRs					
16	Drug interaction				
17	Improper drug selection				
18	Adverse reactions: side effect				

Patients' knowledge

Q	Content	Rating			Comment
		+1	0	-1	
1	What do you think the cause of a seizure is? (Check all that you think apply) 1. [ ] an abnormal electrical discharge in the brain [ ] demonic possession 2. [ ] divine punishment 3. [ ] an abnormal movement				
2	What do you think causes epilepsy? (Check all that you think apply) 1. [ ] an evil spirit 2. [ ] a head injury 3. [ ] brain tumor 4. [ ] divine punishment for reneging on a vow 5. [ ] sleep deprivation 6. [ ] alcohol withdrawal or heavy drinking 7. [ ] stroke 8. [ ] genetic disease 9. [ ] high fever 10. [ ] eating pork				
3	What types of seizures exist? (Check all that you think apply) 1. [ ] physical stiffness followed by jerking movements (tonicclonic seizure) 2. [ ] unusual sensations or abnormal jerking with preserved awareness (simple partial seizure) 3. [ ] lost awareness and physical immobility, repetitive involuntary movements (complex partial seizure) 4. [ ] loss of muscle strength and tone: the person collapses (atonic seizure) 5. [ ] staring spell, sudden mental absence, loss of awareness (absence seizure)				
4	Do you think epilepsy can be cured? 1. Yes 2. No				

Q	Content	Rating			Comment
		+1	0	-1	
5	How often should anti-epileptic drugs be taken? 1. [ ] for life 2. [ ] 2-5 years 3. [ ] only at the full moon 4. [ ] only during an episode 5. [ ] for 3-6 months				
6	What limitations do persons with epilepsy face? (Check all that you think apply) 1. [ ] not allowed to drive a motor vehicle 2. [ ] no sexual intercourse 3. [ ] cannot get married 4. [ ] should not work with machinery 5. [ ] cannot get pregnant 6. [ ] abruptly stop anti -epileptic drugs during pregnancy 7. [ ] not able to lactate 8. [ ] should not eat pork 9. [ ] must quit work 10. [ ] should not drink alcoholic beverages				
7	What should be done during a seizure? (Check all that you think apply) 1. [ ] place the person in a semi -prone position to prevent choking 2. [ ] place something in the mouth to prevent biting the tongue 3. [ ] administer an anti -epileptic drug during the episode 4. [ ] restrain the person and perform chest compressions (CPR) 5. [ ] take actions to prevent injury during the episod				
8	What do you think which the adverse reactions related to phenobarbital but it will get better in 2 -3 weeks. : (Check all that you think to apply) 1. [ ] Sedation 2. [ ] Nystagmus 3. [ ] Dizziness				

Q	Content	Rating			Comment
		+1	0	-1	
	4. [ ] Ataxia 5. [ ] Mild drowsiness				
9	What do you think which the adverse reactions related to carbamazepine but it will get better in the first few weeks : (Check all that you think to apply) 1. [ ] Dizziness 2. [ ] Drowsiness 3. [ ] Anorexia 4. [ ] Nausea 5. [ ] Urticaria 6. [ ] Exfoliative dermatitis				
10	What do you think which the adverse reactions related to valproic acid but it will get better in 2 -3 weeks. : (Check all that you think to apply) 1. [ ] Gastrointestinal tract 2. [ ] Weight gain (use long term) 3. [ ] Anorexia 4. [ ] Nausea 5. [ ] Vomiting 6. [ ] Alopecia (use long term)				
11	What do you think which the adverse reactions related to valproic acid but it will get better in 2 -3 weeks. 1. [ ] Nystagmus 2. [ ] Dizzniess 3. [ ] Sedation 4. [ ] Fatique 5. [ ] Behavior change 6. [ ] Ataxia				

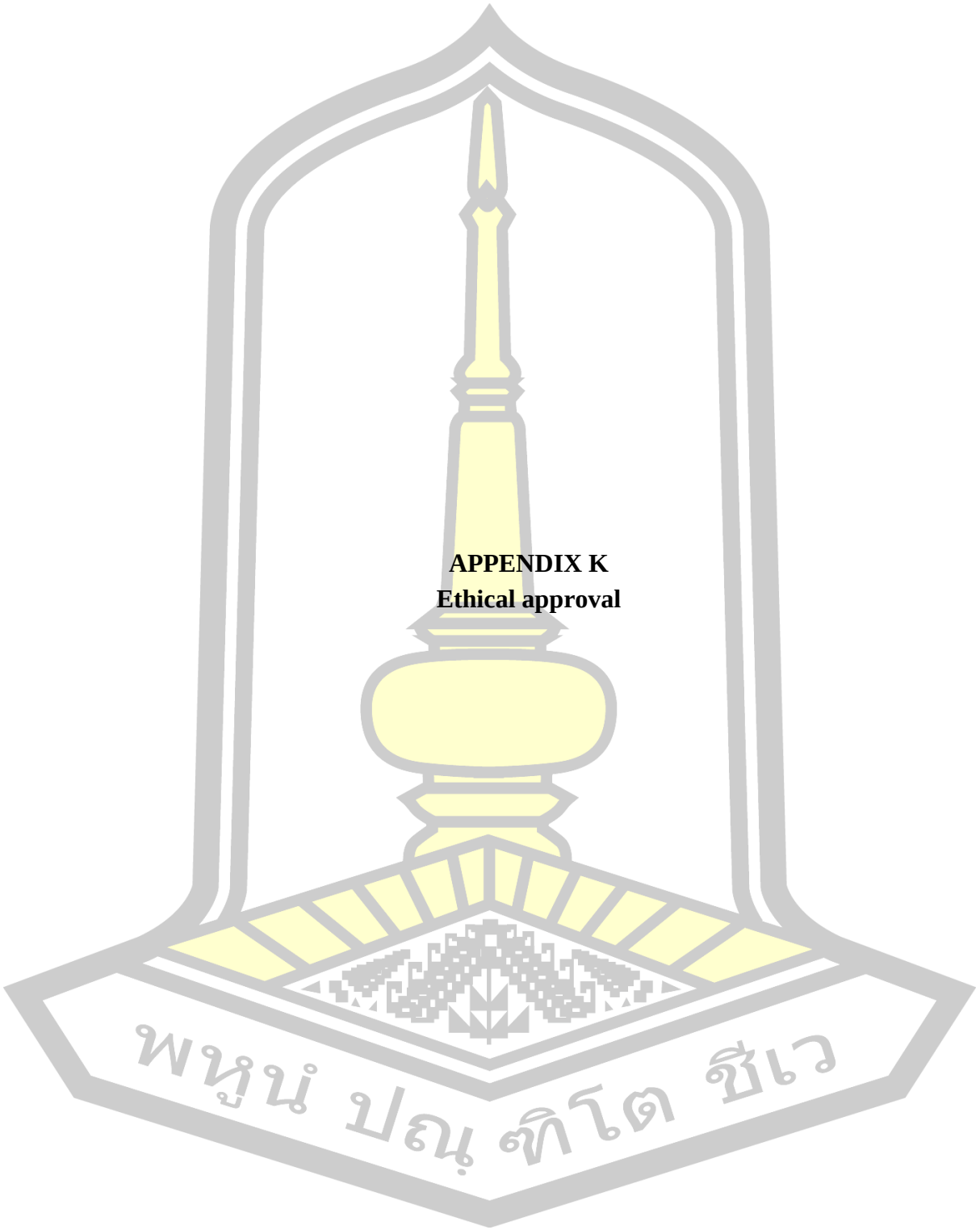
Patients' quality of life

Q	Content	Rating			Comment
		+1	0	−1	
1	Did you have a lot of energy? 1. All of the time 2. Most of the time 3. A good bit of the time 4. Some of the time 5. A little of the time 6. None of the time				
2	Have you felt downhearted and low? 1. All of the time 2. Most of the time 3. A good bit of the time 4. Some of the time 5. A little of the time 6. None of the time				
3	Driving (or other transport) 1. A great deal 2. A lot 3. Somewhat 4. Only a little 5. Not at all				
4	How much do your work limitations bother you? 1. Not at all bothersome 2. A little 3. Somewhat 4. A lot 5. Extremely bothersome				
5	How much do your social limitations bother you? 1. Not at all bothersome 2. A little 3. Somewhat 4. A lot Extremely bothersome				
6	How much do your memory difficulties bother you? 1. Not at all bothersome 2. A little 3. Somewhat				

Q	Content	Rating			Comment
		+1	0	−1	
	4. A lot Extremely bothersome				
7	How much do physical effects of antiepileptic drugs bother you? 1. Not at all bothersome 2. A little 3. Somewhat 4. A lot Extremely bothersome				
8	How much do psychological effects of antiepileptic drugs bother you? 1. Not at all bothersome 2. A little 3. Somewhat 4. A lot Extremely bothersome				
9	How afraid are you of having a fit during the next 4 weeks? 1. Very afraid 2. Somewhat afraid 3. Not very afraid 4. Not afraid at all				
10	How has your quality of life been during the past 4 weeks (that is, how have things been going for you) 1. Very good: could hardly have been better 2. Pretty good 3. Good & bad about equal 4. Pretty bad 5. Very bad: could hardly have been worse				

Score IOC

Patients' data collecting form (13 items)				
Q	Expert no. 1	Expert no. 2	Expert no. 3	IOC
1	1	0	1	0.6
2	1	0	1	0.6
3	1	1	0	0.6
4	1	0	1	0.6
5	1	1	0	0.6
6	1	0	1	0.6
7	1	1	0	0.6
8	0	1	1	0.6
9	0	1	1	0.6
10	1	1	0	0.6
11	0	1	1	0.6
12	1	1	0	0.6
13	1	1	0	0.6
Patients' knowledge (11 items)				
1	1	1	0	0.6
2	1	1	0	0.6
3	1	1	0	0.6
4	1	0	1	0.6
5	1	1	0	0.6
6	1	1	0	0.6
7	1	1	0	0.6
8	0	1	1	0.6
9	1	0	1	0.6
10	1	0	1	0.6
11	1	1	0	0.6
Patients' knowledge (10 items)				
1	1	1	0	0.6
2	1	1	0	0.6
3	1	1	0	0.6
4	1	0	1	0.6
5	1	0	1	0.6
6	1	0	1	0.6
7	0	1	1	0.6
8	1	0	1	0.6
9	1	1	0	0.6
10	1	1	0	0.6



APPENDIX K
Ethical approval

Lao People's Democratic Republic
Peace Independence Democracy Unity Prosperity
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Ministry of Health
National Ethics Committee
for Health Research (NECHR)

No 021 /NECHR
Vientiane Capital 30/04/2021

Approval Notice

Ms. Saysamooth Phanouvong
Email: mooth phanouvong@ gmail.com

RE: Ethical Approval for Health Research

Title: "Outcome of multidisciplinary team for epilepsy management at Setthathirat hospital in LAO PDR." (Submission ID: 2021.10.Vie)

Dear Ms. Saysamooth Phanouvong,

The National Ethics Committee for Health Research of the Lao People's Democratic Republic have reviewed and approved your research.

Please note the following information about your approved research protocol:

Approval period: April 2021 – April 2022
Approved Subject Enrollment: 68
Study Site: Vientiane Capital
Sponsor: Pierre Fabre Foundation, France **Budget**: 23 000 000Kip (LAK)
Implementing Panel/Project Investigator: Ms. Saysamooth Phanouvong

Please note that the Ethics Committee reserves the right to ask for further questions, seek additional or monitor the conduct of your research and consent process.

Principle Investigator is required to notify the Secretary of the National Ethic Committee for Health Research:

- Any significant change to the project and the reason for that change, including an indication of ethical implications (if any);
- Serious adverse effects on participants and the action taken to address those effects;
- Any other unforeseen events or unexpected developments that merit notification;
- The inability of the Principal Investigator to continue in that role, or any other change in research personnel involved in the project;
- Any expiry of the insurance coverage provided with respect to sponsored clinical trials and proof of re-insurance;
- A delay of more than 12 months in the commencement of the project; and,
- Termination or closure of the project.

Additionally, the Principal Investigator is required to submit a progress report on the anniversary of approval and on completion of the project.

President of NECHR

MAHASARAKHAM UNIVERSITY ETHICS COMMITTEE FOR RESEARCH INVOLVING HUMAN SUBJECTS

Certificate of Approval

Approval number: 257-206/2021

Title : Outcome of multidisciplinary team for epilepsy management at Setthathirat hospital in LAO PDR.

Principal Investigator : Mrs. Saysamooth Phanouvong

Responsible Department : Faculty of Pharmacy

Research site : Outpatient clinic, department of neurology, Setthathirat hospital (LAO PDR)

Review Method : Expedited Review

Date of Manufacture : 19 August 2021 **expire :** 18 August 2022

This research application has been reviewed and approved by the Ethics Committee for Research involving Human Subjects, Mahasarakham University, Thailand. Approval is dependent on local ethical approval having been received. Any subsequent changes to the consent form must be re-submitted to the Committee.

Ratree S.

(Asst. Prof. Ratree Sawangjit)

Chairman

Approval is granted subject to the following conditions: (see back of this Certificate)

BIOGRAPHY

NAME	Ms.Saysamooth Phanouvong
DATE OF BIRTH	9 August 1984
PLACE OF BIRTH	Oudomxay province, Lao PDR
ADDRESS	House number 572, Unit 64, Nonkhilex Village, Sikottabong District, Vientiane, Lao PDR
POSITION	Assistant Lecturer at Faculty of Pharmacy, University of Health Sciences, Vientiane, Lao PDR
PLACE OF WORK	Department of Pharmaceutical Care, Faculty of Pharmacy, University of Health Sciences, Samsenthai Rd, Kaoyord Village, Sisattanak District, Vientiane, Lao PDR, Zip code 7444
EDUCATION	2012 Bachelor's degree of Pharmacy, Faculty of Pharmacy, University of Health ScieHnoi University, VietNam 2023 Master degree in Clinical Pharmacy, Faculty of pharmacy, Mahasarakham University, Thailand
Research grants & awards	Thesis support fund for graduate students, Faculty of Pharmacy, year 2019