ORIGINAL ARTICLE

Trends and Costs of Antiepileptic Drugs in a University Hospital in Thailand

Nanthaphan Chainirun BP[1,3], Kittisak Sawanyawisuth MD, PhD[2], Somsak Tiamkao MD[2,3]

[1] Department of Pharmacy Service, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

[2] Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

[3] Integrated Epilepsy Research Group, Khon Kaen University, Khon Kaen, Thailand

Objective: Epilepsy is a common disease and can be treated with anti-epileptic drugs (AEDs). The present study aimed to evaluate trends and cost of AEDs use in university hospital, Thailand.

Materials and Methods: This was a retrospective descriptive study conducted at Srinagarind Hospital, a university hospital of Khon Kaen University. The inclusion criteria were patients with epilepsy who received AEDs both new and standard categories. The present study period was between 2015 and 2021. Trends and costs of AEDs were reported and categorized as new and standard AEDs.

Results: There were nine new and 6 standard AEDs prescribed during the study period. There were 958,968 prescribed tablets for the new AEDs with the total cost of 37,143,927.25 Baht, while there were slightly more prescribed standard AED (1,818,049 tablets) with the total cost of 10,689,034.75 Baht. For the new AEDs group, three common AEDs were lamotrigine, levetiracetam and topiramate with an increasing trend. For the standard AEDs group, sodium valproate and phenytoin had decreasing trend.

Conclusion: The new AEDs had an increasing trend particularly lamotrigine, levetiracetam, and topiramate resulting in higher costs than the standard AEDs.

Keywords: Lamotrigine; Epilepsy; Cost; Trend

J Med Assoc Thai 2023;106(Suppl.1):S31-5

Website: http://www.jmatonline.com

Epilepsy is a common neurological disease in clinical practice. A meta-analysis showed that the prevalence of epilepsy was 6.38 per 1,000 persons[1]. Even though there were comparable of epilepsy prevalence by age or sex, the prevalence was high in some particular countries such as Tanzania at 13.56 per 1,000 persons. It is also related to several conditions such as sleep apnea or hypertension[2–8]. The cornerstone treatment for epilepsy is antiepileptic drugs (AEDs).

There are several available AEDs and can be categorized as new or standard types. The standard AEDs are those available in market before 1991, while the new AEDs are those available in market after 1991[9]. The new AEDs may have better properties such as low drug interactions with comparable safety profile. Treatments with AEDs are dynamic and changing by time. A study conducted in 2000 to 2010 in UK found that carbamazepine and phenytoin were prescribed less, while lamotrigine and levetiracetam were prescribed more[10]. Another study from Korea in the same period showed higher new AEDs from 52.6% in 2001 to 74.3% in 2012[9]. A later study conducted in 2003 to 2016 in UK indicating higher use of levetiracetam from 2.6% from 2007 to 26.2% in 2016[11]. There is limited data of AEDs and cost in Thailand. The present study aimed to evaluate trends and cost of AEDs use in university hospital, Thailand.

Correspondence to:

Tiamkao S.

Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

Phone: +66-43-363664

Email: somtia@kku.ac.th

How to cite this article:

Chainirun N, Sawanyawisuth K, Tiamkao S. Trends and Costs of Antiepileptic Drugs in a University Hospital in Thailand. J Med Assoc Thai 2023;106: S31-5.

DOI: 10.35755/jmedassocthai.2023.S01.13758

Materials and Methods

This was a retrospective descriptive study conducted at Srinagarind Hospital, a university hospital of Khon Kaen University. The inclusion criteria were patients with epilepsy who received AEDs both new and standard categories. The study period was between 2015 and 2021. The study protocol was approved by the ethics committee in human research, Khon Kaen University, Thailand (HE460830).

Eligible patients were retrieved from the electronic medical records of the hospital. Baseline characteristics of eligible patients were published elsewhere. Numbers and

costs of each AED were evaluated and reported by studied year. AEDs were categorized as standard and new type; those standard AEDs were sodium valproate, phenytoin, carbamazepine, clonazepam, phenobarbitone, diazepam, while the new AEDs included levetiracetam, lamotrigine, topiramate, perampanel, lacosamide, oxcarbazepine, gabapentin, zonisamide, and pregabalin.

Price of each AED were as follows: Depakine 200 mg (valproate) TAB (6 Baht), Dilantin Kapseal 100 mg (phenytoin) CAP (4.5 Baht), Carbamazepine 200 mg (1.5 Baht), clonazepam 2 mg (1.5 Baht), phenobarbitone 30 mg and 60 mg (0.5 Baht), diazepam 2 mg and 5 mg (0.5 Baht), Keppra 500 mg (levetiracetam) (43.5 Baht), Lamictal 100 mg (lamotrigine) (46 Baht), Topamax 100 mg (topiramate) (45.5 Baht), Fycompa 8 mg (perampanel) (186 Baht), Vimpat 100 mg (lacosamide) (103 Baht), Trileptal 300 mg (oxcarbazepine) (19.5 Baht), Gabapentin 300 mg (Gabutin) (6.25 Baht), Zonegran 100 mg (oxcarbazepine) (32 Baht), and pregabalin 75 mg (Sandoz) (17.50 Baht).

Results

There were nine new and 6 standard AEDs prescribed during the study period. There were 958,968 prescribed tablets for the new AEDs with the total cost of 37,143,927.25 Baht, while there were slightly more prescribed standard AED (1,818,049 tablets) with the total cost of 10,689,034.75 Baht (Table 1 to 4).

For the new AEDs group, lamotrigine had increasing trend, while levetiracetam and topiramate had slightly decreasing trend (Figure 1). The other six new AEDs had somewhat steady trend except oxcarbazepine, lacosamide, and gabapentin had decreasing trend particularly

Table 1. Numbers of prescribed new antiepileptic drugs (AED) from 2015 to 2021

AED/year	2015	2016	2017	2018	2019	2020	2021	Total
Levetiracetam	47,796	57,396	51,464	58,076	62,924	55,461	40,129	373,246
Lamotrigine	35,263	41,522	47,394	56,091	59,039	48,489	36,054	323,852
Topiramate	21,964	22,112	25,093	30,762	34,081	24,766	18,368	177,146
Gabapentin	2,976	4,652	5,412	6,665	6,181	5,882	5,019	36,787
Oxcarbazepine	5,199	6,156	6,930	3,548	1,651	510	420	24,414
Perampanel	0	1,076	1,719	1,651	2,447	4,146	2,268	13,307
Lacosamide	0	932	900	1,640	1,430	1,008	210	6,120
Zonisamide	0	0	0	450	357	1,133	735	2,675
Pregabalin	350	180	0	0	0	336	555	1,421

Table 2. Costs of prescribed new antiepileptic drugs (AED) from 2015 to 2021

AED/year	2015	2016	2017	2018	2019	2020	2021	Total
Levetiracetam	2,001,530	2,371,079	2,128,655	2,437,958	2,622,133.50	2,333,040.50	1,157,163	15,051,559
Lamotrigine	1,315,269	1,564,443	1,709,900	2,039,888	2,296,023	1,752,416	1,433,562	12,111,501
Topiramate	884,594	903,840	1,039,587.50	1,236,983	1,379,389.50	1,009,445	731,997.50	7,185,836.50
Perampanel	0	82,088.50	116,194	152,723.50	259,687	445,593	297,675	1,353,961
Lacosamide	0	95,996	92,700	168,920	147,290	103,824	21,630	630,360
Oxcarbazepine	101,380.50	120,042	135,135	69,186	32,194.50	9,945	8,190	476,073
Gabapentin	18,600	29,313.50	31,568.25	42,345.75	38,563.75	36,053.75	30,599.25	227,044.25
Zonisamide	0	0	0	14,400	11,424	36,256	23,520	85,600
Pregabalin	7,525	3,870	0	0	0	5,880	4,717.50	21,992.50

Table 3. Numbers of prescribed standard antiepileptic drugs (AED) from 2015 to 2021

AED/year	2015	2016	2017	2018	2019	2020	2021	Total
Sodium valproate	110,542	111,338	98,339	104,929	96,872	82,950	59,784	664,754
Phenytoin	96,988	92,594	95,179	94,961	78,249	71,808	49,440	579,219
Carbamazepine	42,876	46,367	47,775	41,161	44,940	37,990	27,111	288,220
Clonazepam	20,398	28,142	26,075	24,973	26,504	21,588	15,408	163,088
Phenobarbitone	17,884	17,835	20,499	17,646	14,984	10,620	8,837	108,305
Diazepam	2,931	3,639	3,336	905	1,429	1,154	1,069	14,463

Table 4. Costs of prescribed standard antiepileptic drugs (AED) from 2015 to 2021

AED/year	2015	2016	2017	2018	2019	2020	2021	Total
Sodium valproate	1,179,728	1,181,330	1,071,189	1,100,174	1,031,920	901,529	664,111	7,129,981
Phenytoin	428,268	419,759.50	435,162	429,792.50	352,157.50	320,945	220,496.50	2,606,581
Carbamazepine	116,246.25	112,450.25	107,793.75	102,074.25	101,343.75	87,265.75	63,525.75	690,699.75
Clonazepam	23,840	34,142.50	32,412	31,260	32,155	25,983.50	19,212	199,005
Phenobarbitone	8,942	8,917.50	10,249.50	8,823	7,492	5,310	4,418.50	54,152.50
Diazepam	1,585.50	2,139.50	1,828	740.50	838.50	757	726.50	8,615.50

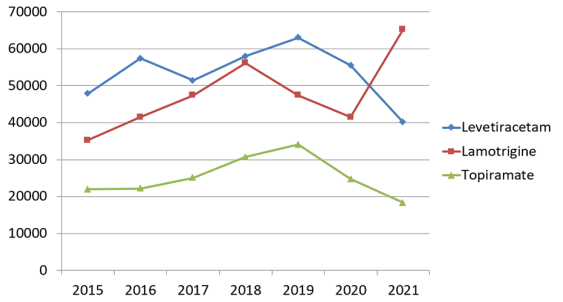

Figure 1. Numbers of prescribed new antiepileptic drugs (AED) from 2015 to 2021 (Top 3).

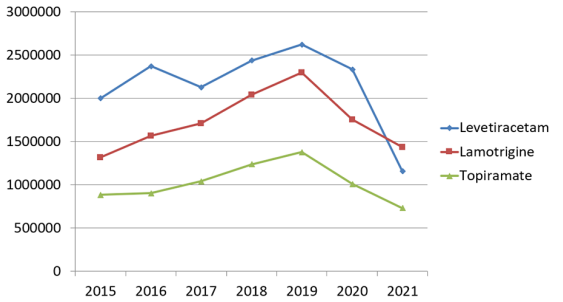

Figure 3. Costs of prescribed new antiepileptic drugs (AED) from 2015 to 2021 (Top 3).

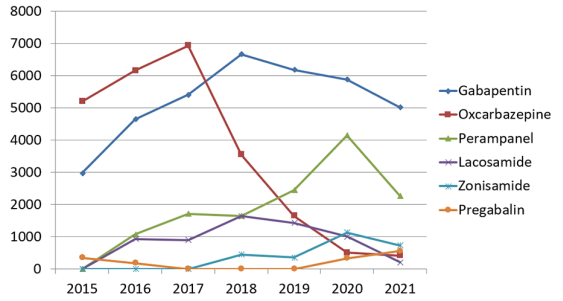

Figure 2. Numbers of prescribed new antiepileptic drugs (AED) from 2015 to 2021 (ranked 4 to 9).

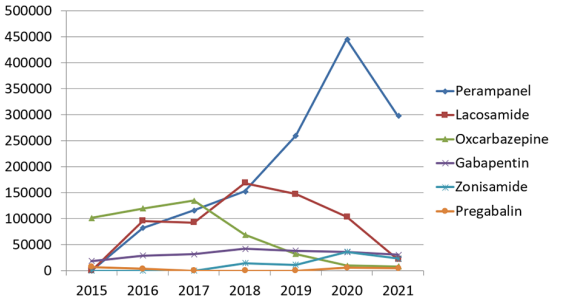

Figure 4. Costs of prescribed new antiepileptic drugs (AED) from 2015 to 2021 (ranked 4 to 9).

oxcarbazepine (Figure 2). Perampanel had slightly increasing use (Figure 2). Regarding costs, the top 3 new AEDs had somewhat steady costs with slightly decreasing in the past two years (Figure 3). The other 6 new AEDs, perampanel had dramatically increasing cost (Figure 4). Oxcarbazepine and lacosamide had decreasing costs (Figure 4).

For the standard AEDs group, the most commonly used standard AED was sodium valproate (Figure 5). The five standard AEDs had slightly decreasing trend except diazepam which had quite steady trend (Figure 5, 6). The costs of six standard AEDs had similar pattern with the numbers used (Figure 7, 8).

Discussion

The present study found similar findings as previously reported[9-11]. Sodium valproate and phenytoin had a slightly decreasing trend, while other standard AEDs such as carbamazepine, clonazepam, phenobarbitone, and diazepam had quite steady rate. These findings may explain by replacement of new AEDs for sodium valproate and phenytoin as the new AEDs may have higher seizure control rate. A study from UK found rapid reduction use of carbamazepine from 34.9% to 10.7%, while phenytoin was lower from 7.6% to 2.1%[11]. For the other four standard AEDs had steady rate as these AEDs may be used in those patients with seizure- controlled resulting in steady rates of these AEDs.

For the new AEDs, lamotrigine is the most commonly used in the 2021 and has an increasing trend continuously. Unlike lamotrigine, levetiracetam and topiramate were prescribed less in the past two years. The advantage of lamotrigine is less teratogenic effects[12,13]. Additionally, a recent review supported to use lamotrigine as the first line treatment for partial onset seizure[14]. Regarding costs

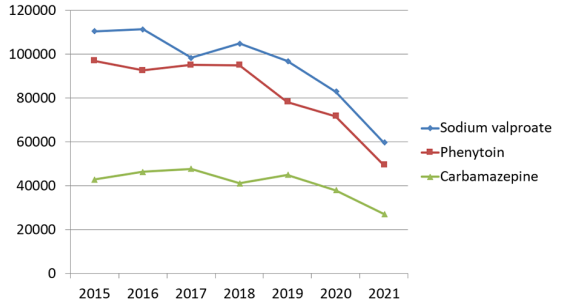

Figure 5. Numbers of prescribed standard antiepileptic drugs (AED) from 2015 to 2021 (top 3).

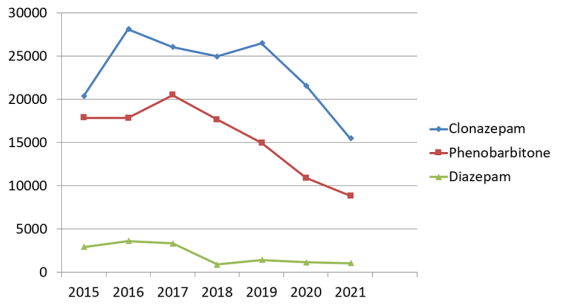

Figure 6. Numbers of prescribed standard antiepileptic drugs (AED) from 2015 to 2021 (ranked 4 to 6).

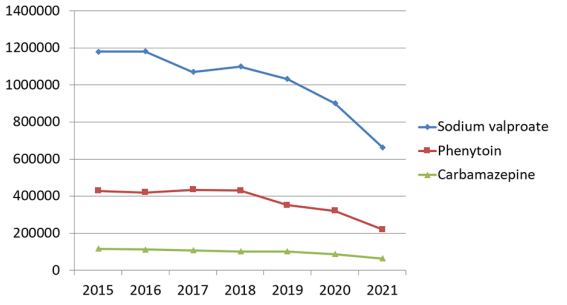

Figure 7. Costs of prescribed standard antiepileptic drugs (AED) from 2015 to 2021 (top 3).

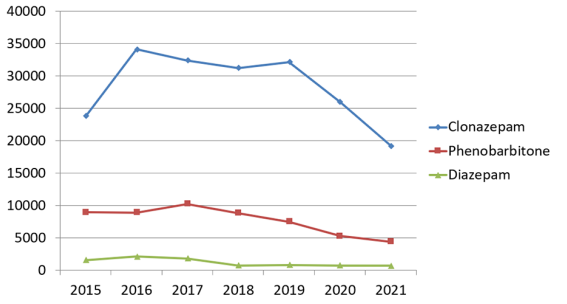

Figure 8. Costs of prescribed standard antiepileptic drugs (AED) from 2015 to 2021 (ranked 4 to 6).

of AEDs, new AEDs had higher costs than the standard AEDs particularly perampanel which had the highest price at 186 Baht/tab.

There are some limitations in the present study. First, the costs and usage data were reported as total costs and total prescribed; not an individual data. Second, some clinical factors related to epilepsy were not studied as well as predictors of seizure controlled using logistic regression analysis or systematic review[15-21]. Finally, no clinical outcomes or cost-effectiveness were evaluated. Even though our results showed that new AEDs had an increasing trend, further studies are required to evaluate the cost-effectiveness of these AEDs.

Conclusion

The new AEDs had an increasing trend particularly lamotrigine, levetiracetam, and topiramate resulting in higher costs than the standard AEDs.

What is already known on this topic?

Trends of using new antiepileptic drugs were reported in several countries but not in Thailand.

What this study adds?

New antiepileptic drugs had an increasing trend in a university hospital, Thailand resulting in higher costs.

Acknowledgements

The authors thank the Department of Medicine, Faculty of Medicine, Khon Kaen University for publication support.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Fiest KM, Sauro KM, Wiebe S, Patten SB, Kwon CS, Dykeman J, et al. Prevalence and incidence of epilepsy: A systematic review and meta-analysis of international studies. Neurology 2017;88:296-303.
2. Sethi S, Barjaktarevic IZ, Tashkin DP. The use of nebulized pharmacotherapies during the COVID-19 pandemic. Ther Adv Respir Dis 2020;14:1753466620954366.
3. Gasparini S, Ferlazzo E, Sueri C, Cianci V, Ascoli M, Cavalli SM, et al. Hypertension, seizures, and epilepsy: a review on pathophysiology and management. Neurol Sci 2019;40:1775-83.
4. Khamsai S, Mahawarakorn P, Limpawattana P, Chindaprasirt J, Sukeepaisarnjaroen W, Silaruks S, et al. Prevalence and factors correlated with hypertension secondary from obstructive sleep apnea. Multidiscip Respir Med 2021;16:777.
5. Khamsai S, Kachenchart S, Sawunyavisuth B, Limpawattana P, Chindaprasirt J, Senthong V, et al. Prevalence and risk factors of obstructive sleep apnea

in hypertensive emergency. J Emerg Trauma Shock 2021;14:104-7.
6. Soontornrungsun B, Khamsai S, Sawunyavisuth B, Limpawattana P, Chindaprasirt J, Senthong V, et al. Obstructive sleep apnea in patients with diabetes less than 40 years of age. Diabetes Metab Syndr 2020;14:1859-63.
7. Sanlung T, Sawanyawisuth K, Silaruks S, Chattakul P, Limpawattana P, Chindaprasirt J, et al. Clinical characteristics and complications of obstructive sleep apnea in Srinagarind hospital. J Med Assoc Thai 2020;103:36-9.
8. Manasirisuk P, Chainirun N, Tiamkao S, Lertsinudom S, Phunikhom K, Sawunyavisuth B, et al. Efficacy of generic atorvastatin in a real-world setting. Clin Pharmacol 2021;13:45-51.
9. Cho YS, Ah YM, Jung AH, Kim KJ, Lee JY. Trends in antiepileptic drug prescriptions for childhood epilepsy at a Tertiary Children's Hospital in Korea, 2001-2012. Paediatr Drugs 2015;17:487-96.
10. Pickrell WO, Lacey AS, Thomas RH, Lyons RA, Smith PE, Rees MI. Trends in the first antiepileptic drug prescribed for epilepsy between 2000 and 2010. Seizure 2014;23:77-80.
11. Powell G, Logan J, Kiri V, Borghs S. Trends in antiepileptic drug treatment and effectiveness in clinical practice in England from 2003 to 2016: a retrospective cohort study using electronic medical records. BMJ Open 2019;9:e032551.
12. Shi X, Wang Y, Zhang Y, Song C, Jiang Y, Zhao J, et al. Effects of antiepileptic drugs polytherapy on pregnancy outcomes in women with epilepsy: An observation study in northwest China. Epilepsy Behav 2022;135:108904.
13. Pa B, G SS, Thomas G, Kp A. Dosage optimization of lamotrigine in pregnancy: A pharmacometric approach using modeling and simulation. J Clin Pharmacol 2022;62:1557-65.
14. Nevitt SJ, Sudell M, Weston J, Tudur Smith C, Marson AG. Antiepileptic drug monotherapy for epilepsy: a network meta-analysis of individual participant data. Cochrane Database Syst Rev 2017;12:CD011412.
15. Sawunyavisuth B. What personal experiences of CPAP use affect CPAP adherence and duration of CPAP use in OSA patients? J Med Assoc Thai 2018;101 Suppl 7:S245-9.
16. Jeerasuwannakul B, Sawunyavisuth B, Khamsai S, Sawanyawisuth K. Prevalence and risk factors of proteinuria in patients with type 2 diabetes mellitus. Asia Pac J Sci Technol 2021;26:APST-26-04-02.
17. Charoentanyarak S, Sawunyavisuth B, Deepai S, Sawanyawisuth K. A point-of-care serum lactate level and mortality in adult sepsis patients: A community hospital setting. J Prim Care Community Health 2021;12:21501327211000233.
18. Boonwang T, Namwaing P, Srisaphonphusitti L, Chainarong A, Kaewwong SC, Kaewwong T, et al. Esports may improve cognitive skills in soccer players: A systematic review. Asia Pac J Sci Technol 2022;27:APST-27-03-03.
19. Namwaing P, Ngamjarus C, Sakaew W, Sawunyavisuth B, Sawanyawisuth K, Khamsai S, et al. Chest physical therapy and outcomes in primary spontaneous pneumothorax: A systematic review. J Med Assoc Thai. 2021;104 Suppl 4:S165-8.
20. Tongdee S, Sawunyavisuth B, Sukeepaisarnjaroen W, Boonsawat W, Khamsai S, Sawanyawisuth K. Clinical factors predictive of appropriate treatment in COPD: a community hospital setting. Drug Target Insights 2021;15:21-5.
21. Sawunyavisuth B, Ngamjarus C, Sawanyawisuth K. A meta-analysis to identify factors associated with CPAP machine purchasing in patients with obstructive sleep apnea. Biomed Rep 2022;16:45.