


The 8th Asian Conference on Clinical Pharmacy: "Toward Harmonization of Education and Practice of Asian Clinical Pharmacy"

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# Anti-epileptic Drugs Utilization and Seizure Outcome among Pediatric Patients in a Malaysian Public Hospital



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## Study Information

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Conducted by

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The research was carried out in General Hospital In Penang under the supervision of lecturers from Universiti Sains Malaysia

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1-4 July 2008, Hyatt Regency Surabaya  
Hotel-Indonesia

## Introduction

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- Epilepsy is the most common neurological disorder in children characterized by spontaneous propensity for recurrent and unprovoked seizures and it remains a challenge to treat.
- Despite the increase in antiepileptic drugs, more than 25% of children with childhood epilepsy continue to have seizures (1). Four to ten percent of children suffer at least one seizure in the first 16 years of life (2).

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- Treatment should aim at controlling seizures associated with the lowest possible occurrence of adverse effects allowing the child to become an active member of the community and this at the lowest possible overall cost.
- The use of antiepileptic drugs in pediatrics circle around the neurologists who prescribed drugs on the basis of their personal experiences due to lack of scientific data for various types of seizure in children.

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- Epidemiologic studies reveal that approximately 150,000 children will sustain a first-time unprovoked seizure each year, and of those, 30,000 will develop epilepsy (2).
- The current antiepileptic drug development system essentially renders children with epilepsy "therapeutic orphans" who can only benefit from this development if drug developed for adults, happens to also be effective for pediatric population (4).

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The ultimate outcome of antiepileptic drug treatment in epilepsy is to attain "no seizures and no side effects." <sup>(5)</sup>

## Objectives

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### Review of Anti-epileptic Drug Utilization

- To review the utilization pattern of newer and older anti-epileptic drugs among pediatric patients.

### Outcome of Anti-epileptic Drugs

- Another objective was to assess the outcome of the anti-epileptic drugs in terms of number of seizure.

## Materials & Methods

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- This is a prospective study including both descriptive and inferential analysis, carried out over a 2-month period.

- All epileptic patients (in- and out-patients) aged between 1 to 15 years who were prescribed with at least one antiepileptic drug were included in the study.

- Patients were identified through the neurologist and pharmacy drug prescriptions.

- The data collection was divided in to two parts comprising of one month each, in first month the demographic data was collected and in second month epileptic patients were followed for the number of seizures that they experienced throughout the month and change in drug therapy.

- The information for the number of seizures experienced by the patients attending the out-patient clinic was collected from the parents and other family members through convenient means of communication, telephone or emails.

- However, the first hand information was obtained from the attending doctors, nurses and family members for the number of seizures experienced by the patients admitted in the ward on daily basis.

## Statistics

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- The descriptive and inferential statistical were carried out using SPSS version 13 for the analysis of the data with 0.05 level of significance.
- Mann-Whitney test was applied to find out the difference between sets of mono-therapy and poly-therapy, AED and AED/BZD in term of number of seizure.
- While Kruskal-Wallis test was applied to find out the difference among old, new and new/old combination AEDs, established, recurrent and new-onset cases.
- The post-hoc analysis was done using Mann-Whitney test with Berfoni's correction.

## Results

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A study cohort of 70 patients with the diagnosis of epileptic seizure and who were receiving at least one AED during the study period were included in the study. Of these, all the patients were diagnosed by the neurologist according to classification of international league against epilepsy (8)

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Table 1: Demographic Characteristics of the study population

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		n	%
Gender	Male	44	62.9
	Female	26	37.1
	Total	70	100
Age (yr)	1 to 5	29	41.4
	6 to 10	32	45.7
	11 to15	9	12.9
	Total	70	100
Race	Chinese	32	45.7
	Malay	25	35.7
	Indian	13	18.6
	Total	70	100

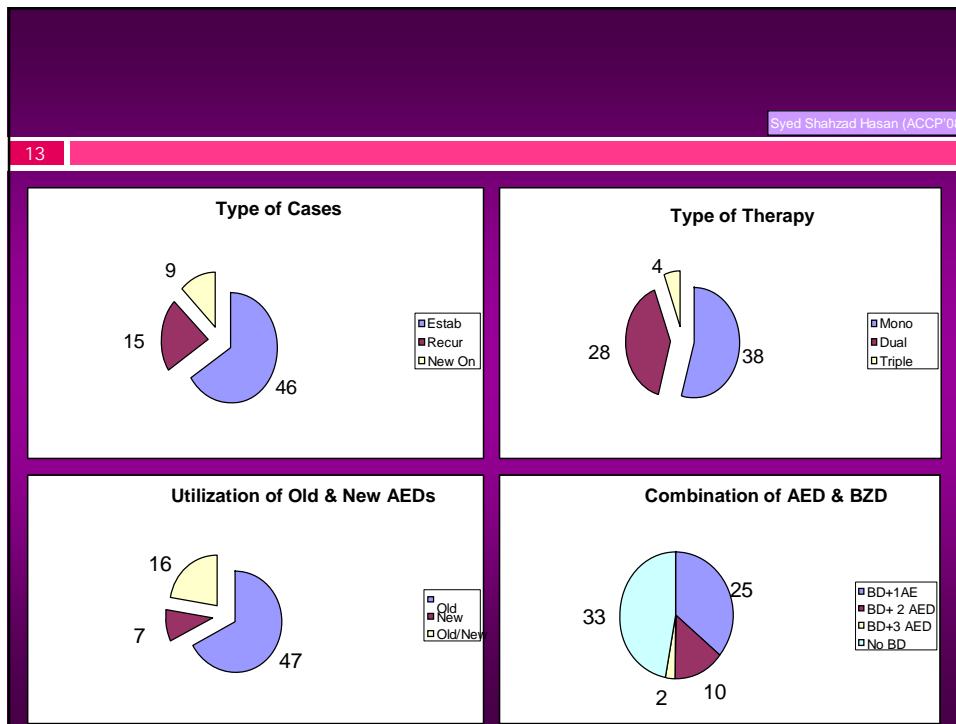
Table 2: Clinical Characteristics

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	n	%
Partial seizure	33	47.1
GTC	21	30
Absence seizure	6	8.6
Myoclonic	1	1.4
Infantile spasm	8	11.4
Unclassified	1	1.4
Total	70	100

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**Table 3: AED Utilization Pattern**

	n	%
<b>Partial seizures group</b>		
Monotherapy	19	27.1
Dual therapy	11	15.7
Triple therapy	3	4.3
<b>Generalized seizures group</b>		
Monotherapy	19	27.1
Dual therapy	8	11.4
Triple therapy	1	1.4
Others	9	13
Total Patients	70	100

Table 4: Overall AED utilization (n=106)

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	n	%
VPA	39	36.8
CBZ	32	30.2
LMT	11	10.4
TOP	8	7.5
PHT	8	7.5
LEV	5	4.7
VGB	3	2.9
Total AEDs	106	100

Table 5: Overall AED utilization (n=106)

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<u>Most common dual combination</u>	n	%
CBZ/VPA	8	11.4
VPA/LMT	6	8.6
VPA/PHT	6	8.6
VPA/TOP	3	4.3
Others	5	7.1
Total Patients	28	40
<u>Most common mono-therapy</u>		
CBZ	20	28.6
VPA	12	17.1
LMT	3	4.3
TOP	2	2.9
PHT	1	1.4
Total Patients	38	54.3

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Table 6: Comparison of antiepileptic drug pattern among Asian countries

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Total percentage for each antiepileptic drug				
<u>Countries (ref &amp; yr)</u>	<u>VPA</u>	<u>CBZ</u>	<u>PHE</u>	<u>PB</u>
India (17, 1999)	21	44	25	8
Taiwan (10, 2000)	31	57	32	14
Oman (9, 2002)	49	44	12	3
Prev. study (7, 2005)	36.1	21.1	0	1.1
Present study (2007)	36.8	30.2	7.5	0

Table 7: Comparison of antiepileptic drug pattern among Asian countries

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	<u>n</u>	<u>Seizure free pat.</u>	<u>%</u>
<u>AED and BZD combination</u>			
AED only	33	13	61.9
AED+BZD	37	8	38.1
<u>Types of AED and BZD combination</u>			
BZD with 1 AED	25	6	28.6
BZD with 2 AED	10	2	9.5
BZD with 3 AED	2	0	0
<u>Type of Treatments</u>			
Monotherapy	38	12	57.1
Polytherapy	32	9	42.9
<u>Type of antiepileptic drugs</u>			
Old AED	47	18	85.7
New AED	7	0	0
Old/New AED	16	3	14.3

Table 8: Number of seizures experienced by the patients per month (n=49)

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19	n	1 to 5 seizures	6 to 10 seizures	>10 seizures
<b>AED + BZD</b>				
AED only	33	11(22.4%)	3(6%)	6(12.2%)
AED+BZD	37	10(20.5%)	10(20.5%)	9(18.4%)
<b>Types of AED and BZD combination</b>				
BZD with 1 AED	25	9(18.4%)	6(12.2%)	4(8.2%)
BZD with 2 AED	10	1(2.1%)	4(8.2%)	3(6.1%)
BZD with 3 AED	2	0	0	2(4.1%)
<b>Type of treatments</b>				
Monotherapy	38	12(24.5%)	9(18.4%)	5(10.2%)
Polytherapy	32	9(12.7%)	4(5.7%)	10(20.4%)
<b>Type of antiepileptic drugs</b>				
Old AED	47	13(26.5%)	11(22.4%)	5(10.2%)
New AED	7	4(8.2%)	1(2.1%)	2(4.1%)
Old/New AED	16	4(8.2%)	1(2.1%)	8(16.2%)

Table 9: Characteristics of seizure-free patients (n=21)

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20	n	seizures free patients	%
<b>AED + BZD</b>			
AED only	33	13	61.9
AED+BZD	37	8	38.1
<b>Types of AED and BZD combination</b>			
BZD with 1 AED	25	6	28.6
BZD with 2 AED	10	2	9.5
BZD with 3 AED	2	0	0
<b>Type of Treatments</b>			
Mono-therapy	38	12	57.1
Poly-therapy	32	9	42.9
<b>Type of antiepileptic drugs</b>			
Old AED	47	18	85.7
New AED	7	0	0
Old/New AED	16	3	14.3

## Results

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- As indicated by Kruskal-Wallis test, no significant difference ( $p = 0.092$ ) was noted among established, recurrent and new onset cases in term of number of seizures.
- However, the results showed that there was a significant difference ( $p = 0.027$ ) among old, new and combination of old/new AEDs in terms of number of seizure.
- Mann-Whitney test with Berfoni's correction was applied for post-hoc analysis. The Berfoni's corrected value was calculated as 0.016, and based on that value there was no difference found between old and new AEDs (0.712), old and old/new AEDs combination (0.018), and new and old/new AEDs combination (0.092).

## Discussion

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- Most of the studies done earlier were on adult population (9, 10, 11, 12 and 13), but study carried out in pediatric population of age confined between 1-15 years.
- In agreement with earlier studies (7, 10, 14, 15, 16 and 17), in present study epileptic seizures were more common in male than female.
- In contradiction with previous study in Malaysia (7), partial seizures was the most common epileptic seizure followed by generalized seizures.
- Study data showed that the use of newer anti-epileptics as mono-therapy and poly-therapy have been increased against phenytoin and phenobarbitone.
- The increase in utilization of newer antiepileptic drug is attributed by many factors such as 1) newer antiepileptic drugs have been reported to have better side effects profile (18), 2) better awareness about the side effects of older antiepileptic drugs particularly in children (19, 20).

## Discussion

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- In present study, a total of 106 antiepileptic drugs were prescribed with an average of 1.51 antiepileptic drugs per patient, which is at the higher end than studies done in Oman (1.34) and Taiwan (1.41).
- Mono-therapy (54.3%) was the type of treatment most frequently utilized (45.7%), consistent with a general estimate where 70% of childhood epilepsy can be controlled using mono-therapy (19)
- Mono-therapy was found to be the drug of choice in majority of the epileptic patients which is consistent with the findings of other studies (9, 10, 22, and 23).
- Twenty one patients remained seizure-free during that period while 49 patients experienced seizure with an average of 8.61 seizures per month.
- Mono-therapy was found superior to poly-therapy in controlling seizure as 57.1% of seizure-free patients were from this group as compared to 42.9% seizure-free patients from poly-therapy group. Similarly older antiepileptic drugs were more effective in producing seizure free cases (85.7%).

## Conclusion

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- ▣ Mono-therapy was the most frequently used remedy in all forms of epilepsy.
- ▣ Sodium valproate was the most commonly used drug in both mono-therapy as well as poly-therapy while carbamazepine was found to be more frequently used as mono-therapy.
- ▣ In the study population, carbamazepine was found to be more effective than sodium valproate as mono-therapy in terms of producing more seizure-free cases.
- ▣ There was a significant difference found between older and newer antiepileptic drugs with 87.5% of seizure-free patients were on older antiepileptic drugs

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