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RESEARCH ARTICLE

Study of Drug Utilization, Cost-Effectiveness and Outcome of Antiepileptics Used in Paediatric Ward of Tertiary Care Hospital in Tamil Nadu, India

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ABSTRACT

The primary purpose of this study was to evaluate the utilisation pattern, cost-effectiveness and seizure outcome of newer and older antiepileptic drugs in paediatric clinical practice in a Indian hospital setting (Rajah Muthiah Medical College & Hospital (RMMCH), Annamalai Nagar-608 002, Tamilnadu). Over a six-month period, all paediatric epilepsy patients from RMMCH, who were diagnosed according to the classification of the International League against Epilepsy, were followed up prospectively, and the patient's information was gathered with the help of a validated data collection form. An average of 1.30 antiepileptic drugs per patient was prescribed, with 59.09 % of them on monotherapy and 40.90 % on polytherapy. Phenytoin (39.65%) was the most commonly used AED as monotherapy, followed by carbamazepine (27.59%). Valproic acid (22.41%) and lamotrigine (10.34%), the only new AED as monotherapy, were used in this study. Benzodiazepines were used as adjuvant therapy. The most common BZD therapy was clobazam (64.58%) followed by midazolam (35.42%). A significant difference was observed between AED alone and AED+BZD (p =0.013) in terms of seizure control, *which suggests that the addition of BZDs to the AED therapy did improve the seizure profile of the patients in the present study*. Similarly, a significant difference was observed between Older AED's and older & newer combination (p =0.048) in terms of seizure control. Old AED's were more cost – effective than New AED's for treatment of epilepsy in paediatric patients, and the *INCREMENTAL COST EFFECTIVE RATIO (ICER) OF NEW AED's TO OLD AED's was found to be Rs.73.33/APCCS (additional patient classified as complete success).*

KEYWORDS

Antiepileptic's, Cost-effectiveness, Paediatric Epilepsy, Drug Utilization

INTRODUCTION

"It is thus with regard to the disease called sacred: it appears to me to be in no way more divine nor more sacred than other diseases. The brain is the cause of this affliction"…Hippocrates.

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These were the famous words by the Greek physician Hippocrates, who wrote the first book on EPILEPSY, titled "***On the Sacred Disease"***, around 400 BC. Hippocrates recognized that Epilepsy was a brain disorder, and he spoke out against the ideas that seizures were a curse from the Gods and that people with Epilepsy held the power of prophecy. Epilepsy can be defined as a chronic disorder characterized by recurrent unprovoked seizures due to an underlying process[1].

Epilepsy is the utmost common neurological disorder in children, and it is characterised by recurrent and unprovoked seizures that are spontaneous in nature. Epilepsy, particularly childhood epilepsy, remains a challenge to treat. Despite the increased number of antiepileptic drugs (AEDs), more than 25% of children with childhood epilepsy continue to have seizures.[2,3]

New antiepileptic drugs (AEDs) which were introduced in 1993, provide further varied options in the treatment of epilepsy. Despite the equivalent efficacy and better tolerability of these drugs, more than 25% of patients remain obstinate to that treatment. Moreover, the issues for paediatric patients are different from those for adults, and have not been addressed in the development and application of the new AEDs[4].

Drug utilization was defined by world health organization (WHO) in 1977 as "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences". The management of epilepsy is primarily based on use of AEDs. The choice of drugs varies considerably among physicians and across countries and do not always indicates a rational clinical decision making. The cost of drugs should be an important consideration in the choice especially in developing countries. The practitioners should weigh the cost against the potential clinical benefits especially with newer AEDs[5]. Dan Chisholm, on behalf of WHOCHOICE reported that older first line AEDs (Phenobarbital and Phenytoin) were more cost effective on account of their similar efficacy but lower acquisition costs. The main objectives of the study were to describe the drug utilization pattern of anti- epileptic drugs (AEDs). To get an insight into the medication use in various form of epileptic seizures and determine the outcome and cost-effectiveness of various antiepileptic drugs used in this hospital[6].

Aim of the Study

The primary purpose of this study was to evaluate the utilisation pattern, cost-effectiveness and seizure outcome of newer and older antiepileptic drugs in paediatric clinical practice in a Indian hospital setting (Rajah Muthiah Medical College & Hospital (RMMCH), Annamalai Nagar-608 002, Tamilnadu)

METHOD

This was an observational, prospective, cohort, study carried out over a six-month period, incorporating both descriptive and inferential analyses. The study was designed to evaluate the utilisation and outcome of AED therapy in children with epilepsy in a public hospital and to determine the cost – effectiveness of the two types of AED's used to treat paediatric epilepsy. All epileptic patients aged 0–12 years who were prescribed with at least one AED were included in the study. The patients were further classified into different age groups: 0–5, 6–9 and 10–12 years. Patients having seizures induced by drugs, or due to any trauma or disease were excluded from the study.

Convenience sampling was used to recruit all eligible patients in this study. Patients were identified through the neurologist and pharmacy drug prescriptions. The data collection form for this research was piloted on a sample of ten participants to ascertain the validity of the data collection forms. Participants who agreed to take part in the pilot were given a copy of the background information of the study, together with a consent form to read and sign before providing their comments. Participants were asked about their understanding of and comments on the form upon completing it. The feedbacks were then used to improvise the data collection form. A total of 117 patients were approached, of whom 85 agreed to participate in the study. The following data was retrieved from the prescriptions, medical records, attending doctors, nurses and family members: demographics, details of AEDs used frequency of seizures and change in drug therapy during the study. The epileptic seizures were categorised according to the classifications of the International League Against Epilepsy[7]. However, patients with more than one type of seizures were categorised as unclassified or a mixed type of seizure. The diagnosis was

confirmed by a paediatric neurologist based on the clinical presentation of seizures, electroencephalography and scan tests. In addition, all the prescriptions were originated from the hospital paediatric neurologist.

Data collection was divided into two parts. First part consisted of data collected during the hospital stay of the patient and the second part consisted of the follow-up data. The epileptic patients were followed up on the number of seizures they experienced throughout the follow up period of ten days. Information on the number of seizures experienced by the patient during follow-up period was collected from the parents or other family members via telephone or by person during revisits. However, first-hand information on the number of seizures experienced by patients in the ward was obtained from the attending doctors, nurses and family members on a daily basis. Depending on number of seizures experienced during follow-up period, patients were grouped into 3 groups of 1-3 seizures, 4-6 seizures and >6 seizures, along with the medication used by the patient during their sta in the hospital and during their follow-up period.

The descriptive and inferential statistical analyses were carried out using the Statistical Package for Social Sciences version 16 (SPSS Inc, Chicago, IL, USA) for the analysis of the data at 0.05 level of significance. The Students t-test was applied to determine the difference in the number of seizures between sets of monotherapy and polytherapy, AED and AED/benzodiazepine (BZD),type of AED's(older and newer AED's), older and old/new AED combination. The cost of antiepileptic's used were obtained directly from hospital pharmacy, from where the drugs were purchased. Total cost incurred during hospital stay was found out from hospital administrative staff and cost effective analysis comparing older and newer AED's was performed. All the information was collected with the permission and approval of the Clinical Research Centre, the hospital director, and the research and ethics committee. All patients who agreed to take part in the study were given a copy of the study background information together with a consent form. In addition, strict confidentiality was assured for the information collected.

RESULTS

A study cohort of 85 patients with a diagnosis of epilepsy and who were receiving at least one AED during the study period were included in the study. The demographic characteristics of the patients, including gender and age are presented in Table I.

Table 1: Demographic Characteristics

		n	%
Gender	Male	54	63.53
	Female	31	36.47
	Total	85	100
Age (In Yrs)	0 to 5	39	45.88
	6 to 9	33	38.82
	10 to 12	13	15.29
	Total	85	100

Among the 85 patients, majority were male patients (63.53%) as compared to female patients (36.47%).Overall 39 patients belonged to the age group of 0-5 yrs, accounting for 45.88 % of total. A total of 33 patients belonged to the age group of 6-9 yrs., accounting for 38.82%. The remaining 13 patients belonged to the age group of 10-12 yrs., accounting for 15.29 % of total patients included in the study. The patients were also classified based on the type of epilepsy. A total of 40 patients were diagnosed to have Generalised tonic-clonic seizures, 23 patients were diagnosed to have partial seizures, 7 experienced absence seizures, 2 patients had myoclonic type of seizures and 10 infantile seizures. However the type of seizures could not be identified in 3 patients (fig 1).

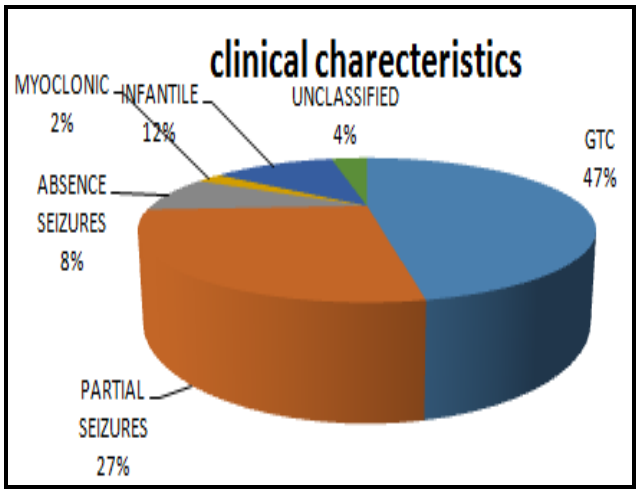

Figure 1: Clinical Characteristics

The pattern of AEDs prescribed and the different therapeutic approaches of epilepsy treatment utilised are presented in Tables II and III. A total of 111 AEDs were prescribed to a total of 85 patients during the study period, which corresponded to an average of 1.30 AED per patient.

Antiepileptic drugs can be categorised into two groups:

1) Old AED's: These include, phenytoin, valproic acid, carbamazepine, phenobarbitone & clonazepam
2) New AED's: These include, lamotrigine, gabapentin, felbamate, oxcarbazepine, etc.

Table 2: Type of Therapy

Type of therapy	No.(%)
Monotherapy	58 (68.23)
Dual therapy	22 (25.88)
Triple therapy	5 (5.90)
Older AED's	74 (87.05)
Newer AED's	6 (7.05)
Older/Newer AED's	5 (5.88)

AED: antiepileptic drug

Table 3: AED's Prescribed

Type of AED	No.(%)
Most frequent Mono-therapy (n=58)	
Phenytoin	23(39.69)
Carbamazepine	16(27.59)
Valproic Acid	13(22.41)
Lamotrigine	6(10.34)
Most frequent Dual-Combination (n=22)	
Phenytoin/Phenobarbitone (Inj)	7(31.81)
Phenytoin/Carbamazepine	6(27.27)
Valproic Acid/Phenytoin	6(27.27)
Valproic Acid/Lamotrigine	3(13.63)
Most frequent Triple-Combination (n=5)	
Phenobarbitone/Phenytoin/Sodium Valproate (Inj)	3(60)
Phenytoin/Sodium Valproate/Lamotrigine	2(40)

Adjuvent Therapy

Benzodiazepines were used as adjuvant therapy to treat epilepsy in the included paediatric patients. As shown in table IV, a total of 48 prescriptions, out of the 85 prescriptions analysed, included adjuvant therapy. The most common drug used was frisium (clobazam) and this was followed by the use of midazolam.

Table 4: Adjuvent Benzodiazepine Therapy

Drugs	n	%
Clobazam	31	64.58
Midazolam	17	35.42
Total	48	100

Benzodiazepines were used in combination with either a single AED or benzodiazepine with 2 AED's or a benzodiazepine with 3 AED's. As shown in Fig. 2, the most common combination was a benzodiazepine with a single AED.

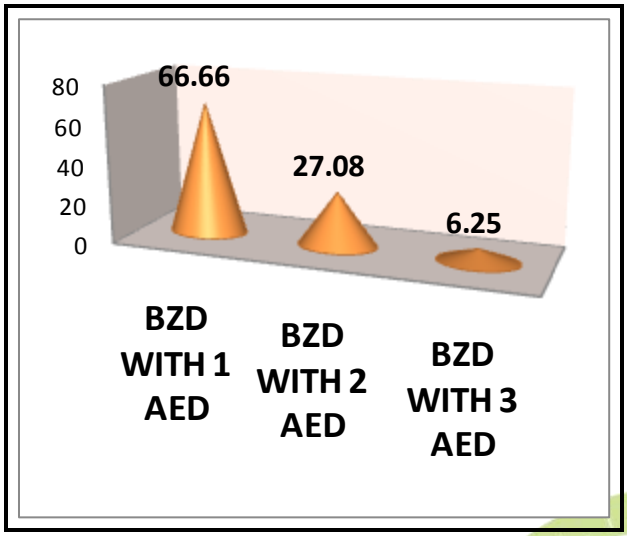

Figure 2: Adjuvent Therapy

Outcome of Pharmacotherapy

All the patients included in the study had an acute episode of seizure and were hospitalized for management. An appropriate treatment regimen was established for each patient and doses were carefully titrated. The outcome of pharmacotherapy was measured in terms of lowered number of seizure episodes, eventually leading to seizure free patients at the end of treatment for 10 follow up days. A total of 44 patients, out of the 85 included were seizure free at the end of treatment (for 10 observation days after discharge). Table V – Table VI and Fig. 3 depict the characteristics of seizure free patients after treatment.

Table 5: Characteristics of Seizure Free Patients

	n	***Seizure Free Patients***	**%**
AED only	37	29	65.90
AED + BZD	48	15	34.09
BZD WITH 1 AED	32	9	20.45
BZD WITH 2 AED	13	5	11.36
BZD WITH 3 AED	3	1	2.27
Total	85	44	100

Table 6: Characteristics of Seizure Free Patients

	n	**Seizure free patients**	**%**
Mono-therapy	58	26	59.09
Poly-therapy	27	18	40.90
Total	85	44	100

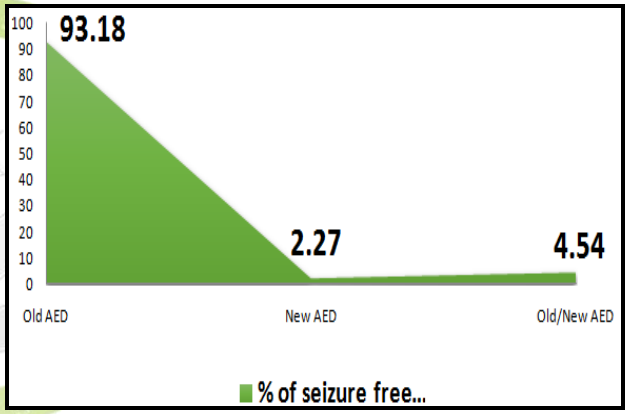

Figure 3: Characteristics of Seizure Free Patients

Average Per Day Cost of Drugs Prescribed for the Treatment of Paediatric Epilepsy in Rajah Muthaiah Medical College Hospital (India)

The study showed that an acute episode of seizure in children (age 0-12 yrs) require hospitalization of about 10(9.60) days on average (SD = 0.1091). An average cost spent on antiepileptic drugs during hospitalization was found to be Rs 278.97 (SD = 1.185). The small value of standard deviation indicates that the data consists of narrow range of values.

The *average per day cost of drugs per patient* for treatment of epilepsy in children (age 0-12 yrs) is approximately found to be INR Rs 29.06 (SD = 3.262)

The total indirect cost spent for treatment of epilepsy in children (age 0-12 yrs) included in the study was found to be approximately Rs. 1,04,085 and the average indirect cost spent per patient was found to be INR Rs. 1224.52 (SD = 338.73).

The average indirect cost spent per patient per single day was found to be INR Rs.122.45

Therefore the total average per day cost per patient for treatment of paediatric epilepsy was found to be INR Rs. 151.51

Cost – Effective Analysis

The total cost spent on individual AED's during the entire study period were, INR Rs.7,065 for Phenytoin, INR Rs.837.54 for Sodium valproate, INR Rs.388.8 Carbamazepine, INR Rs.1,950 Phenobarbitone and INR Rs.572 for Lamotrigine.

The total cost of individual AED's taken into consideration for cost - effective analysis (including cost of drugs involved in monotherapy and combinations, while excluding drugs involved in Old AED/New AED combination therapy) were, Rs. 6,764.4 for Phenytoin, Rs.682.4 for Sodium Valproate, Rs. 388.7 for Carbamazepine, Rs.1,950 for Phenobarbitone, Rs. 312 for Lamotrigine.

The outcomes were gauged in terms of improvement of symptoms after initiating therapy with the drugs, eventually leading to symptom (seizure) free patients (patients classified as complete success). Patients were considered symptom free if they did not experience even a single episode of seizures for 10 observational days following the completion of treatment regimen. (Table VII and VIII).

Total population-level treatment effects (measured in patients classified as complete success) and treatment costs (measured in INR) were combined to form ratios of cost-effectiveness

The probability of complete success was 0.488 for phenytoin, 0.454 for sodium valproate, 0.227 for carbamazepine, 0.400 for phenobarbitone and 0.166 for lamotrigine.

Lamotrigine (NEW AED) was thus the reference strategy and all other treatment alternatives except phenobarbitone were non – dominated. Only phenobarbitone was more expensive and less effective compared to lamotrigine. (Fig. 4)

The incremental cost per additional patient classified as complete success was Rs.73.33 for Old AED's relative to lamotrigine (New AED).

Table 7: Cost-effective analysis in old AED's

Drugs	No. of Patients (Taking Drug)	Avg. Cost/Patient (in Rs.)	Total Cost (in Rs.)	No. of Seizure Free Patients	Expected Probability of Complete Success
Phenytoin	45	150.32	6,764.4	22	0.488
Valproic Acid	22	31.02	682.4	10	0.454
Carbamazepine	22	17.67	388.7	5	0.227
Phenobarbitone	10	195	1,950	4	0.4
Total	99	394.01	9,785.5	41	0.414

Table 8:Cost-effective analysis in new AED

Drugs	No. of Patients (Taking Drug)	Avg. Cost/Patient (in Rs.)	Total Cost (in Rs.)	No. of Seizure Free Patients	Expected Probability of Complete Success
Lamotrigine	6	52	312	1	0.166

The incremental cost per additional patient classified as complete success was Rs.4.53 for phenytoin relative to lamotrigine, Rs. 243.74 for sodium valproate relative to lamotrigine and Rs.234.6 for carbamazepine relative to lamotrigine.

Graph Showing Cost Involved Along With Number of Seizure Free Patients Associated With the Antiepileptic Drugs

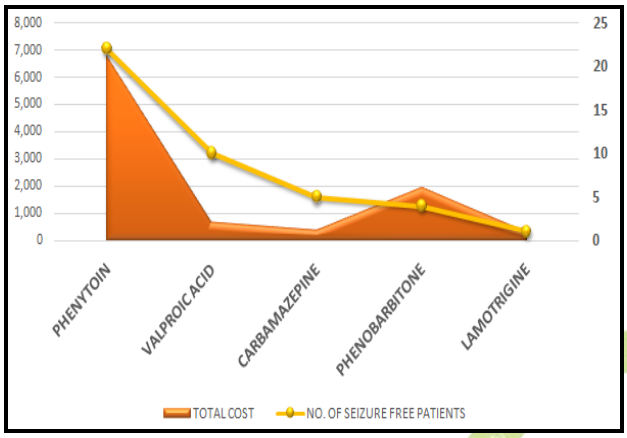

Figure 4: Cost Involved along with Number of Seizure Free Patients Associated with the Antiepileptic Drugs

Incremental Cost-Effective Ratio of Individual Drugs (Old AED'S compared to New AED'S)

1) ICER For Phenytoin Relative To Lamotrigine :-

- Total cost spent on phenytoin = Rs.6,764.4
- Total seizure free patients = 19
- Cost involved to produce single
  = Rs. (6764.4/22) = 307.47

Seizure free patient (additional patient Classified as complete success) (with phenytoin)

- Cost involved to produce single

Seizure free patient (additional patient Classified as complete success)

(With lamotrigine) = Rs. 312

- ICER = 312 – 307.47/1
  = **4.53** Rupees/APCCS

Similarly

2) ICER for Valproic Acid Relative To Lamotrigine:

- **ICER** = 312 – 68.24/1
  = **243.76** Rupees/APCCS

3) ICER for Carbamazepine Relative To Lamotrigine:

- **ICER** = 312 – 77.4/1
  = **234.6** Rupees/APCCS

DISCUSSION

This study described the utilisation, seizure outcomes and cost - effectiveness of AEDs in a cohort of 85 paediatric patients observed and followed up in a tertiary care hospital for duration of six months. The aim of AED therapy is to stop the occurrence or reduce the frequency of seizures with minimal adverse effects, and to improve the patients quality of life. Unlike a previous study.[3,32,58] the present study was a prospective, outcome-based and cost – effective study conducted in a indian tertiary teaching hospital. In addition, most of the previous studies were carried out on adults with epilepsy.[7,8,38,39,58,59]

Patient Demographic Characteristics

Overall, 97 patients were enrolled during the study period. Of these, 85 patients completed study. In keeping with earlier studies.[3,9,10,11,32] epileptic seizures were found to be more common in male than female patients in the present study. Almost 85% of patients were under 10 years of age. Rest, around 15% were in the 10 – 12 years age group. Unlike the study by Hassan S S et a [3], generalised seizures followed by partial seizures were the most common seizure type in our study, which was in line with the findings of Ab Rahman AF et al[32], and . Ravat et al Antiepileptic drugs in paediatric epilepsy[12], where generalized seizures were found to be the most common seizure type.

Drug Utilisation

The choice of drug depends on the proper classification of the type of seizure that occurs.

In this study, average number of antiepileptic drugs prescribed per patient were 1.30, which was lesser then previous studies.[3,13] Monotherapy was the most common type of therapy used in this study, which is consistent with the findings of other studies.[3,6,38] Phenytoin(39.65%) was the most commonly used AED as monotherapy, followed by carbamazepine (27.59%), this was in contradiction with previous studies (*Hassan SS et al and Shih – Hui et al.),*[3,14] where carbamazepine was found to be most commonly used AED as monotherapy. Valproic acid (22.41%) and lamotrigine (10.34%) were the other monotherapy drugs used in this study. The most commonly used polytherapy was dual therapy with phenytoin/phenobarbitone injection. In this study, phenytoin was most commonly used for Acute Symptomatic seizures and sodium valproate was the most commonly used drug for idiopathic generalized epilepsies (tonic clonic, absence seizures), and this was in accordance to Indian Guidelines for Diagnosis and Management of Epilepsy.[15] The present study showed that older AEDs (93.18%) were the most widely used for epilepsy treatment. A trend of prescribing newer AEDs as monotherapy was found in 2.27% of epileptic patients, and prescriptions with combination of old/new antiepileptics was found in 4.54 %, old new combination includes sodium valproate with lamotrigine, whereas the use of older AEDs, such as phenytoin and phenobarbitone, was higher when compared to a previous study[3]. The AEDs were also utilised in combination with BZDs, such as clobazam and midazolam, which are commonly used in adults as AEDs. The present study showed that more than half (56.47%) of the patients were on a AED+BZD therapy. The most common BZD therapy was clobazam (64.58%) followed by midazolam (35.42 %).

Outcome of Pharmacotherapy

Controlling seizures with minimal adverse effects and maintaining the patient's ability to perform daily activities are the critical measures of treatment outcome. In this study, the outcome of the AED therapy was measured in terms of the number of seizures experienced by the patients throughout the follow-up period of 10 days upon completion of treatment. 44 patients remained seizure-free during that period, while 41 experienced an average of 4.39 seizures 10 days. Among the 44 seizure free patients, Monotherapy was found to be superior to polytherapy in controlling seizures as 59.09% of the seizure-free patients were from this group as compared to 40.9% seizure free patients from the polytherapy group. Likewise 41 seizure free prescriptions (93.18%) consisted of old AED's and only 1 (2.27%) prescription consisted of new AED's, rest of the two seizure free prescriptions consisted of combination of old/new AED's. It was noted that 65.90 % (29) of seizure free patients received AED only, and 34.09 % (15) of seizure free patients received adjuvant BZD therapy along with AED.

Statistical Analysis

The statistical student t – test was used to determine whether there is any significant difference in terms of seizure control between

1. Type of treatments
2. Type of antiepileptic drugs and
3. AED therapy compared to combination with adjuvant therapy, in terms of number of seizures produced.

It was found that there was **significant difference between AED alone and AED+BZD(p =0.013)** in terms of seizure control, ***which suggests that the addition of BZDs to the AED therapy did improve the seizure profile of the patients in the present study.*** This was the striking feature of this study when compared to older studies (Hassan SS et al.)[3], where they did not find any significant difference between AED alone and AED+BZD combination.

With regard to drug category (older, newer and their combinations), a significant difference was found among the drug categories older AED's compared to their combination in terms of the number of seizures (p = 0.048), as older AEDs were utilised more frequently in seizure-free patients (93.18%) than their combinations

(4.54%). However no significant difference was found between Old AED's and New AED's (P = 0.059), this being in contradiction with previous studies[3].

No significant difference was found between monotherapy and polytherapy (p = 0.051), although the majority of the seizure-free patients were from the monotherapy group. One possible explanation could be polytherapy and newer AEDs were administered to the more refractory cases that were less likely to do well no matter what one did.

In this study, in contradiction to previous studies[3], phenytoin was the most commonly used monotherapy drug among seizure free patients, it was used in 50% of seizure free patients and was associated with the largest value (0.488) of expected probability of complete success. This finding indicates that phenytoin was more effective as monotherapy compared to all other AED's used in our study. Valproic acid was found to have an expected probability of complete success of 0.454, followed by phenobarbitone (0.400), carbamazepine (0.227) and lamotrigine (0.166).

Cost-effective Analysis

The cost - effectiveness was measured in terms of superfluous amount associated, to produce an additional patient classified as complete success, with New AED's (lamotrigine) compared to Old AED's (phenytoin, valproic acid, carbamazepine and phenobarbitone).Our study found that Old AED's were more cost – effective then New AED's for treatment of epilepsy in paediatric patients, and the *INCREMENTAL COST EFFECTIVE RATIO (ICER)OF NEW AED's TO OLD AED's was found to be Rs.73.33/APCCS (additional patient classified as complete success).* Lamotrigine (NEW AED) was thus the reference strategy and all other treatment alternatives except phenobarbitobe were non – dominated. Only phenobarbitone was more expensive and less effective compared to lamotrigine. This may be attributed to the fact that phenobarbitone was given only as combination therapy and not as monotherapy. However phenobarbitone was found to have much greater value of expected probability of complete success (0.400) than lamotrigine (0.166). No other study previously compared cost – effectiveness along with expected probability of complete success, taking outcome of therapy into consideration among New and Old AED's used in pediatric epilepsy patients in India. This makes our study anomalous from other studies on pediatric epilepsy.

Pharmacoeconomics of Pediatric Epilepsy

In this study a major disparity was not seen in the cost of treatment for individual patients which can be said to be fairly predictable given the not much varying symptoms of the disorder. An average cost spent on antiepileptic drugs during hospitalization was found to be Rs 278.97 (SD = 1.185). The small value of standard deviation indicates that the data consists of narrow range of values. The *average per day cost of drugs per patient* for treatment of epilepsy in children (age 0-12 yrs) is approximately found to be Rs 29.06 (SD = 3.262).The total indirect cost spent for treatment of epilepsy in children (age 0-12 yrs) included in the study was found to be approximately Rs. 1,04,085 and the average indirect cost spent per patient was found to be Rs. 1224.52 (SD = 338.73).The average indirect cost spent per patient per single day was found to be Rs.122.45. Therefore the total average per day cost per patient for treatment of paediatric epilepsy was found to be Rs. 151.51.

CONCLUSION

Epilepsy is the most common neurological disorder in children, and it is characterised by a spontaneous propensity for recurrent and unprovoked seizures. The antiepileptic drug of choice has to be carefully selected for each patient keeping in mind factors such as adverse drugs reaction, over dose and response to drug at recommended doses. Additional care must be taken to titrate dose for paediatric patient based on age and weight of the child.

The study shows that monotherapy was the most common approach in all form of epilepsies.

Phenytoin was the most common drug in both monotherapy as well as polytherapy, while phenobarbitone was found to be used only in polytherapy. Lamotrigine was the only New AED used in the study. Benzodiazepines (clobazam and midazolam) were used as adjuvant therapy in few patients for treatment of epilepsy.

In the study population, phenytoin was found to be more effective than sodium valproate and carbamazepine as monotherapy in terms of producing more seizure free cases, and phenytoin was also associated with the largest value of expected probability of complete success, followed by sodium valproate and phenobarbitone.

A significant difference between AED alone and AED+BZD ($p = 0.013$) in terms of seizure control, *suggesting that the addition of BZDs to the AED therapy did improve the seizure profile of the patients in the present study*, was the striking feature of this study when compared to older studies (Hassan SS et al.)[3], where they did not find any significant difference between AED alone and AED+BZD combination. With regard to drug category (older, newer and their combinations), a significant difference was found among the drug categories older AED's compared to their combination in terms of the number of seizures ($p = 0.048$), as older AEDs were utilised more frequently in seizure-free patients (93.18%) than their combinations (4.54%).

Cost - effectiveness was measured in terms of superfluous amount associated, to produce an additional patient classified as complete success, with New AED's (lamotrigine) compared to Old AED's(phenytoin, valproic acid, carbamazepine and phenobarbitone).

Our study found that Old AED's were more cost – effective then New AED's for treatment of epilepsy in paediatric patients, and the *INCREMENTAL COST EFFECTIVE RATIO (ICER) OF NEW AED's TO OLD AED's was found to be Rs.73.33/APCCS (additional patient classified as complete success).*

Pharmacoeconomical analysis was performed and it was found that the average per day cost of drugs per patient for treatment of epilepsy in children (age 0-12 yrs) is approximately found to be Rs 29.06 (SD = 3.262).

The average indirect cost spent per patient per single day was found to be Rs.122.45. Therefore the total average per day cost per patient for treatment of paediatric epilepsy was found to be Rs. 151.51.

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