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COST-EFFECTIVENESS ANALYSIS (CEA) OF ANTIEPILEPTIC DRUG (AED) TREATMENT IN NEWLY DIAGNOSED PATIENTS WITH EPILEPSY: FINDINGS FROM A TERTIARY CARE HOSPITAL IN INDIA

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ABSTRACT

Objective: To compare cost-effectiveness between newer *vs* older anti-epileptic drug (AED) treatment in patients with newly diagnosed epilepsy. **Material and Methods**: The socio-demographic data of patients with epilepsy (PWE), clinical characteristics and cost components were collected prospectively for 12 months. A decision analysis was carried out to compare cost-effectiveness of treatment strategies between older and newer AEDs with clobazam as add-on. We considered two outcome groups namely the complete success and the failure of seizure control. **Results:** There were 76 (43 males and 33 females) newly diagnosed PWE. Their median age at AED treatment initiation was 23 years (18-46 IQR 19-30) and 35(46%) were from lower/upper lower socioeconomic class. The probability of obtaining complete success varied from 73% with Carbamazepine (CBZ) - CBZ+CLB to 84% with Topiramate (TPM)-TPM+ Clobazam (CLB). Treatment strategy (CBZ) - CBZ+CLB) which recorded lowest cost was considered as reference cost. The expected annual total cost (direct + indirect cost) of treatment per patient during the first year were US$ 416.85; the total direct costs were US$351.45 and AED costs were US$26.17. The TPM-TPM+CLB was a non-dominated strategy, with ICER US$764.98 for total costs relative to CBZ-CBZ+CLB per additional patient with complete success. The AEDs for PHT, VPA, OXC, and LEV alone, and with CLB as add on were dominated (more costly, but less effective). ICER values with highest direct and total treatment cost estimates using one-way sensitivity analysis for CBZ and TPM were found to be non-dominated compared to least costly strategy PHT. However, the ICER value was not found to be cost-effective compared to WHO thresholds. **Conclusion**: The use of newer AED TPM alone and followed by CLB as add on strategy was found to be cost-effective compared to CBZ alone followed by CLB which is justified considering the GDP per capita.

KEYWORDS: epilepsy, antiepileptic drugs (AEDs), patients with epilepsy (PWE), cost-effectiveness analysis (CEA), and decision tree model.

KEY POINT BOX: i) The newer AED with topiramate strategy (TPM-TPM+CLB) was found to be cost-effective compared to older carbamazepine (CBZ-CBZ+CLB). ii) The treatment strategy CBZ-CBZ+CLB was found to have lowest cost and LEV-LEV+CLB the highest cost.

INTRODUCTION

Epilepsy is one of the most common neurological disorders affecting over 69 million people worldwide that imposes heavy burden on individuals, families, and also on healthcare system.[1] It is estimated that there are more than 10 million people with epilepsy in India.[2]

The six major AEDs - carbamazepine, phenobarbital, phenytoin, primidone, valproic acid, and ethosuximide were available for the treatment of all forms of epilepsy prior to 1990.[3] However, in the last decade several newer antiepileptic drugs (AEDs) like felbamate, gabapentin, lamotrigine, topiramate, tiagabine, oxcarbazepine, levetiracetam, and zonisamide have been approved for use by the United States - Food and Drug Administration (US-FDA). This development was based on the fact that the available AEDs did not provide optimal care for patients with epilepsy (PWE) as evidenced by inadequate seizure control or occurrence of side effects.[4] Selecting an AED is based on many factors such as relative efficacy, drug interactions, tolerability and cost.[5] It is well established that the

acquisition costs of newer AEDs are generally higher than the older AEDs, but are superior to older AEDs in controlling seizures. However, there are studies that suggest newer AEDs offer little or no more improved effectiveness compared to older AEDs when used as monotherapy, despite being significantly more expensive.[6,7]

The recent interest in studies involving economic aspects of treating epilepsy by conducting evaluation of drug utilization is due to an increase in the use of newer AEDs, which are considered to dramatically escalate the costs of epilepsy treatment. Therefore, frequent use of newer AEDs is debated in developing nations like India due to relatively greater health needs, coupled with scarcity of resources, demanding efficient use of finances. The pharmacoeconomic (PE) studies are therefore proposed to help in formulating suitable cost-effective treatment options. Hence the present study was designed to evaluate the cost-effectiveness of newer vs older AEDs as first line treatment strategy at a tertiary care hospital located in Bangalore, India.

MATERIAL AND METHODS

Study Design and Site

This was a prospective, observational study conducted at a tertiary care hospital, in Bangalore. The study protocol was reviewed and approved by the Institutional Ethics Review Board. Adult patients with newly diagnosed epilepsy (NDE) ≥ 18 years age, visiting the inpatient/outpatient facilities of the Neurology department were recruited after obtaining written informed consent from each patient and were followed up for one year.

Collection of Data and Treatment Outcome

Data was collected using a specially designed case record form (CRF) which included detailed socio-demographic characteristics, family history, seizure history including frequency, duration; and AEDs prescribed with details on AED type and dose. The data on number of seizure episodes before initiating AED treatment was recorded at the time of enrolment, at the end of six months after treatment and at the end of one year from the date of first visit. The societal perspective was used for the economic analysis. The data on costs of epilepsy treatment in hospital was obtained from the medical records of patients and hospital information systems. Data on AED costs were collected from Current Index of Medical Services (CIMS). The treating physician considered each patient under two categories - complete treatment success when seizure free or as failure when there was no seizure control and/or when seizure reduction was less than 50%. The daily maintenance doses of AEDs were as defined in the decision model suggested by Perucca et al.[8] The above information was collected prospectively over a period of one year during 2012.

Economic Analyses

Cost-effectiveness analysis (CEA) was used for comparing costs of treatment between newer and older AEDs as first-line treatment strategy in NDE patients. Since newer AEDs are generally used either as second-line monotherapy or as adjunctive therapy with older AEDs,[6] we have considered these categories for analysis with decision tree as a modeling instrument. A societal perspective was adopted for the economic evaluation and costs during the first year of AED treatment were considered where the cost and effectiveness measures were not discounted.

Decision Tree Model

In order to depict the potential clinical pathways for AED treatment and its outcomes in the first year, TreeAge software [Williamstown, MA (version 2015)] was used for the decision tree analysis. The model was constructed for the natural progression of epilepsy with a cohort of patients with NDE. Six first-line older AEDs were considered for analysis, namely - phenytoin (PHT), valproic acid (VPA) and carbamazepine (CBZ) and the newer AEDs - levetiracetam (LEV), oxcarbazepine (OXC) and topiramate (TPM). Using these AEDs, six treatment strategies were evaluated comprising of the first-line and add-on treatment. **Figure 1** shows the structure of the model, and is similar to a recently published decision tree model by Knoester et al.[9] In our study the effectiveness of first-line AED was analyzed after 6 months and was continued for the next 6 months if the patient became seizure-free. Physician added the second-line treatment with the first-line AED when seizure control was inadequate. Thus, at the end of the first year, it was assumed that all patients would be grouped into one of the two AED treatment outcome groups, i.e. complete success or failure.

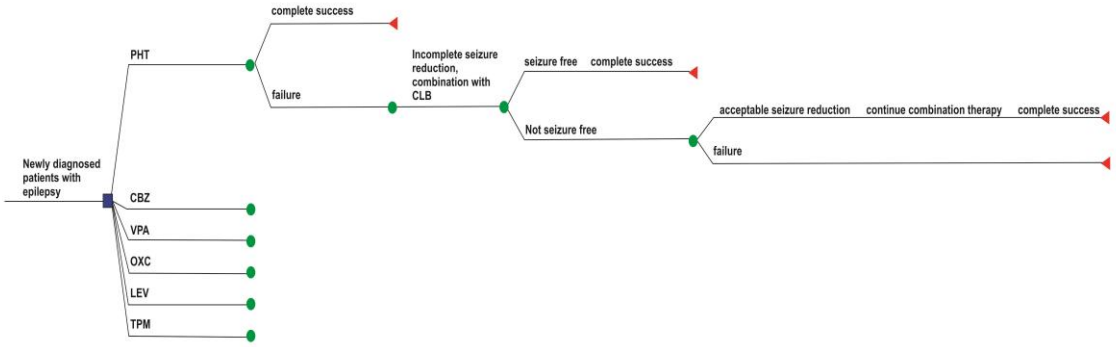

Figure 1: The model shows six first-line AED strategies with carbamazepine (CBZ), followed by clobazam (CLB) in case of failure (CBZ–CBZ+ CLB). The structure of the model applies to all strategies. Circles represent chance nodes, and triangles represent outcome groups of patients during the first year of treatment.

Decision Model Input

The path probabilities for the AED treatment strategies commonly used at the study centre were calculated from data in published literature.[10,11-14]

The available literature on studies which were comparable, with study designs that reported the effectiveness of six AEDs as first-line therapy were searched and reviewed.

The inclusion criteria for the selection procedure for effectiveness of AEDs were:

- patients with NDE >12 years of age
- seizure type - partial and/or generalised tonic–clonic
- evaluation period of minimum 24 weeks/6 months

The first-line AED treatment probabilities of seizure freedom and failure due to the insufficient seizure reduction were calculated from the selected studies **(Table 1)**. All analyses were performed on a per protocol basis. Individual probabilities, as derived from different studies were based on weighted probabilities and the sample size.

Similarly, one study reporting the effectiveness of AEDs as add-on therapy was selected from literature[15] and the effectiveness was assumed to be same for all the add-on treatments after discussing with an expert neurologist **(Table 1)** Three studies related to add-on therapy using newer AEDs – LEV,[16] OXC[17] and clobazam[18] were identified; however, they were not included due to variation in the probabilities. The probabilities for all add-on therapies were based on the findings of a study by Brodie et al.[15] since this was the most frequently used strategy at the study center.

Table 1: Studies referred for incorporating AED effectiveness categories in decision model.

AED	N	Doses mg/day	Starting doses (mg)	Titration	Complete success		Failure		Reference
					Number	%	Number	%	
Phenytoin	072	200	200	300/2weeks	022	30.55	050	69.44	Steiner et al, 1999[10]
Carbamazepine	105	600	200	200mg/2 weeks	064	61.00	041	39.00	Reunanen et al, 1996[11]
Valproic acid	098	Flexible	300	No fixed scheme	057	58.16	041	41.83	Christea et al, 1997[12]
Oxcarbazepine	112	900-2400	300	No fixed scheme	060	53.57	052	46.42	Christea et al, 1997[12]
Levetiracetam	228	500	500	1500mg/2 weeks	111	48.70	117	51.31	Brodie, et al, 2007[13]
Topiramate	262	100-200	25	25mg/week	128	48.85	134	51.14	Privitera et al, 2002[14]

The choice of secondary poly-therapy with AEDs after the first monotherapy regimen was based on the decision of the expert neurologist.

AED Cost Valuation

Unit costs for each AED were calculated by recording the cost incurred per day by each patient, depending on the number of prescribed AEDs and their average. The costs were collected, in Indian rupees, adjusted for inflation for the year 2015 and converted to USD with conversion rate (1INR = US$ 0.014) as on Oct 28, 2016, for analysis.

Table 2: Unit cost per investigational item [USD].

	Baseline	Cost measure
Investigations*	93.78	Per procedure
MRI CT EEG Hemat Bio	89.75 30.42 42.03 10.67 15.07	per procedure
OPD	0.75	per visit
Supplements	0.74	per patient
ADR management	7.44	per patient
Hospitalization †	141.44	per admission
Cost of travel (patient) ‡	5.33	per trip
Cost of travel (caregiver) ‡	3.69	per trip
Loss of wages (patient) §	15.41	per day
Loss of wages (caregiver) §	13.81	per day
Phenytoin	0.10	per day
Phenytoin+ Clobazam	0.25	per day
Valproic acid	0.25	per day
Valproic acid+ Clobazam	0.40	per day
Carbamazepine	0.04	per day
Carbamazepine+ Clobazam	0.19	Per day
Oxcarbazepine	0.29	per day
Oxcarbazepine+ Clobazam	0.22	per day
Levetiracetam	0.47	per day
Levetiracetam+ Clobazam	0.61	per day
Clobazam	0.14	per day
Topiramate	0.25	per day
Topiramate+ Clobazam	0.40	per day

*- Weighted composition of tariffs for different laboratory investigations

†- Weighted composition of tariffs across hospital for various class of beds

‡ - Weighted composition of different modes of transport

§ - Weighted composition of different wages.

AED Cost-Effectiveness Analysis (CEA)

The analysis of the decision tree model was considered in probabilities of a theoretical patient in one of two outcome groups, i.e. complete success or failure, the so-called path probabilities. The probability of these outcomes were then calculated by considering number of patients who responded to the treatment under these two groups from the available study data for each AED **(Table 1)**. [Probability of complete success/failure = (Number of PWE responding to the treatment*100/total number of patients enrolled)].

The expected cost was determined based on the obtained path probabilities, for each of the six AED strategies. The general principles of CEA were then applied to the derived results. Our first objective was to check if certain strategies were dominated by other strategies. The background rule we followed was that a dominated strategy was costlier, but less effective than any other strategy. For the non-dominated strategies, the expected costs and the probability of complete success were combined by the CEA (i.e. the incremental cost-effectiveness ratio [ICER]. Beginning with the least costly strategy, non-dominated alternatives were compared with the calculated incremental ratio using a formula given below.

ICER

$$\frac{\text{(mean annual cost per patient) strategy 2} - \text{(mean annual cost per patient) strategy 1}}{\text{(complete success) strategy 2} - \text{(complete success) strategy 1}}$$

In the absence of validated national thresholds, we used WHO thresholds, i.e. three times the GDP, to establish 'very-cost-effective strategy'.[19]

Sensitivity Analysis

One-way sensitivity analysis was performed using highest and lowest costs for treatment from our sample.

RESULTS

Majority 35(46%) of NDE patients were from the lower socioeconomic class. The cost-effectiveness evaluation of AEDs was carried out in 76 NDE patients under two outcome groups of which 60 (34 men, 26 women) were in the complete success and 16 patients (6 men, 6 women) in the failure groups. **Table 3** presents the average monthly treatment costs per patient, with the exception of drug costs. In both the outcome groups, costs on hospitalization contributed to the highest costs followed by the costs of investigations. Indirect costs contributed to 20% and 11.53% of the total costs in the complete success and failure categories, respectively.

Table 3: Average breakdown of costs with lower and higher estimates [USD] per patient group in rupees per month (and range).

Cost-item	Complete success group			Failure group		
	Average	Lower	Higher	Average	Lower	Higher
Investigations	93.62	4.67	160.26	110.30	20.17	161.12
OPD	3.08	0.75	5.98	3.07	2.99	4.48
Supplements used	7.59	0.52	38.33	7.90	0.97	4.26
ADR management	9.65	0.20	38.94	7.81	0.24	9.60
Hospitalization	148.20	44.08	623.45	197.30	0.00	230.06
Cost of travel (PWE)	21.60	2.24	432.03	24.30	1.49	28.02
Cost of travel (caregiver)	16.69	2.24	186.78	17.48	2.24	28.02
Loss of wages (PWE)	36.49	1.20	301.90	14.29	11.21	28.02
Loss of wages (caregiver)	38.99	5.60	205.46	33.71	9.34	149.43
Total direct Costs medical	262.13	50.22	866.96	326.38	24.37	409.53

Total direct non medical costs	38.29	4.48	618.82	41.78	3.74	56.04
Total Direct costs	300.42	54.70	1485.78	368.16	28.11	465.56
Total Indirect costs	75.48	6.80	507.36	48.01	20.55	177.45
Total Costs	375.90	61.50	1993.14	416.17	48.65	643.01

Cost-Effectiveness Analysis using Decision Tree

Table 4 presents the results of CEA, ranked in ascending order of expected costs. The probability to achieve complete success ranged from 73% (CBZ - CBZ+CLB strategy) to 84% (TPM-TPM+CLB strategy). The treatment strategy that recorded the lowest cost was with combination of older and newer AED i.e CBZ-CBZ+CLB; this is considered here as the reference cost. The expected annual costs per patient during the first year of treatment including, drug costs, total direct costs and total costs (direct + indirect) were found to be US$26.17, US$351.45 and US$416.85 respectively, with the probability of complete success at 73%. The treatment strategy with newer AEDs LEV-LEV+CLB showed the highest costs, US$182.95 for annual drug costs alone, US$516.52 for direct costs, and US$578.56 for total costs (direct+indirect cost), with probability of success at 71%. Only one strategy with newer AEDs, i.e. TPM-TPM+CLB was found to be non-dominated with ICER US$764.98 for total costs relative to CBZ-CBZ+CLB per additional patient under complete success. All the other alternatives, i.e. PHT-PHT+CLB, VPA-VPA+CLB, and OXC-OXC+CLB, were dominated strategies i.e. more expensive and less effective.

Table 4: Cost-effectiveness analysis [CEA] of treatment AEDs in PWE (amount in USD).

Treatment Regimen	Complete success	Annual drug costs	#ICER	Annual direct treatment costs	#ICER	Annual total treatment costs	#ICER
CBZ CBZ+CLB	0.73	26.17	Reference	351.45	Reference	416.85	Reference
PHT PHT+CLB	0.72	56.05	-2987.19 (Dominated)	400.45	-4899.51 (Dominated)	458.09	-4123.77 (Dominated)
TPM TPM+CLB	0.84	105.40	720.21 (Very cost-effective)	438.96	795.56 (Very cost-effective)	501.00	764.98 (Very cost-effective)
VPA VPA+CLB	0.72	103.28	-7710.97 (Dominated)	430.48	-7902.29 (Dominated)	495.10	-7824.63 (Dominated)
OXC OXC+CLB	0.71	117.46	-4564.50 (Dominated)	447.21	-4787.64 (Dominated)	510.80	-4697.10 (Dominated)
LEV LEV+CLB	0.71	182.95	-7838.80 (Dominated)	516.52	-8253.17 (Dominated)	578.56	-8085.06 (Dominated)

ICER-Incremental Cost-effectiveness ratio; CBZ-Carbamazepine, PHT-Phenytoin, VPA-Valproic acid, TPM-Topiramate, OXC- Oxcarbazepine, LEV- Levetiracetam, CLB- Clobazam.

Sensitivity Analysis for AEDs

One-way sensitivity analysis using highest and lowest resource costs from the study sample presented in **(Tables 5 and 6)**, the ICER values of lower treatment costs were similar to those of the annual treatment cost The ICER values with highest direct and total treatment cost estimates for AEDs - CBZ and TPM were found to be non-dominated compared to PHT which was the least expensive strategy. Even though CBZ and TPM were non dominated these were not found to be cost-effective when compared to WHO thresholds.

Table 5: The sensitivity analysis of AED treatment in PWE (amount in USD, lower estimates of resource costs).

Treatment Regimen	Complete success	Annual direct treatment costs	#ICER	Annual total treatment costs	#ICER
CBZ CBZ+CLB	0.73	65.54	Reference	82.96	Reference
PHT PHT+CLB	0.72	89.49	-2394.73 (Dominated)	109.21	-2624.62 (Dominated)
TPM TPM+CLB	0.84	142.97	703.93 (Very cost-effective)	160.61	705.94 (Very cost-effective)
VPA VPA+CLB	0.72	143.29	-7775.09 (Dominated)	159.71	-7674.72 (Dominated)
OXC OXC+CLB	0.71	156.50	-4547.92 (Dominated)	173.40	-4522.20 (Dominated)
LEV LEV+CLB	0.71	220.52	-7749.27 (Dominated)	238.17	-7760.24 (Dominated)

ICER-Incremental Cost-effectiveness ratio; CBZ-Carbamazepine, PHT-Phenytoin, TPM-Topiramate, VPA-Valproic acid, OXC- Oxcarbazepine, LEV-Levetiracetam, CLB-Clobazam.

Table 6: The sensitivity analysis of AED treatment in PWE (amounts in USD, higher estimates of resource costs).

Treatment Regimen	Complete success	Annual direct treatment costs	#ICER	Annual total treatment costs	#ICER
PHT PHT+CLB	0.72	626.03	Reference	1172.65	Reference
CBZ CBZ+CLB	0.73	725.28	9924.83 (Not cost-effective)	1515.51	-34286.21 (Dominated)
OXC OXC+CLB	0.71	786.44	-16041.02 (Dominated)	1523.88	-35123.06 (Dominated)
VPA VPA+CLB	0.72	789.48	-16345 Dominated	1526.25	-35359.66 (Dominated)
LEV LEV+CLB	0.71	826.10	-20007.22 (Dominated)	1562.88	-39023 Dominated
TPM TPM+CLB	0.84	748.55	1020.99 (Cost-effective)	1437.96	2210.91 (Cost-effective)

ICER-Incremental Cost-effectiveness ratio; CBZ-Carbamazepine, PHT-Phenytoin, VPA-Valproic acid, OXC-Oxcarbazepine, LEV-Levetiracetam, TPM-Topiramate, CLB-Clobazam.

DISCUSSION

The goal of any healthcare system is to improve and preserve health, and it is becoming increasingly important to identify the therapies that achieve this efficiently. Assessing the burden of illness and provisioning effectively are priorities for providers, payers and health authorities. It is, therefore, important to choose interventions that are effective, both clinically and economically to ensure access, availability and acceptability to patients. The evidence for such decision making comes from clinical and pharmacoeconomic studies that demonstrate cost-effectiveness - the evidence of which often drive market access and reimbursement strategies.

The recent advancements in drug development have made it possible for pharmacotherapy as one of the main options in the treatment of epilepsy. Evidences for the randomized clinical trials and meta-analysis have shown that newer AEDs compared to placebo are superior in decreasing seizure frequency when used as adjunctive therapy in patients with refractory partial or generalized seizures.[20] There are reports that the newer AEDs, in addition to efficacy have offered improved safety and tolerability profiles than the older AEDs.[21] However, head to head comparison between the older and newer AEDs in newly diagnosed patients with epilepsy have largely failed to detect any significant differences in efficacy outcome.[22] Hence, Chung and colleagues[23] have raised doubts regarding superiority of newer AEDs as well as on their long term value for the reasons mentioned. Since AEDs are diverse in their mechanisms of actions and clinical characteristics, the economic analysis which considers both costs and outcomes is hypothesized to help in informed decision making process. With a dearth of well designed trials comparing newer AEDs, economic modelling techniques are becoming popular and are employed to evaluate the cost-effectiveness of treatment options for epilepsy. In addition, while clinical trials are usually reported to predict the treatment outcomes for a shorter duration, the economic models are said to predict treatment outcomes over a longer duration of time.

Our study presents a decision model for treatment of newly diagnosed PWE. We found that the cost of treatment in patients with NDE was lowest using the newer strategy TPM-CLB. The results of earlier monotherapy studies in patients with NDE show newer AEDs having apparently similar effectiveness but significantly higher acquisition costs than the older AEDs. Based on a decision model that included quantification of uncertainty associated with the decision regarding the cost-effectiveness of AEDs[24] the newer AEDs used as monotherapy for newly diagnosed partial epilepsy which was most frequent types encountered at our study center in the present study showed similar benefits but were more expensive than the older AEDs. In patients with refractory epilepsy, newer AEDs were more effective but more expensive than the older AEDs, and were cost-effective at a higher threshold. Knoester et al[9] have reported older AED valproate as more cost-effective than lamotrigine (LTG) in patients with newly diagnosed generalized epilepsy. However, this difference in study outcome is difficult to explain. The only exception was that the study on cost-effectiveness with topiramate (TPM) over a 15 year time horizon dominated several older and newer generation AEDs at a 6% discount rate with fairly high ICER value.[25]

A study by Maltoni and Messori reported the cost-effectiveness of TPM as an adjunctive therapy in patients with refractory epilepsy where the cost per additional QALY was $US 40078.[26] Further, Selai et al[27] compared cost per satisfied patient receiving TPM with LTG as an adjunctive therapy and found it to be $US132 and $US256 respectively.

A cost-effectiveness study by Frew et al[28] reported that though the newer AEDs are expensive, they are equal in efficacy. Studies conducted by Knoester et al, and Connek et al[9,29] in NDE patients support the use of older

AEDs. A study by Boon et al[30] has shown the favourableness of surgery in patients with refractory epilepsy compared to conventional treatment. These differences in reporting AED treatment outcomes may be attributed to differences in study populations (NDE and refractory epilepsy) as well as design.

It is therefore suggested that each country establish threshold values on which to base funding decisions for new treatment interventions, which could be a major challenge. The WHO has proposed to consider the wealth of an individual country in deciding thresholds for economic value - specifically, multiples of a country's per-capita GDP.[19,31] Also, the cost-effectiveness of new treatments with an ICER of less than or equal to the per-capita GDP are considered very cost-effective, one to three times the GDP as cost-effective, and more than three times as not cost-effective. In our study, the new AED - TPM compared to conventional regimens was cost-effective and is justified considering the GDP per capita. Among the new AEDs prescribed at our center, TPM can be considered to be cost-effective in comparison with CBZ (as reference) in treating adult patients with NDE. Other newer AEDs (oxcarbazepine and levetiracetam) for treating the target population, do not appear to be cost-effective compared to older AEDs.

Studies suggest second-generation AEDs are preferred because of their more favorable pharmacokinetic and pharmacodynamic profiles compared to the first-generation[32] In our study clobazam was most frequently used add on therapy similar to another Indian study by Joshi et al[33] where clobazam was used as add on drug.

The present study has several strengths such as, study data was collected for 12-month duration; the treatment costs for two outcome groups namely, probability of complete success and failure where combination AED therapy was used, have been corroborated using recently published decision tree model,[9] the drug costs were from the latest reference of Current Index of Medical Services (CIMS), and patient outcomes were considered from a practicing senior neurologist at the study hospital.

There are a few limitations of the study. Clinical data was collected from a referral single center, from a large city in South India, and hence may not represent the costs in other parts of India; the cost-effectiveness was not done alongside single randomized clinical trial (RCT). We have considered the average resource utilization costs of our entire sample along with the drug costs to calculate the ICER values. When we evaluated the costs of individual AEDs and the subsequent utilization of resources, we observed that with two AEDs, VPA and LEV the average cost of complete failure was more than 20% in comparison with the average total costs, this implies that we may have underestimated the resource utilization in our model. Further, the determinants of quality of life to estimate utility values could have been incorporated. However, our study illustrates that the outcome of CEA for choice of AED effectiveness depends on the inclusion criteria as reported by Knoester et al.[9]

CONCLUSIONS

The use of newer AED TPM alone and followed by CLB as add on strategy was found to be cost-effective compared to CBZ alone followed by CLB which is justified considering the GDP per capita. The need for prospective real world studies with sufficient sample size to compare strategies of first line AEDs and add on treatment for future economic evaluation may be suggested especially for resource poor countries like India.

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