

COST ANALYSIS OF LONG ESTABLISHED AND NEWER ORAL ANTIEPILEPTIC DRUGS AVAILABLE IN THE INDIAN MARKET

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ABSTRACT

Background: Large number of pharmaceutical companies manufactures antiepileptic drugs in India. The price variations among the marketed drugs are wide. **Aims:** The present study was aimed to find the cost of different oral antiepileptic drugs available in Indian market as monotherapy, combination therapy and number of manufacturing companies for each, to evaluate difference in cost of different brands of same dosage of same active drug by calculating percentage variation of cost. **Methods and Materials:** Cost of a drug being manufactured by different companies, in the same strength and dosage forms was obtained from "Indian Drug Review" Vol. XXI, Issue No.4, 2014 and "Current Index of Medical Specialties" July-October 2014. The difference in the maximum and minimum price of the same drug manufactured by different pharmaceutical companies and percentage variation in price was calculated. **Results:** The percentage price variation noted of long-established drugs was – Phenytoin (50mg): 140%, Carbamazepine (100mg): 1033%, Phenobarbital (30mg) : 730%, Valproic acid (300mg) : 420%. Newer drugs –Levetiracetam (250mg): 75%, Lamotrigine (25mg): 66%, Topiramate (50mg): 108%, Zonisamide (100mg): 19%. **Conclusion:** The percentage price variation of different brands of the same commonly used long-established oral antiepileptic drug manufactured in India is very wide. The formulation or brand of Antiepileptic drugs (AED's) should preferably not be changed since variations in bioavailability or different pharmacokinetic profiles may increase the potential for reduced effect or excessive side effects. Hence, manufacturing companies should aim to decrease the price variation while maintaining the therapeutic efficacy.

INTRODUCTION

Epilepsy is a chronic non-communicable disorder of the brain that affects people of all ages often interfering with education and employment. Epilepsy is defined by International League Against Epilepsy (ILAE) as a condition characterized by recurrent (two or more) epileptic seizures, unprovoked by any immediate identified cause.^[1] According to the World Health Organization (WHO), of the 50 million people with epilepsy worldwide, 80% reside in developing countries.^[2] It is estimated that there are more than 10 million persons with epilepsy in India. Its prevalence is about 1% in Indian population.^[3] The prevalence is higher in the rural (1.9%) compared to urban population (0.6%).^[4,5] The estimated burden of epilepsy using the disability adjusted life years (DALYs) accounts for 1% of the total burden of disease in the world, excluding that due to social stigma and isolation, which further add to the disease burden.^[6] In many developing countries, people with epilepsy do not receive appropriate treatment for their condition, a phenomenon called treatment gap (TG), which is defined as the number of people with active epilepsy not on treatment (diagnostic and therapeutic) or on inadequate treatment, expressed as a percentage of the total number with active epilepsy.^[7] The magnitude of epilepsy

treatment gap in India ranges from 22% among urban, middle-income people to 90% in rural India.^[8]

In order to reduce this gap in the context of limited resources, it would be necessary to specify the important causes of gap for a particular community and the most cost-effective resource for a particular situation.^[9,10-12] The Indian pharma market size is expected to grow to US\$ 85 billion by 2020. The growth in Indian domestic market will be on back of increasing consumer spending, rapid urbanization, and raising healthcare insurance and so on.^[13]

The cost of drug plays a crucial role in patient's care especially in developing countries and constitutes an essential part of rational drug prescription. In recent years more emphasis has been given on cost effective practice which should be adopted by clinicians. Cost of drugs is an important factor influencing compliance with treatment.^[14]

The epileptic seizures are a common disorder for which patients have to take medication for a prolonged period, sometimes even life-long. It is necessary for the clinicians to prescribe most effective, appropriate and economical treatment regimen available.

Estimation of the economic burden of epilepsy is of pivotal relevance to enable a rational distribution of healthcare resources. Being one of the common brain disorders with

varying etiologies, which can present at any age, requiring prompt therapy and with the aim to promote rational pharmacotherapy we decided to study the cost of different brands of antiepileptic drugs available in Indian market.

MATERIALS AND METHODS

Study design: This was an analytical study.

Exclusion criteria: The drug formulation being manufactured by only one company was excluded.

The study was conducted by the Department of Pharmacology, Topiwala National Medical College & B.Y.L. Nair Charitable Hospital, Mumbai.

Methodology: Price in Indian rupees (INR) of oral antiepileptic drugs manufactured by different pharmaceutical companies in India, in the same strength was obtained from "Indian Drug Review" (IDR) Vol. XXI, Issue No.4, 2014 and "Current Index of Medical Specialties"(CIMS)⁽¹⁵⁾ July-October 2014. The prices of 18 oral antiepileptic drugs (16 single and 2 combinations), available in 56 different formulations were analyzed.

Cost of the oral antiepileptic drug formulation was calculated for an average of 10 tablets as the number of tablets available per strip varied. Difference in the maximum and minimum price of the same drug formulation manufactured by different pharmaceutical

companies and percentage variation in price was calculated.

Percentage cost variation was calculated as follows:^[14]

$$\%CV = \frac{\text{Price of most expensive brand} - \text{least expensive brand}}{\text{Price of least expensive brand}} \times 100$$

(CV= Cost variation)

Statistical analysis: Findings of our study were expressed as absolute numbers as well as percentage.

RESULTS

Table 1 shows variation in cost of long - established oral antiepileptic drugs used as a single drug therapy. The percentage variation noted in the cost was - Carbamazepine (100 mg): 1033%, Phenobarbital (30 mg): 730%, Valproic acid (300 mg): 420%, Divalproax sodium (500 mg): 378% and Diazepam (5 mg): 374%.

Table 2 shows variation in cost of oral antiepileptic drugs used in combination. The percentage variation noted in the cost was Sodium valproate + Valproic acid (333+145 mg): 76.67%, Phenobarbital + Phenytoin (30+100 mg): 354.55%.

Table 3 shows variation in cost of newer oral antiepileptic drugs used as single drug therapy. The percentage variation noted in the cost was - Pregabalin (75 mg): 143%, Topiramate (50 mg): 108%, Levetiracetam(250 mg): 75%, Oxcarbazepine (150 mg): 59%.

Table 1: Price variation in long-established oral antiepileptic drugs

Drug	Formulation	Doses(mg)	No.of Manuf. Companies	Minimum price (INR)	Maximum price (INR)	% Price variation
Carbamazepine	4	100	13	6.18	70.00	1033
		200	22	11.17	120.00	974
		300	5	18.24	28.28	55
		400	11	24.24	37.71	56
Phenytoin	3	50	3	7.49	18.00	140
		100	9	8.36	21.10	152
		300	2	50.19	56.66	13
Phenobarbitone	2	30	3	4.95	41.08	730
		60	3	8.25	28.02	240
Divalproex sodium	7	125	7	17.00	30.30	78
		250	21	24.00	84.00	250
		500	25	32.00	153.00	378
		750	9	85.00	106.05	25
		1000	6	99.00	115.00	16
		200	3	29.50	35.00	19
Valproic acid	3	200	15	19.50	42.00	115
		300	8	25.90	56.00	420
		500	9	39.90	93.00	133
Diazepam	3	2	3	12.65	20.20	60
		5	9	7.00	33.21	374
		10	8	11.75	40.85	248
Lorazepam	2	1	11	7.80	30.00	285
		2	10	10.59	35.00	230
Clonazepam	4	0.25	9	7.00	16.25	132
		0.5	23	9.63	45.00	367
		1	13	12.50	37.00	196
		2	16	31.68	67.00	111
Clobazam	3	5	9	23.00	53.52	133
		10	9	43.00	106.37	147
		20	4	79.90	146.00	83

INR: Indian rupees. The prices of 18 oral antiepileptic drugs (16 single and 2 combinations), available in 56 different formulations were analyzed.

Table 2: Price variation among combination therapy

Drug	Formulation	Doses (mg)	No of Manufa. Companies	Minimum price (INR)	Maximum price (INR)	% Price variation
Na valproate+ valproic acid	2	200+87	7	36.50	62.50	71.23
		333+145	7	60.00	106.00	76.67
Phenobarbital+ phenytoin	1	30+100	3	6.60	30.00	354.55

INR: Indian rupees, Na: sodium

Table 3: Price variation in newer oral antiepileptic drugs

Drug	Formulation	Doses (mg)	No. of Manufacturing Companies	Minimum price (INR)	Maximum price (INR)	% Price variation
Lamotrigine	3	25	4	30.00	50.00	66
		50	7	54.50	90.00	65
		100	7	98.00	158.00	61
Gabapentin	3	100	3	36.20	44.00	22
		300	10	98.75	131.00	33
		400	5	119.50	152.00	27
Pregabalin	3	50	2	58.20	59.00	1
		75	17	56.83	138.00	143
		150	14	114.14	169.00	48
Topiramate	3	25	4	19.00	38.00	100
		50	4	36.00	75.00	108
		100	2	108.00	158.00	46
Levetiracetam	4	250	5	55.00	96.00	75
		500	5	110.00	189.00	72
		750	4	168.00	280.00	67
		1000	2	290.00	360.00	24
Zonisamide	2	50	2	57.00	59.40	4
		100	3	87.79	104.70	19
Oxcarbazepine	4	150	11	26.39	42.00	59
		300	12	48.33	75.00	55
		450	2	110.00	120.00	9
		600	10	90.00	134.00	49

INR: Indian rupees

DISCUSSION

The epilepsies are a spectrum of brain disorders ranging from mild, benign forms to severe, life-threatening and disabling ones. Epilepsies can occur in children, adults and the elderly, as well as following brain trauma, stroke, and brain tumors. There is lack of sufficient data in India comparing the cost of the same antiepileptic drug sold under different brand names by different pharmaceutical companies.^[15]

The drug prices available in CIMS and IDR were compared as they are one of the available sources of drug information that are updated on a regular basis.

In our study, we have found that there were 56 formulations of antiepileptic drugs of which 31 were of long-established antiepileptic drugs, 22 of newer and 3 of combination drugs. So it is not practically possible for any

health care provider to remember the prices of all these brands.

Variations in costs were found to be significant. The ones with significant variations were the cost of the brands of Carbamazepine 100mg varied from Rs.6.18 to Rs.70.00; Phenobarbital 30mg varied from Rs.4.95 to Rs.41.08. Valproic acid 300mg cost varied from Rs.25.90 to Rs. 56.00. Among newer antiepileptics, Pregabalin 75mg varied from Rs.56.83 to Rs. 138.00; Topiramate 50 mg cost varied from Rs. 36.00 to Rs. 75.00. Among the combination therapy, Phenobarbital + Phenytoin (30 mg+100 mg) showed maximum price variation i.e. 354.55%.

Thus, in our study of cost-analysis of various anti-epileptic brands, it has been observed that there is substantial variation in the cost of different brands of same generic

drugs. Anand Krishnan, Ritvik, DebashishChowdhary (2007) have also observed a lot of variation in the cost of anti-epileptic drugs.^[16] Findings of our study is similar to their studies. The intrabrand comparison of newer anti-epileptic drugs also showed wide variation in the cost. Our study is in agreement with the study of Beghi, Ettore, et al (2008) as they have noticed a higher cost of newer anti-epileptic drugs.^[17]

The reasons for this price variation could be as follows-^[18]

1. Government regulations and pricing policies
2. The existing market structure of the pharmaceutical industry
3. Industry costs

Drugs are the mainstay of treatment for epilepsy, and are effective for most patients. It is switching from brand-name to generic antiepileptic or from one generic antiepileptic to another that should be avoided in clinical practice, since subtle differences in bioavailability may disturb optimal degree of seizure control to which the patient was previously successfully titrated.^[19] Even using a parent compound, antiepileptic medication levels can fluctuate if the product source has changed, resulting in toxicity.^[20] In this regard, therapeutic drug monitoring becomes essential specially for phenytoin since it has narrow therapeutic index. It is vital therefore those patients should receive the same brand consistently to avoid loss of control.

In India, a large number of patients are not covered under any individual or government medical insurance. Hence, the patients have to purchase the prescribed drugs by themselves. These wide variations in the prices of different formulations of the same drug have severe economic implications on the Indian Population.

The Government of India has unveiled 'Pharma Vision 2020' aimed at making India a global leader in end-to-end drug manufacture. It has reduced approval time for new facilities to boost investments. Further, the government has also put in place mechanisms such as the Drug Price Control Order (DPCO) and the National Pharmaceutical Pricing Authority (NPPA) to address the issue of affordability and availability of medicines.

There are few antiepileptic drugs included in The National list of essential medicines but still there are many drugs especially the newer antiepileptic drugs such as oxcarbazepine, topiramate etc. having better safety, efficacy profile but not included in the list.^[21-24]

Limitations of this study: Being sources of information were limited to IDR and CIMS. There are various other brands which are marketed in India but not published in the above mentioned sources. Also we have not assessed the prices of parenteral preparations.

CONCLUSION

The percentage price variation of different brands of the same antiepileptic drug manufactured in India is very wide. Considering the prevalence of epilepsy especially in rural India where there are limited resources and poverty, providing a broad overview of available antiepileptic drugs and their prices is of utmost importance. There should be education programs and marketing strategies so that prescribers can select proper medication for their patients

which is cost-effective, tolerable as well as efficacious in accordance to the principles of rational pharmacotherapy.

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