Cost variation analysis of different brands of oral anti-epileptic drugs available in India

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ABSTRACT

Background: Epilepsy is a group of neurological disorders, characterized by seizures, loss of consciousness, muscular contraction. Prevalence of epilepsy in India is about 1%. High medical care cost should be cause of concern for policy makers and service providers. Hence, a study was planned to analyse cost ratio and percentage cost variations of oral antiepileptic drugs available in India.

Methods: An analytical study with maximum and minimum price of 10 tablets/capsules and syrup of one bottle of available strength of each drug was noted in Indian Rupee, using “Current Index of Medical Specialties” July to October 2020; “Drug Today” July To October 2020 volume-1 and “Indian Drug Review” 2020 volume-26 issue 6. Percentage cost variation and cost ratio for individual drugs was compared.

Results: Significant cost variations were found in different brands of same drug. Among established oral antiepileptic drugs, Divalproex sodium 250 mg has highest cost ratio 16.071 and 1507.14% price variation and Clonazepam 0.25 mg with cost ratio 16.005 and 1500.55% price variation. Diazepam 2 mg has lowest cost ratio 1.024 and 2.43% price variation. Among newer oral antiepileptic drugs, Levetiracetam 500 mg has highest cost ratio 66.389 and 6538.93% price variation; least is Oxcarbazepine 450 mg with cost ratio 1.317 and 31.75% price variation.

Conclusions: Epilepsy has long course of treatment. Increased adherence to treatment is achieved by switching to cost-effective therapy and by making Pharmacoeconomics an integral part of Undergraduate and Postgraduate Curriculum.

Keywords: Anti-epileptic drugs, Cost ratio, Percentage cost variation

INTRODUCTION

Epilepsy is a group of neurological disorders characterized by seizures, loss of consciousness, muscular contraction. The etiology in most cases is not known. Some of the causes may bestroke, brain tumors, injury andinfections of the brain, and birth defects through a process known as epileptogenesis. About 50 million people worldwide suffer from epilepsy. There are about 10 million people with epilepsy in India with a prevalence of 1.4

The treatment of epilepsy is a challenging task while selecting an appropriate drug or a combination of drugs that controls seizures most effectively at an acceptable level of adverse effects, taking into account the cost of the drug.

Poverty and Poor health infrastructure are reasons for large treatment gap in epilepsy. Usually, the difference between expensive and inexpensive drugs is not properly appreciated by clinicians. This could be due their ignorance about drug cost. Overestimating the price of
inexpensive drugs or underestimating the price of expensive drugs can result in overall increase in expenditures of patients for a drug.\(^6\) Hence a study was conducted to analyze and compare the cost of various brands and strengths of oral antiepileptic drugs available in India.

**METHODS**

In this analytical study the maximum and minimum price in INR (per 10 tablets/capsules and syrup of one bottle) of all available strengths and dosage form of antiepileptics, manufactured by different companies were noted using Current Index of medical specialties (CIMS), July to October 2020; Drug Today, July To October 2020 volume-1 and Indian Drug Review (IDR) 2020 volume 26 issue 6.\(^7,8\) Antiepileptic drugs in combinations with other classes of drugs were not included in the study.

Percentage cost variation is calculated as Cost variation (%) = \((\text{Maximum cost} - \text{minimum cost}) / \text{Minimum cost}\) x 100\(^9,10\)

Cost ratio is calculated as Cost ratio = Price of the costliest brand/Price of the least costly brand.\(^11\)

**Statistical analysis**

The collected data was noted in MS excel and same was used to generate cone diagrams which involves comparing % price variation and cost ratio of antiepileptics.

**RESULTS**

Significant cost variations were found in different brands of same drug. Among well-established oral antiepileptic drugs, Divalproex sodium 250 mg has highest cost ratio 16.071 and 1507.14% price variation, followed by Clonazepam 0.25 mg with cost ratio 16.005 and 1500.55% price variation. Diazepam 2 mg has lowest cost ratio 1.024 and 2.43% price variation.

Table 1: The different available strengths, maximum and minimum prices of each available strength, % price variations and cost ratios for well-established oral antiepileptic drugs.

| Drug               | Dose (mg) | No. of brands | Max Price (INR) | Min Price (INR) | Cost Ratio | % Price variation |
|--------------------|-----------|---------------|-----------------|-----------------|------------|------------------|
| Carbamazepine      | 100       | 16            | 70              | 6.19            | 11.308     | 1030.85          |
|                    | 200       | 31            | 120             | 19.04           | 24.77      | 49.89            |
|                    | 300       | 4             | 38.42           | 1.995           | 12.743     | 1174.36          |
|                    | 400       | 14            | 37.13           | 1.498           | 1.294      | 29.40            |
| Phenytion          | 50        | 6             | 15.85           | 6.49            | 2.442      | 14.22            |
|                    | 100       | 14            | 170             | 13.34           | 12.743     | 1174.36          |
|                    | 300       | 4             | 67.20           | 51.93           | 1.294      | 29.40            |
| Clobazam           | 5         | 20            | 78.30           | 5.5             | 14.236     | 1323.63          |
|                    | 10        | 20            | 137.70          | 41              | 3.348      | 235.85           |
|                    | 20        | 7             | 313.03          | 81              | 3.864      | 286.45           |
| Divalproex sodium  | 125       | 5             | 80              | 19.37           | 4.13       | 313.01           |
|                    | 250       | 28            | 90              | 5.5             | 16.071     | 1507.14          |
|                    | 500       | 34            | 141.08          | 32              | 4.408      | 340.87           |
|                    | 750       | 9             | 182             | 12.2            | 14.918     | 1391.08          |
| Valproic acid      | 200       | 32            | 119             | 21              | 5.666      | 466.66           |
|                    | 300       | 16            | 68.96           | 34              | 2.028      | 102.82           |
| Lorazepam          | 500       | 24            | 111             | 58.30           | 1.903      | 90.39            |
|                    | 0.25      | 32            | 28.81           | 1.8             | 16.005     | 1500.55          |
|                    | 0.5       | 57            | 48.92           | 3.2             | 15.287     | 1428.75          |
|                    | 1         | 28            | 47.16           | 4.1             | 11.502     | 1050.24          |
|                    | 2         | 29            | 99              | 7.2             | 13.75      | 1275             |
|                    | 2         | 4             | 16.39           | 16              | 1.024      | 2.43             |
|                    | 5         | 6             | 15.83           | 8.9             | 1.778      | 77.86            |
|                    | 10        | 4             | 77.98           | 12.30           | 6.339      | 533.98           |
|                    |           |               |                 |                 |            |                  |
|                    | 1         | 14            | 27              | 7.68            | 3.515      | 251.56           |
|                    | 2         | 14            | 35              | 15.17           | 2.307      | 130.71           |
Among newer oral antiepileptic drugs, Levetiracetam 500 mg has highest cost ratio 66.389 and 6538.93% price variation while Oxcarbazepine 450 mg has least cost ratio 1.317 and 31.75% price variation.

The different available strengths, maximum and minimum prices of each available strength, % price variations and cost ratios for well-established oral antiepileptic drugs are given in Table 1.

Highest percentage price variation among available strengths for well-established oral antiepileptic drugs are given in Figure 1.

Lowest percentage price variation among available strengths for well-established oral antiepileptic drugs are given in Figure 2.

Highest cost ratio among available strengths for well-established oral antiepileptic drugs are given in Figure 3.
Lowest cost ratio among available strengths for well-established oral antiepileptic drugs are given in Figure 4.

| Drug            | Highest % Price Variation | Lowest Cost Ratio |
|-----------------|---------------------------|-------------------|
| Lorazepam 1 mg | 51.5                      | 2.55              |
| Diazepam 10 mg  | 1000.0                    | 6.33              |
| Clonazepam 0.25 mg | 1500.05            | 16.005            |
| Valproic acid 200 mg | 1507.44             | 5.666             |
| Divalproex sodium 250 mg | 1323.67         | 14.071            |
| Clonazepam 5 mg | 1174.36                   | 12.743            |
| Phenytoin 100 mg | 1100                      | 11.308            |
| Carbamazepine 200 mg | 1100                  |                   |

Figure 1: Highest % price variation among available strengths for well-established oral antiepileptic drugs.

The different available strengths, maximum and minimum prices of each available strength, percentage price variations and cost ratios for newer oral antiepileptic drugs are given in Table 2.

Highest percentage price variation among available strengths for newer oral antiepileptic drugs are given in Figure 5.

Lowest percentage price variation among available strengths for newer oral antiepileptic drugs are given in Figure 6.

Highest cost ratio among available strengths for newer oral antiepileptic drugs are given in Figure 7.

| Drug            | Lowest % Price Variation | Lowest Cost Ratio |
|-----------------|--------------------------|-------------------|
| Lorazepam 1 mg | 45.0                     | 1.498             |
| Diazepam 10 mg  | 1050.24                  | 1.294             |
| Clonazepam 0.25 mg | 1387.85           | 3.348             |
| Valproic acid 200 mg | 1620.71          | 4.13              |
| Divalproex sodium 250 mg | 1050.24       | 11.502            |
| Clonazepam 5 mg | 20.13                    | 1.024             |
| Phenytoin 100 mg | 124.43                   | 2.307             |
| Carbamazepine 200 mg | 410.72                  |                   |

Figure 3: Highest cost ratio among available strengths for well-established oral antiepileptic drugs.

Lowest cost ratio among available strengths for newer oral antiepileptic drugs are given in Figure 8.

| Drug            | Lowest Cost Ratio |
|-----------------|-------------------|
| Carbamazepine 400 mg | 47.00            |

Figure 4: Lowest cost ratio among available strengths for well-established oral antiepileptic drugs.

Oxcarbazepine 600 mg | 91.62
Zonisamide 100 mg | 124.43
Lacosamide 50 mg | 41.55
Levetiracetam 500 mg | 1938.63
Topiramate 25 mg | 140
Pregabalin 75 mg | 1478.75
Gabapentin 400 mg | 229.92
Lamotrigine 25 mg | 1446.66

Figure 5: Highest % price variation among available strengths for newer oral antiepileptic drugs.
The different available strengths, maximum and minimum prices of each available strength, percentage price variations and cost ratios for fixed dose combination (FDC) of well-established oral antiepileptic drugs are given in Table 3.

The following figures illustrate the price variation and cost ratio among available strengths for newer oral antiepileptic drugs:

**Figure 6:** Lowest % price variation among available strengths for newer oral antiepileptic drugs.

**Figure 7:** Highest cost ratio among available strengths for newer oral antiepileptic drugs.

**Figure 8:** Lowest cost ratio among available strengths for newer oral antiepileptic drugs.

Highest percentage price variation and cost ratio among available strengths for fixed dose combinations of antiepileptic drugs are given in Figure 9.

**Figure 9:** Highest % price variation and cost ratio among available strengths for fixed dose combinations of antiepileptic drugs.

**Figure 10:** Lowest % price variation and cost ratio among available strengths for fixed dose combinations of antiepileptic drugs.

**DISCUSSION**

According to a study conducted by Sai NP et al., highest cost ratio and percentage price variation is shown by Carbamazepine 200 mg and lowest by Oxcarbazepine 450 mg. According to Shukla et al highest cost ratio and percentage price variation is shown by Divalproex 500 mg. In our study, among well-established oral antiepileptic drugs, Divalproex sodium 250 mg has highest cost ratio and percentage price variation while least is by Diazepam 2 mg. And among the newer oral antiepileptic drugs, Levetiracetam 500 mg has highest cost ratio and percentage price variation while least is Oxcarbazepine 450 mg. There is huge price variation among antiepileptic drugs similar to earlier mentioned studies.

Factors like age, sex, psychomotor development or seizure type do not influence adherence of patient to medication. Medication adherence which influences health outcome is mainly affected by cost. Higher medication cost has been
found to be reason for poor adherence of treatment which leads to adverse health outcomes.\(^1\)

Gupta et al had also observed more than 100% variation in the cost of selected anti-epileptics. A lot of variations in different brands of same strength of the newer anti-epileptic drugs like gabapentin, clobazam, levetiracetam in comparison to older first line antiepileptic drugs like phenytoin, phenobarbitone, carbamazepine and valproic acid.\(^1\)

Treatment with generic antiepileptic drugs have been associated with increased adherence and decreased adverse clinical outcomes compared to treatment with branded antiepileptics.\(^1\) Prescribing doctors should give importance to drug prices in country like India where majority of medical bill is paid by patient. 80% of health financing is borne by patients in India.\(^1\) Sincere effort should be made by the concerned authorities to bring more number of antiepileptic drugs under price control since only a few medicines are under drug prices control order currently. Some of the effective tools for regulating drug prices are Drug price control order (DPCO) and National Pharmaceutical pricing (NPPA).\(^1\)

The wide variation in prices of different brands of same drug have severe economic implications in India.\(^2\) Hence there is need to draw attention to reduce cost of therapy. Studies have shown that providing a manual of comparative drug prices with explanatory prescribing advice to physicians helped in reducing the patient’s expenditure, especially those who need long term treatment.\(^9\)

**CONCLUSION**

Epilepsy has a long course of treatment. The percentage price variation of different brands of same antiepileptic drug is very wide. In developing countries like India where patient bears majority of medical bill, prices are of utmost importance. There is urgent need to reduce unnecessary cost variation by changing drug pricing policy from government authorities so that the drugs are affordable to common man. Increased adherence to treatment can be ensured by switching to cost effective therapy by physicians and making Pharmacoeconomics an integral part of undergraduate and postgraduate curriculum.

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