

Cost Variation Analysis of Anti-Migraine Drugs Available in Indian Market

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Abstract: *Introduction:* Migraine afflicts 10%–20% of the population. There are various drugs available in the market for treating acute attack as well as for chronic prophylaxis of migraine. It is beneficial to know about the cost variation of various anti-migraine drugs of different brands available in the Indian market so that whenever possible, a cheaper effective brand can be prescribed to ensure better patient adherence and reduce drug cost as well as total health care cost. *Results:* Among the drugs used for treatment of migraine the highest cost ratio and highest percentage cost variation is shown by Acetaminophen (Paracetamol) 650mg that is (1700) and (169900) respectively. Among the drugs used for prophylaxis of migraine the highest cost ratio and highest percentage cost variation is shown by Amitriptyline 10mg that is (47.57785467) and (4657.785467) respectively.

Keywords: Migraine, prophylaxis, percentage cost variation, cost ratio, Acetaminophen, Amitriptyline

1. Introduction

The most common disorder of central nervous system is the headache disorder. Migraine is the primary headache disorder. Globally, approximately 15% of people are affected by migraine^[1]. In the Global Burden of Disease Study of 2010, it was ranked as the third most prevalent disorder in the world. As of 2016, it is one of the most common causes of disability.

Migraine often begins after puberty and most commonly affects people within the age group of 35-45years. Females are affected more than males in the ratio of 2:1, this is said to be due to hormonal influence.

Migraine headache is characterised by recurrent throbbing headaches which can be of moderate to severe intensity, often aggravating with physical activity, is mostly unilateral, pulsating type, may be associated with nausea, vomiting, increased sensitivity to light, sound and smell. Most commonly these headaches are triggered by stress. The exact cause of the headaches is not known but genetics and environmental factors play a significant role. Migraine is believed to be primarily a neurological disorder, while others believe it to be a neurovascular disorder with blood vessels playing the key role, although current evidence does not support this completely.

Migraine can be divided into two major sub-types.

- 1) Migraine without aura is a clinical syndrome characterised by headache.
- 2) Migraine with aura is primarily characterised by the focal neurological symptoms that usually precede or sometimes accompany the headache.
 - Some patients also experience a pre-migratory phase, occurring hours or days before the headache, which include hyperactivity, hypoactivity, depression, craving for particular foods, repetitive yawning and other less typical symptoms.
 - and a headache resolution phase which includes soreness at the area where migraine occurred,

cognitive difficulty, tiredness, abdominal symptoms, impaired thinking^[6]

Drugs used for treatment and prophylaxis of migraine are as follows:

(A) For acute attack

- 1) Ergot alkaloids: Ergotamine tartrate, dihydroergotamine mesylate
- 2) Triptans: Sumatriptan, zolmitriptan, rizatriptan, naratriptan, almotriptan, frovatriptan, eletriptan⁰.
- 3) NSAIDs: Aspirin, paracetamol, ibuprofen, naproxen, ketoprofen
- 4) Miscellaneous: Caffeine, domperidone, metoclopramide

(B) For prophylaxis

- 1) Beta-blockers: Propranolol, metoprolol, atenolol
- 2) Antidepressants: Amitriptyline, venlafaxine
- 3) Calcium antagonists: Flunarizine, verapamil
- 4) 5HT antagonists: Cyproheptadine, pizotifen, methysergide
- 5) Antiepileptics: Divalproex sodium, topiramate
- 6) Others : Candesartan, riboflavin, botulinum toxin-A

Since there are so many different anti migraine drugs available in the market, there is a high chance of price variation in the different brands of these drugs. According to (Global Burden of Disease 2016 and Disease and Injury Incidence and Prevalence Collaborators, 2017) the economic burden of migraine is the second highest of all brain diseases^[2]

2. Materials and Methods

This research was conducted to compare the cost of different brands of drugs available in India for the treatment and prophylaxis of the migraine. The study was started after getting the approval from Institutional Ethics Committee. We gathered information regarding the prices of various anti migraine drugs manufactured by various companies. Drugs of same formulations and strength were compared together.

The maximum and minimum price of a particular drug was obtained from various sources such as the latest issue of (CIMS) Current Index of Medical Specialties, and from mobile apps like Pharma Sahi Daam, G-Dawa and Indian Drug Index.

Prices were mentioned in Indian Rupee (INR). Following parameters were calculated using the data:

- 1) Difference: calculated as maximum price - minimum price
- 2) Ratio: calculated as $\frac{\text{maximum price}}{\text{minimum price}}$
- 3) Percentage Cost Variation: calculated as $\frac{\text{maximum price} - \text{minimum price}}{\text{minimum price}} \times 100$

Statistical Analysis

- The collected data was entered in Microsoft Excel software in tabulated manner.
- Tables included the minimum and maximum price of the drugs, the ratio, and cost variation analysis.
- Data was analyzed using percentage and proportions.

3. Results

All anti migraine drugs available in the Indian market were included in this study. A total of 30 drugs (21 drugs used in the treatment and 9 drugs used in the prevention of migraine) available in 57 various formulations were analysed.

Among the drugs used for treatment of migraine the highest cost ratio is seen with Acetaminophen (Paracetamol) 650mg (1700), Prochlorperazine 5mg (544.444444), Acetaminophen (Paracetamol) 500mg (319.444444), Domperidone 10mg (256.684492) and lowest cost ratio is

seen with Almotriptan 12.5mg (1.03908956), Almotriptan 6.25mg (1.093920455), Lisuride 25mg (1.163043478). This is depicted in the table number 1.1

Among the drugs used for prophylaxis of migraine the highest cost ratio is seen with Amitriptyline 10mg (47.57785467), Amitriptyline 75mg (33.405), Cyproheptadine 4mg (31.49350649) and lowest ratio is seen with Valproic Acid 125mg (1.918), Valproic Acid 300mg (2.016666667), Valproic Acid 500mg (2.126666667). This is depicted in the table number 1.2

A significant cost variation is seen in same anti migraine drugs of different brands and also of different strength and formulation.

Among the drugs used to treat migraine, the highest percentage cost variation is seen with Acetaminophen (Paracetamol) 650mg (169900), Prochlorperazine 5mg (54344.44444), Acetaminophen (Paracetamol) 500mg (31844.44444), Domperidone 10mg (25568.4492) and lowest cost ratio is seen with Almotriptan 12.5mg (3.908955962), Almotriptan 6.25mg (9.392045455), Lisuride 25mg (16.30434783). This is depicted in the table number 1.1

Among the drugs used to prevent the migraine, highest percentage cost variation is shown by Amitriptyline 10mg (4657.785467), Amitriptyline 75mg (3240.5), Cyproheptadine 4mg (3049.350649) and lowest ratio is seen with Valproic Acid 125mg (91.8), Valproic Acid 300mg (101.6666667), Valproic Acid 500mg (112.6666667). This is depicted in the table number 1.2

S.No	Drug	Strength	Quantity	Formulations	Max	Min	Diff	Ratio	% Variation
1	Amitriptyline	10mg	10	tab	137.5	2.89	134.61	47.57	4657.7
		25mg	10	tab	60.2	5	55.2	12.04	1104
		50mg	10	tab	174.65	15.6	159.05	11.19	1019.5
		75mg	10	tab	66.81	2	64.81	33.405	3240.5
2	Cyproheptadine	4mg	10	tab	48.5	1.54	46.96	31.49	3049.3
		200mg	60ml	syp	143.25	19	124.25	7.53	653.94
3	Flunarizine	5mg	10	tab	80	10	70	8	700
		10mg	10	tab	265.5	20	245.5	13.275	1227.5
4	Fremanezumab	225mg	1	inj	8500	3278	5222	2.59	159.30
5	Propranolol	10mg	10	tab	30.96	3	27.96	10.32	932
		20mg	10	tab	57.1	9.69	47.41	5.892	489.26
		40mg	10	tab	49	9.36	39.64	5.23	423.504
		80mg	10	tab	64.35	7.71	56.64	8.346	734.63
6	Gabapentin	100mg	10	tab	111.13	39.86	71.27	2.788	178.80
		300mg	10	tab	312	83	229	3.759	275.90
		400mg	10	tab	159	19.98	139.02	7.957	695.79
7	Pizotifen	0.5mg	10	tab	200	40.27	159.73	4.96	396.64
8	Topiramate	25mg	10	tab	98.5	23	75.5	4.28	328.260
		50mg	10	tab	203	46	157	4.413	341.30
		100mg	10	tab	402	77.29	324.71	5.201	420.10
9	Valproic Acid	125mg	10	tab	38.36	20	18.36	1.918	91.8
		200mg	10	tab	71.07	21	50.07	3.384	238.42
		250mg	10	tab	68.75	30	38.75	2.29	129.16
		300mg	10	tab	121	60	61	2.016	101.66
		500mg	10	tab	70.18	33	37.18	2.126	112.6

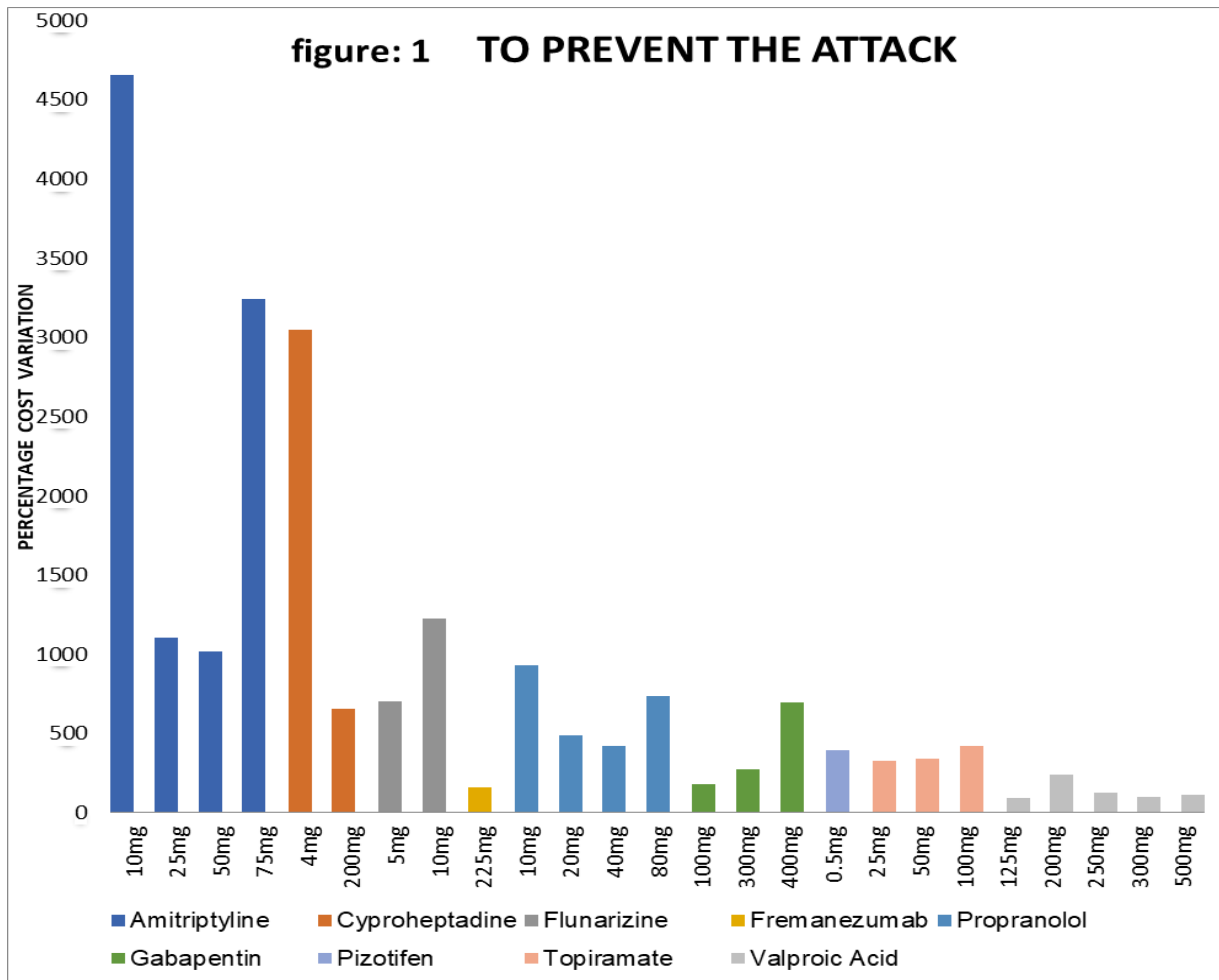


Table 1.2

TO TREAT THE ATTACK

S.No	Drug	Strength	Quantity	Dosage Form	Max	Min	Diff	Ratio	% Variation
A ANTIEMETICS									
1	Domperidone	10mg	10	tab	480	1.87	478.13	256.68	25568.44
2	Metoclopramide	5mg	2ml	Inj	5	1.5	3.5	3.33	233.33
		10mg	10	tab	100	1.8	98.2	55.55	5455.56
3	Prochlorperazine	5mg	30ml	Syp	250	5.34	244.6	46.81	4581.64
		5mg	10	tab	980	1.8	978.2	544.4	54344.44
4	Promethazine	12.5mg	2ml	inj	18.62	4.05	14.57	4.59	359.75
4	Promethazine	25mg	10	tab	300	2.16	297.8	138.8	13788.88
B ERGOT ALKALOIDS									
1	Dihydro-ergotamine	4mg	1	nasal spray	5292	3763	1529	1.40	40.63
2	Ergotamine	1mg	10	tab	142.86	25	117.8	5.71	471.44
		1mg	1ml	inj	45.39	5.09	40.3	8.91	791.74
3	Lisuride	25mg	10	tab	107	92	15	1.16	16.30
4	Methysergide	1mg	60	tab	4890	3259	1631	1.50	50.046
C NSAIDS									
1	Diclofenac	0.10%	5ml	eye drops	55	14.6	40.4	3.76	276.71
		0.10%	10ml	eye drops	135	5.5	129.5	24.54	2354.54
2	Ibuprofen	200mg	10	tab	244.62	3.06	241.5	79.94	7894.11
		200mg	100	tab	432.25	26	406.2	16.62	1562.5
		400mg	10	tab	34.6	3.93	30.67	8.80	780.40
		400mg	100	tab	188	35	153	5.37	437.14
		300mg	10	cap	69.51	8.17	61.34	8.50	750.79
		10mg	60ml	suspension	35.21	6.36	28.85	5.53	453.61
3	Mefenamic acid	100mg	10	tab	38.5	8.5	30	4.52	352.94
		250mg	10	tab	187.5	4.3	183.2	43.60	4260.46
		500mg	10	tab	65	6.61	58.39	9.83	883.35
		250mg	10	cap	5940	6	5934	990	98900
4	Naproxen	100mg	60ml	syp	36	22	14	1.63	63.63
4	Naproxen	250mg	10	tab	75	25.39	49.61	2.95	195.39

		500mg	10	tab	103.37	55.75	47.62	1.85	85.41
D	SELECTIVE 5-HT AGONIST								
1	Almotriptan	6.25	10	tab	192.53	176	16.53	1.09	9.39
		12.5	10	tab	84	80.84	3.16	1.03	3.90
2	Rizatriptan	5mg	10	tab	232.66	37.25	195.4	6.24	524.59
		10mg	10	tab	231.72	63.5	168.2	3.64	264.91
3	Sumatriptan	25mg	10	tab	37.15	19	18.15	1.95	95.52
		50mg	10	tab	57.53	36	21.53	1.59	59.80
		100mg	10	tab	199	72	127	2.763	176.38
4	Zolmitriptan	2.5mg	10	tab	50	18.28	31.72	2.73	173.52
E	SIMPLE ANALGESICS								
1	Acetaminophen (Paracetamol)	500mg	10	tab	575	1.8	573.2	319.44	31844.44
		650mg	10	tab	204	0.12	203.88	1700	169900
2	Aspirin	75mg	10	tab	159.62	1.82	157.8	87.70	8670.32
		150mg	10	tab	42.1	2.85	39.25	14.77	1377.19
3	Codeine	10mg	100ml	syp	62	51.77	10.23	1.19	19.76
4	Dipyron	500mg	10	tab	59.11	8.33	50.78	7.09	609.60
F	MISCELLANEOUS								
1	Rimegepant	75mg	8	tabs	1,09,615.78	71,461.65	38154.13	1.53	53.39

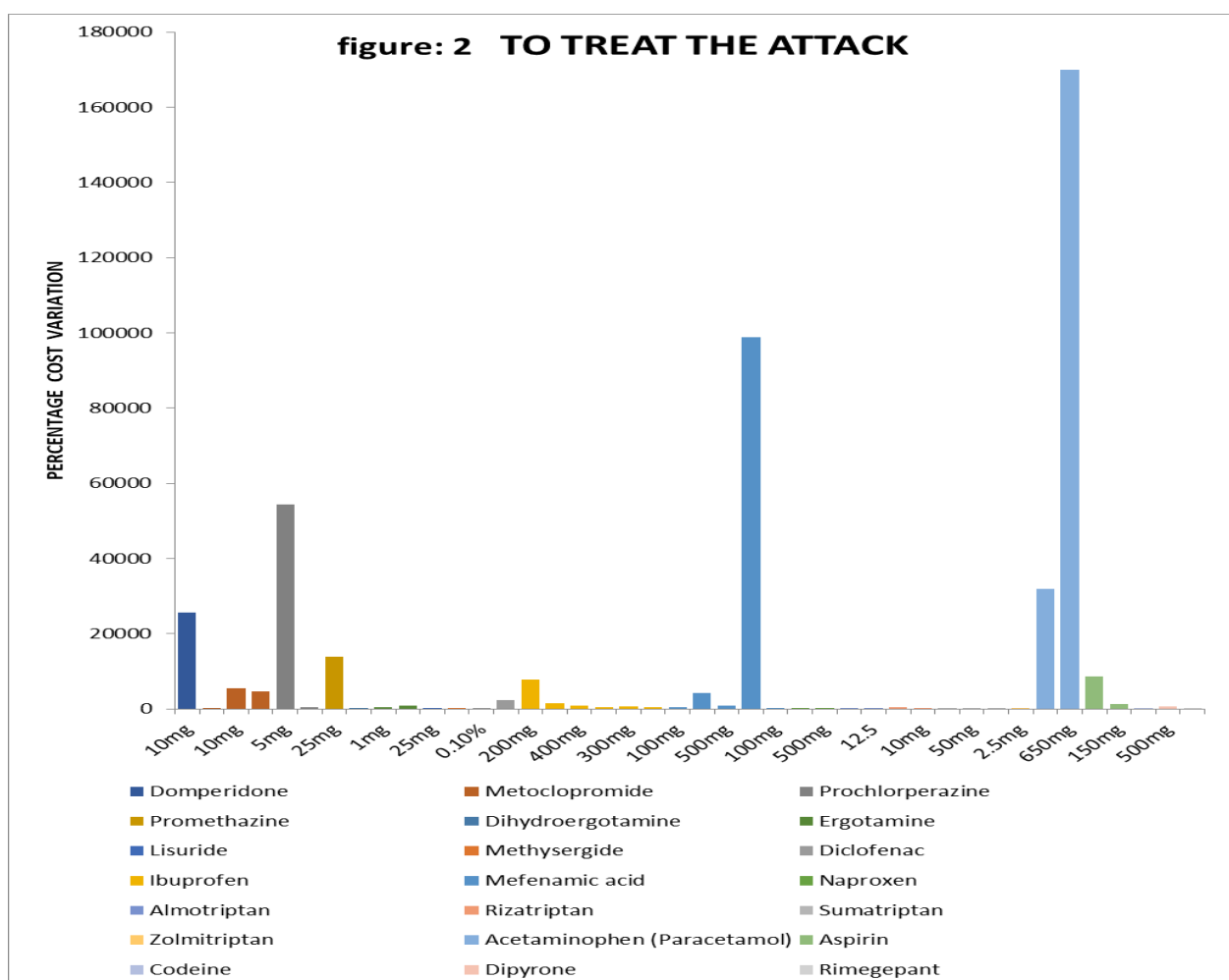


Table 2.1: Minimum and maximum cost, cost difference, cost ratio and percent cost variation in different brands of anti-emetic drugs

S. No	Drug	Strength	Quantity	Dosage Form	Max	Min	Diff	Ratio	% Variation
1	Domperidone	10mg	10	tab	480	1.87	478.13	256.684492	25568.4492
2	Metoclopramide	5mg	2ml	Inj	5	1.5	3.5	3.333333333	233.3333333
		10mg	10	tab	100	1.8	98.2	55.55555556	5455.555556
		5mg	30ml	Syp	250	5.34	244.66	46.8164794	4581.64794
3	Prochlorperazine	5mg	10	tab	980	1.8	978.2	544.4444444	54344.44444
		12.5mg	2ml	inj	18.62	4.05	14.57	4.597530864	359.7530864
4	Promethazine	25mg	10	tab	300	2.16	297.84	138.8888889	13788.88889

Table 2.2: Minimum and maximum cost, cost difference, cost ratio and percent cost variation in different brands of ergot alkaloids drugs

S.No	Drug	Strength	Quantity	Dosage Form	Max	Min	Diff	Ratio	% Variation
1	Dihydroergotamine	4mg	1	nasal spray	5292	3763	1529	1.406324741	40.63247409
2	Ergotamine	1mg	10	tab	142.86	25	117.86	5.7144	471.44
		1mg	1ml	inj	45.39	5.09	40.3	8.917485265	791.7485265
3	Lisuride	25mg	10	tab	107	92	15	1.163043478	16.30434783
4	Methysergide	1mg	60	tab	4890	3259	1631	1.500460264	50.04602639

Table 2.3: Minimum and maximum cost, cost difference, cost ratio and percent cost variation in different brands of NSAIDS.

S. No	Drug	Strength	Quantity	Dosage Form	Max	Min	Diff	Ratio	% Variation
1	Diclofenac	0.10%	5ml	eye drops	55	14.6	40.4	3.767123288	276.7123288
		0.10%	10ml	eye drops	135	5.5	129.5	24.54545455	2354.545455
2	Ibuprofen	200mg	10	tab	244.62	3.06	241.56	79.94117647	7894.117647
		200mg	100	tab	432.25	26	406.25	16.625	1562.5
		400mg	10	tab	34.6	3.93	30.67	8.804071247	780.4071247
		400mg	100	tab	188	35	153	5.371428571	437.1428571
		300mg	10	cap	69.51	8.17	61.34	8.507955936	750.7955936
		10mg	60ml	suspension	35.21	6.36	28.85	5.536163522	453.6163522
3	Mefenamic acid	100mg	10	tab	38.5	8.5	30	4.529411765	352.9411765
		250mg	10	tab	187.5	4.3	183.2	43.60465116	4260.465116
		500mg	10	tab	65	6.61	58.39	9.833585477	883.3585477
		250mg	10	cap	5940	6	5934	990	98900
		100mg	60ml	syp	36	22	14	1.636363636	63.63636364
4	Naproxen	250mg	10	tab	75	25.39	49.61	2.953918866	195.3918866
		500mg	10	tab	103.37	55.75	47.62	1.854170404	85.41704036

Table 2.4: Minimum and maximum cost, cost difference, cost ratio and percent cost variation in different brands of 5HT receptor antagonists

S. No	Drug	Strength	Quantity	Dosage Form	Max	Min	Diff	Ratio	% Variation
1	Almotriptan	6.25	10	tab	192.53	176	16.53	1.093920455	9.392045455
		12.5	10	tab	84	80.84	3.16	1.03908956	3.908955962
2	Rizatriptan	5mg	10	tab	232.66	37.25	195.41	6.24590604	524.590604
		10mg	10	tab	231.72	63.5	168.22	3.649133858	264.9133858
3	Sumatriptan	25mg	10	tab	37.15	19	18.15	1.955263158	95.52631579
		50mg	10	tab	57.53	36	21.53	1.598055556	59.80555556
		100mg	10	tab	199	72	127	2.763888889	176.3888889
4	Zolmitriptan	2.5mg	10	tab	50	18.28	31.72	2.735229759	173.5229759

Table 2.5: Minimum and maximum cost, cost difference, cost ratio and percent cost variation in different brands of simple analgesics

S. No	Drug	Strength	Quantity	Dosage Form	Max	Min	Diff	Ratio	% Variation
1	Acetaminophen (Paracetamol)	500mg	10	tab	575	1.8	573.2	319.4444444	31844.44444
		650mg	10	tab	204	0.12	203.88	1700	169900
2	Aspirin	75mg	10	tab	159.62	1.82	157.8	87.7032967	8670.32967
		150mg	10	tab	42.1	2.85	39.25	14.77192982	1377.192982
3	Codeine	10mg	100ml	syp	62	51.77	10.23	1.19760479	19.76047904
4	Dipyron	500mg	10	tab	59.11	8.33	50.78	7.096038415	609.6038415

Table 2.6: Minimum and maximum cost, cost difference, cost ratio and percent cost variation in different brands of rimegepant

S.NO	Drug	Strength	Quantity	Dosage Form	Max	Min	DIFF	Ratio	% Variation
1	Rimegepant	75mg	8	tabs	1,09,615.78	71,461.65	38154.13	1.533	53.391

4. Discussion

In this study we have found significant cost variation amongst various anti migraine drugs. Among the drugs used for treatment of migraine the highest cost ratio is seen with Acetaminophen (Paracetamol) 650mg (1700), and lowest cost ratio is seen with Almotriptan 12.5mg (1.03908956). This is depicted in the table number 1.1. Among the drugs used for prophylaxis of migraine the highest cost ratio is seen with Amitriptyline 10mg (47.57785467) and lowest

ratio is seen with Valproic Acid 125mg (1.918). This is depicted in the table number 1.2

A significant cost variation is seen in same anti migraine drugs of different brands and also of different strength and formulation. Among the drugs used to treat the migraine, the highest percentage cost variation is seen with Acetaminophen (Paracetamol) 650mg (169900), and lowest cost ratio is seen with Almotriptan 12.5mg (3.908955962). This is depicted in the table number 1.1. Among the drugs used to prevent migraine, highest percentage cost variation

is shown by Amitriptyline 10mg (4657.785467) and lowest ratio is seen with Valproic Acid 125mg (91.8). This is depicted in the table number 1.2

Similar results were seen in the study carried out by James U. Adelman et al on the cost considerations of acute Migraine treatment, which observed substantial variation in the cost of drugs used in acute migraine treatment. Another study carried out by Vishakha et al (2021) on "Cost Variation Analysis of various brands of topical medications used in Acne vulgaris currently available in Indian Pharmaceutical Market" has shown a wide variation in the prices of different brands of same topical drugs used in treating acne vulgaris in India. Anjali Kushwah et al (2021) conducted a study on "A Pharmacoeconomic Comparison of Cost Variation among Hypolipidemic Drugs Available in Indian Market" that showed a wide variation in cost of hypolipidemic drugs available in Indian market. Many such cost variation studies have been done on different drugs like antihypertensive drugs, anti-diabetic drugs, anti-psychotic drugs, anti-microbial, anti-tuberculosis drugs etc. the results of all such studies also show a wide price variation among various brand of drugs.

5. Conclusion

Migraine is the primary headache disorder. Roughly 1 in 4 to 1 in 8 persons in India suffer from migraine. Only about a half of these patients require migraine treatment. There is significant disability attached to primary headache disorders and the country carries an unseen but huge economic burden. Estimates of the financial cost of headache disorders to society are quite high, mostly due to lost working hours, decreased output and reduced productivity.

In India prices of drugs are very important, as approximately 41.6% of its population are living below the poverty line. So people have to choose between buying medicines or saving that money for their daily needs. Although patients may believe their doctors are aware of the price of the medications they prescribe, but this is frequently not the case. Physicians who treat patients may not always be aware of the cost of the medications. This can lead to prescription of costlier drugs when a cheaper alternative is available in the market. To prevent this, pharmacoeconomics should be incorporated into undergraduate and graduate curriculum. They must be made aware of the price differences between various medicine brands. Doctors must use cost-effective therapies to improve patient compliance with treatment.

In a 2007 systematic study on physician cost awareness, clinicians agreed that knowledge of cost have a significant impact on prescription behaviour and overall patient spending. The price difference between the branded and generic versions of various medications can range from less than 2times to more than 100 times the price. Studies have shown that the branded and costly drugs are in no way superior to their cheaper alternative. This has to be borne in mind while prescribing such drugs.

In today's era where the pharmaceutical companies are competing to be the best, has led to an outburst of many drugs being made available in the market. It is nearly

impossible for an individual to remember the prices of all the drugs. So to tackle these problems doctors should be updated on regular basis so as to make them aware of the cheaper alternatives of the drugs available in the market. This can be done by holding regular seminars, webinars, group discussion, lectures, providing with e-books, etc.

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