

Cost variation analysis of ACE inhibitors in India**Prashant Wadagbalkar¹, Poonam Patel^{2*}, Swati V. Raipurkar³**¹Department of Pharmacology, RKDF Medical College Bhopal, Madhya Pradesh, India²Department of Pharmacology,³Department of Paediatrics, Index Medical College, Indore, Madhya Pradesh, India**Received:** 15 April 2017**Accepted:** 08 May 2017***Correspondence to:**Dr. Poonam Patel,
Email: dr.pp84@gmail.com**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.**ABSTRACT****Background:** Cardiovascular diseases are the most prevalent cause of death and disability in developed and developing countries. There is a wide variation in the prices of antihypertensive drugs marketed in India. Thus, a study was planned to find out variation in cost in the ACE Inhibitors available in India either as a single drug or in combination and to evaluate the difference in cost of various brands of the same ACE Inhibitors and ARBs by calculating percentage variation in cost in Indian rupees.**Methods:** Minimum and maximum costs in rupees (INR) of antihypertensive agents manufactured by different companies, in the same strength and dosage forms were obtained from “current index of medical specialties” January April 2016 and Drug Today October-December 2016. The cost ratio and percentage cost variation were calculated for each generic antihypertensive agent (ACE Inhibitors and ARBs).**Results:** This study shows that there is a wide variation in the prices of different brands of same ACE Inhibitors and ARBs in Indian market.

Highest cost variation 400% is for Lisinopril (2.5mg), followed by Enalapril (10mg) 394.16%, Telmisartan (20mg) 322.22%.

Conclusions: There is a wide difference in the cost of different brands of ACE Inhibitors and ARBs available in India. They have important role in management of hypertension particularly if associated with other morbidities like diabetes. The clinicians prescribing these drugs should be aware of these variations in cost so as to reduce the cost of drug therapy and increase the patient adherence to the therapy.**Keywords:** Adherence, Angiotension converting enzyme inhibitors, Angiotensin receptor blockers, Cost analysis, Compliance, Cost variation, Hypertension**INTRODUCTION**

Hypertension is most common cardiovascular disease leading to morbidity and un-timely death. The World Health Organization describes hypertension as the number one risk factor for mortality, as worldwide annually 7.5 million deaths (13% of all deaths) are attributable to high blood pressure (BP)-related diseases.¹ In India, the situation is more alarming as hypertension attributes for nearly 10% of all death.² Prevalence of hypertension in India is reported to vary from 4-15 % in urban and 2-8% in rural population.³ It is estimated that the worldwide prevalence of hypertension would increase from 26.4% in 2000 to 29.2% in 2025.⁴ It is a major risk factor for stroke, myocardial infarction, vascular disease, and chronic kidney disease. For that reason, the guidelines of hypertension and cardiology societies

emphasize that hypertension treatment should aim at reducing the long-term risk of (cardiovascular) morbidity and Mortality.^{5,6} Hypertension is often referred to as the ‘silent killer’, as its presence is usually symptomless. Antihypertensive drug once started mostly continued through-out life. Antihypertensive drugs were the second largest therapy area in 2011 with the global sales value of more than USD 40 billion, according to the world preview 2018 report by Evaluate Pharma.⁷ Despite extensive research over the past several decades, control of blood pressure is suboptimal in general population. It has estimated that less than 20% of hypertensive patient have adequate control of blood pressure.⁸ Indian pharmaceutical industry being one of the largest pharmaceutical markets in the world has a large number of branded formulations and generic brands of the same drug with a large difference in their selling price.⁹

Variations in cost of drugs which are very commonly used have large economic implications. This affects the compliance of the patients who need to take these drugs regularly to maintain good health.¹⁰ Patient compliance play important role in adequate control of blood pressure.

There are several drug used in treatment of hypertension like diuretics, calcium channel blocker, ACE Inhibitors, ARBs, beta blockers, alfa blocker, vasodilators. National guideline recommended Diuretics as preferred initial therapy for most patients with uncomplicated stages 1 hypertension.⁶ But most of the time patient suffers hypertension along with diabetes and so ACE Inhibitors or ARBs should be the first line drugs. The beneficial effect of ACE inhibitor treatment on all cause mortality for hypertensive patients was well established in a recent meta-analysis.¹¹ Captopril, enalapril, lisinopril, ramipril, benazepril, trandolapril, fasinopril, quinopril, imdapril are the different type of ACE Inhibitors. Olmesartan, Losartan, Candesartan, Irbesartan, Valsartan, Telmisartan are the ARBs used in treatment of hypertension.

METHODS

The prices of 11 oral antihypertensive drug (ACE inhibitors and ARBs), eleven single and thirteen combinations, available in 49 different formulations were analyzed. Price in Indian rupees (INR) of ACEI and ARBs manufactured by different pharmaceutical

companies in India, in the same strength, was obtained from Current Index of Medical Specialties (CIMS), July-October 2016, and DRUG TODAY October-December 2016.

- The drug formulations manufactured by a single company or by different companies, but, in different strengths, were excluded.
- The cost of the oral ACE inhibitors and ARBs drugs was estimated for an average of 10 tablets.
- The difference in the maximum and minimum prices of the same drug formulation manufactured by different pharmaceutical companies and percentage variation in price was calculated.
- Percentage cost variation was calculated as follows:

% Price variation =

$$\frac{\text{Maximum cost} - \text{Minimum cost} \times 100}{\text{Minimum cost}}$$

RESULTS

This study shows that there is a wide variation in the prices of different brands of same ACE Inhibitors and ARBs in Indian market.

Table 1: Variation in cost of single drug therapy.

S. No.	Drugs	Formulation	Dose (mg)	Min. price	Max. price	Range	Price variation
1	Captopril	1	25mg	9.07	35.70	26.63	293.60
2	Enalapril	3	2.5mg	6	22.6	16.6	276.6
			5mg	9	36.7	27.7	307.7
			10mg	12	59.3	47.3	394.16
3	Lisinopril	3	2.5mg	10	50.00	40	400
			5mg	25	69	44	176
			10mg	39	122.30	83.3	213.58
4	Perindopril	2	2mg	56.25	94	37.75	67.11
			4mg	85	123	38	44.70
5	Ramipril	4	1.25mg	14.9	44.30	29.4	197.3
			2.5mg	25.50	79.80	54.3	212.94
			5mg	43.00	128.80	85.8	200
			10mg	63.50	179.30	115.8	182.36
6	Olmesartan	3	10mg	39	53	14	35.89
			20mg	46	87.92	41.92	91.13
			40mg	75	149	74	98.66
7	Losartan	2	25mg	13.20	45	31.8	240.90
			50mg	27.50	67	39.5	143.63
8	Candesartan	2	4mg	27	34.95	7.95	29.44
			8mg	45.27	61.80	16.53	36.51
9	Irbesartan	2	150mg	78.56	240	161.44	205.49
			300mg	168	199.65	31.65	18.83
10	Valsartan	2	80mg	69	93.50	24.5	35.50
			160mg	130	163	33	25.38
11	Telmisartan	3	20mg	18	76	58	322.22
			40mg	28	85.10	57.1	203.92
			80mg	89	134	45	50.56

Table 2: Variation in cost of combination therapy.

S. No.	Drugs	Formulation	Dose (mg)	Min. price	Max. price	Range	Price variation
1	Enalapril+ Hydrochlorothiazide	2	5+12.50 10+25	25 22.75	31.40 75.66	6.4 52.91	25.6 232.57
2	Amlodipine+Enalapril	2	5+2.5 5+5	25 31	29 76.50	4 45.5	16 146.77
3	Lisinopril+ Hydrochlorothiazide	2	5+12.5 10+12.5	10 12.5	52.10 75.75	42.1 63.25	421 506
4	Amlodipine+Lisinopril	1	5+5	32	73.3	41.3	129.06
5	Ramipril+ Hydrochlorothiazide	2	2.5+12.5 5+12.5	34.11 43.13	84.10 136.95	49.99 93.82	146.55 217.52
6	Amlodipine+Ramipril	2	5+2.5 5+5	25.30 71	82 110	56.7 39	224.11 54.92
7	Losartan+ Hydrochlorothiazide	2	25+12.5 50+12.5	28.50 34	50 89	21.5 55	75.43 161.76
8	Amlodipine+Losartan	1	5+50	20.80	88.47	67.67	325.33
9	Olmesartan+ Hydrochlorothiazide	2	20+12.5 40+12.5	67 95	101.75 182	34.75 87	51.86 91.57
10	Olmesartan+Amlodipine	2	20+5 40+5	69.90 109.90	90.50 130	20.6 20.1	29.47 18.28
11	Irbesartan+ Hydrochlorothiazide	1	150+12.5	69	269	200	289.85
12	Telmisartan+ Hydrochlorothiazide	2	40+12.5 80+12.5	38.5 110	85 125	46.5 15	120.77 13.63
13	Telmisartan+Amlodipine	1	40+5	55	101	46	83.63

Table 1 shows single drug percentage price variation for various ACE Inhibitor and ARBs. Highest cost variation 400% is for Lisinopril (2.5mg), followed by Enalapril (10mg) 394.16, Telmisartan (20mg) 322.22%.

Table 2 shows, cost variation of fixed dose combinations of ACE Inhibitors or ARBs.

Lisinopril+ hydrochlorothiazide (10+12.5mg): 506%, (5+12.5mg): 421%, Amlodipine+ Losartan (5+50mg): 325.33%, Irbesartan+ Hydrochlorothiazide (150+12.5mg): 289.85%.

DISCUSSION

The Renin-angiotensin-aldosterone system (RAAS) controls circulating volume and electrolyte balance in the human body and is therefore an important regulator of haemodynamic stability.¹² An overactive RAAS is strongly associated with high BP. Both Angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs) are the first line drugs for hypertension and they effectively reduce the risk of cardiovascular and renal events.¹³ With sales of US\$358 million on the private market, ACE-inhibitors (excluding fixed combinations with diuretics) represent the second largest therapeutic class in the antihypertensive market, just behind the calcium channel blockers. Some 60% of this revenue is shared between three ACE-inhibitors - Lopril (captopril), Renitec (enalapril) and Coversyl

(perindopril) - with others competing for the remaining 40%.¹⁴ As they are very important group for treatment and we didn't find much studies regarding cost variation analysis related to them, so we conducted this study. Hypertensive patient require long term treatment. Inadequate treatment or poor adherence to treatment can leads to stroke, myocardial infarction, vascular disease, and chronic kidney disease which further increase the economic burden to patient and indirectly increases economic burden of the country. Higher medication costs have been found to be a reason for medication nonadherence.¹⁵ Cost related poor medication adherence has been found to be related to adverse health outcomes.¹⁶ In India, there are many pharmaceutical companies which sell a particular drug under different brand names along with the innovator company. There are large numbers of formulations for the same drugs are available leading to large variation in the price of drugs leading to an unnecessary economic burden on Indian population. No correlation has been found between the quality of the medicine and its corresponding price.¹⁷ DPCO is an effective tool for regulation of drug prices. Very few medicines are under drug prices control order. Government should bring more number of antihypertensive drugs under price control.

Many times it is seen that doctors are unaware or underestimate the price of expensive ones which further increase the economic burden over patient and increases the chances of non-adherence with therapy. Physician's awareness about the cost differences should be ensured

by providing a manual of comparative drug prices. Availability of manual has been found to reduce patient's drug expense.¹⁸

CONCLUSION

This study highlights that there is a wide variation in cost among the antihypertensive drugs manufactured by different pharmaceutical companies. Hypertension requires long term treatment, compliance being a key factor for successful treatment. Adherence to the treatment can be increased by decreasing the cost of therapy. The Government of India should take strict and effective measures in bringing uniformity in the cost of the drug for long term benefit of the health.

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