

A Cost Variation Analysis of Drugs used in the Management of Thromboembolic Disorders - A pharmaco-economic study

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Abstract

Background: Cardiovascular diseases (CVDs) have become a major cause of mortality among the Indians. The cost of anticoagulant, antiplatelet, and fibrinolytic drugs which are used to treat thromboembolic disorders and used as prophylactics for individuals at high risk of CVDs varies widely in Indian pharmaceutical market. Our aim of the study is to find different drugs available for managing thromboembolic disorders, either singly or in combination and to evaluate and compare the cost of a particular drug in the same strength, number, and dosage forms being manufactured by different companies.

Methods: The maximum cost and minimum cost of a particular drug in the same strength and dosage forms being manufactured by different companies was obtained from “current index of medical specialties” CIMS website. The cost ratio and the percentage cost variation were noted for each brand.

Results: Amongst single drug therapy, Prasugrel 5mg showed highest price variation (4767.23%). Minimum cost variation was of Rivaroxaban 20mg (0%). In fixed dose combinations, highest cost variation was seen with Aspirin 75+ Clopidogrel 75mg (2770.96%) while minimum cost variation was of Aspirin 75mg + Prasugrel 10mg (8.52%).

Conclusions: There is lot of variation in prices of different brands of the same anticoagulants, fibrinolytics, and antiplatelet drugs available in Indian market. Hence, by reducing the cost variation and improving the affordability of drugs, we can improve compliance and adherence, the health status of community, and the economic burden due to healthcare expenditures.

Keywords: Anti-platelets, Anti-coagulants, Fibrinolytics, Cost variation, Pharmaco-economics.

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1. Introduction

Cost of the drug plays a crucial role in patient care. The cost of therapy for both patients and the physician has been a major concern in developing countries. [1] In the developing countries, the cost of drugs is a major concern to both physician and patient; yet there are very few data on prescribing patterns and expenditure. Rational prescribing implies use of the right drug for a right patient in a right dose and right formulation for the right duration and at the right price, which patient can afford. [2] Physicians have their own way of selecting a P-drug for their patients. Price is one of the major criteria that enable a physician to choose the P-drug.

Hence, the producers of medications need to assess the value of the drugs, in terms of both economic worth and clinical efficacy as well.[3] This data collection regarding the availability of drug, price, and utilization may not only help the health-care professionals but will also the policymakers to make decisions.[4]

Maintenance of proper blood flow is very complex yet a highly regulated physiological process, which involves multiple complementary and opposing mechanisms of control. Imbalances in these mechanisms may lead to a variety of pathological consequences, such as hemorrhage or

obstructive clot (thrombus) formation in veins or in the arteries, and this may cause stroke, pulmonary embolism, heart attack, and other serious conditions.[5] Haemostasis and thrombosis plays an important role in understanding their pathophysiology in both arteries (e.g., thrombotic stroke and MI) as well as in the veins (e.g., deep vein thrombosis and pulmonary embolism).[6] Haemostasis is the stoppage of bleeding from damaged blood vessels and is vital for life. A wound causes constriction of the vessels, along with adhesion and also there is activation of platelets and formation of fibrin. Platelet activation leads the formation of haemostatic plug which halts bleeding and further by fibrin. Thrombosis is the pathological formation of haemostatic plug within the vasculature in the absence of bleeding. [7]

Cardiovascular disease is highly prevalent and is expensive to treat. Many novel anticoagulants, fibrinolytics, and antiplatelet agents have been found to be effective in decreasing the morbidity and mortality associated with cardiovascular disease.[8] In India, 52% of the deaths due to CVD occur before the age of 70 years as compared to 23% in the Western populations.[9] Within the next 15 years, it has been predicted that these diseases will increase rapidly in India and this country will be host to more than half the cases of heart disease in the world.[10] They are expected as fastest growing long-term disease by 2015 expanding at 9.2% every year since 2000.[11] Pharmaceutical industry manufactures many branded formulations of the same drug with large difference in selling price. In India, most of the drugs are available in brands and they are prescribed by clinician mostly in the name of the brand. This ultimately affects the patient's economy if costly brand is prescribed, especially in cardiovascular diseases which need treatment for prolonged duration. [12]

The objective of Pharmacoeconomics study is to influence a policy formulation and to make an effective decision, rational prescribing behaviour and effective utilization of resources, so as to make a person or a group of people to change their behaviour and persuade them a new course of action that is more efficient. [13]

The aim of our study was to analyse cost variation of commonly prescribed anticoagulants, fibrinolytics, and antiplatelet drugs which are available in the Indian market under various brand names. In addition, we have also compared their cost-ratio and percentage cost variation along with their maximum and minimum price.

2. Materials and Methods

An observational, analytical study carried out in department of Pharmacology of a tertiary care teaching hospital Pune in the month of October – December 2021 After Approval from Institutional Ethics Committee. Price in

INR* (Indian National Rupees) of anticoagulants, fibrinolytics, and antiplatelet drugs same strength and dosage form was obtained from the Current Index of Medical Specialities (CIMS) 2021 for cost variation analysis.

Anticoagulants, fibrinolytics, and antiplatelet drug formulations with same strength, dose, and number were included for the study. Drugs manufactured by a single company and fixed-dose combinations (FDCs) were also included. The difference between the maximum and minimum costs of the same drug manufactured by different pharmaceutical companies will be calculated.

The following formula was used to calculate the percentage cost variation [14]:

% Cost variation=

$$\frac{\text{Cost of most expensive brand} - \text{Cost of least expensive brand}}{\text{Cost of the least expensive brand}} \times 100$$

The findings of observational are expressed as absolute numbers and percentages.

3. Results

The prices of anticoagulants, fibrinolytics, and antiplatelets produced by several pharmaceutical companies were analyzed. Tables 1-3 show percentage cost variation of antiplatelets, anticoagulants and fibrinolytics. Wide variation in the prices of several brands of same antiplatelets, anticoagulants and fibrinolytics was found in Indian pharmaceutical market.

According to our present study, as shown in Table 1 there are 7 single preparations available for oral use and 3 injectable antiplatelet drugs. In these, aspirin is available in 9 different formulations of which 162.5mg dose has 2 brands and has least price variation of 33.33% and 75 mg dose has highest price variation of 585.18 %. In addition, dipyridamole is available in 3 different formulations, 25mg, 75mg, 100mg respectively of which 100mg has least price variation of 299.59% and 25 mg dose has highest price variation of 390%. Here, ticlopidine is available only in 250 mg dose and has 11 brands. In addition, prasugrel has 2 different formulations of 5 mg and 10 mg and cost variation of 5mg is 4767.23% while 5mg is least i.e. 38.93%. Clopidogrel was available in 3 different formulations in which 75 mg showed maximum price variation of 444.13% and 300mg has least cost variation of 38.93%. Cilostazol has 50 mg and 100 mg strength but there was no much difference in cost variation. Ticagrelor has 60mg and 90mg strength and had 122.22% and 100% cost variation respectively.

As shown in Table 2, there are 5 oral and 3 injectable forms of anticoagulants. Acenocoumarol has 4

strengths 1mg, 2mg, 3mg, 4mg and 2mg has (193.12%) and 3mg has (153.4%) cost variations. Fondaparinux has strengths of 7.5mg/0.6ml and 2.5mg/0.5ml and has low-cost variations compared to other anticoagulants of (20.416%) and (32.35%) respectively. Dabigatran 75mg, 110mg, 150mg strength and (50.75%), (122.23%), (39.51%) successively. Warfarin also had low range of cost variation, lowest of 4mg strength (45.34%). Rivaroxaban has the lowest cost variations among all the drugs used for thromboembolic disorders of 0% of 20 mg strength, having 2 brands and of same cost. There are 3 injectable, Heparin has 3 strengths 5000/5ml has higher cost variation of (1064.06%) and 25000ml/5ml has lower of 201.35%. Enoxaparin has 4 strengths, 20mg/0.2ml

has 182.06% and 60mg/0.6ml has 31.84% as their highest and lowest cost variations.

Table 3 shows the list of Fibrinolytics, strengths and their cost variation. Streptokinase 0.75MIU has 74.24% and 250000MIU has 131.09% as their cost variation. Tenecteplase has 2 strengths of 30mg and 40mg and cost variation of 15.21% & 5.3% respectively.

Retepase has only 1 strength of 18 mg and its cost variation is of 63.86%.

Table no 4 shows the Fixed dose combinations, the highest cost variation was of Aspirin 75mg+clopidogrel 75mg (2770.96%) and lowest was of Aspirin 75mg+Prasugrel 10 mg (8.52%) respectively.

Table 1: Cost variation of different brands of Antiplatelets

Sr. No	Drug	Strength (mg)	For	Dosage Form	Number of brands	Maximum cost (INR)	Minimum cost (INR)	Cost ratio	Cost variation (%)
1	Aspirin	50mg	10	Tab	3	8.5	2	4.25	325
		75mg	10	Tab	18	6.07	1.46	4.15	315.75
		81mg	10	Tab	2	14.8	11.9	1.24	24.36
		80mg	10	Tab	2	5.7	2	2.85	185
		100mg	10	Tab	4	9.9	1.85	5.35	435.13
		150mg	10	Tab	12	8.5	2.5	3.4	240
		325mg	10	Tab	4	14.8	2.16	6.85	585.18
		350mg	10	Tab	2	11.2	3.13	3.57	257.82
		162.5mg	10	Tab	2	18	13.5	1.34	33.33
2	Clopidogrel	75mg	10	FC	16	102.16	39	2.619	161.94
			10	Tab	78	135	24.81	5.4	444.13
		150mg	10	FC	6	168.75	73.82	2.285	128.59
			10	Tab	7	152.05	67.62	2.248	124.48
		300mg	10	Tab	2	217.25	142.5	1.52	52.45
3	Prasugrel	5mg	10	FC	6	137.55	99	1.38	38.93
			10	Tab	13	2628.57	54	48.67	4767.23
		10mg	10	FC	6	269.2	152.2	1.76	76.87
			10	Tab	16	1430	94.82	15.08	1408.12
4	Ticagrelor	60mg	10	Tab	2	400	180	2.22	122.22
		90mg	10	Tab	6	500	250	2	100
5	Ticlopidine	250mg	10	Tab	11	140.95	65	2.16	116.84
6	Cilostazol	50mg	10	Tab	12	137.55	62	2.21	121.85
		100mg	10	Tab	11	245.02	111	2.207	120.73
7	Dipyridamole	25mg	10	Tab	3	13.3	2.71	4.9	390.7
		75mg	10	Tab	2	38.1	7.9	4.8	382.27
		100mg	10	Tab	5	39	9.76	3.99	299.59
8	Tirofiban	5mg	1	Inj	13	6940	3495	1.98	98.56
9	Eptifibatide	20mg/10ml	10ml	Inj	7	4676	1980	2.36	136.16
		75mg/100ml	100ml	Inj	8	16832.6	4000	4.09	309.56
		2mg/10ml	10ml	Inj	5	2975	2471.51	1.2	20.37
		0.75mg/100ml	100ml	Inj	5	10540	8148.42	1.29	29.35
10	Abciximab	2mg	5ml	Inj	3	21896.8	8100	2.7	170.33

Table 2: Cost variation of different brands of anticoagulants.

Sr. No	Drug	Strength (mg)	for	Dosage Form	Number of brands	Maximum cost (INR)	Minimum cost (INR)	Cost ratio	Cost variation (%)
1	Acenocoumarol	1mg	10	Tab	8	73	27.5	2.6	165.45
		2mg	10	Tab	8	114.32	39	2.93	193.12
		3mg	10	Tab	7	145.96	57.6	2.53	153.4
		4mg	10	Tab	8	155.73	57	2.73	173.21
2	Dabigatran	75mg	10	Tab	6	300	199	1.5	50.75
		110mg	10	Tab	8	300	135	2.2	122.23
		150mg	10	Tab	6	399	286	1.39	39.51
3	Warfarin	1mg	10	Tab	4	26.41	10	2.641	164.1
		2mg	10	Tab	4	29.2	19.83	1.47	47.25
		3mg	10	Tab	2	34.15	22.8	1.49	49.78
		4mg	10	Tab	5	35	24.08	1.45	45.34
4	Rivaroxaban	10mg	10	Tab	3	1015	78.57	12.9	1191.84
		15mg	10	Tab	3	1450	92.86	15.6	1461.49
		20mg	10	Tab	2	1450	1450	1	0
5	Enoxaparin	20mg x 0.2ml	0.2ml	Inj	19	520.32	184.47	2.82	182.06
		40mg x 0.4ml	0.4ml	Inj	49	560	290.85	1.92	92.73
		60mg x 0.6ml	0.6ml	Inj	48	626.72	475	1.31	31.94
		80mg x 0.8ml	0.8ml	Inj	9	1176.61	565	2.08	108.24
6	Heparin	1000IU/5ml	5ml	Inj	12	126.8	27	4.69	369.62
		5000IU/5ml	5ml	Inj	25	298	25.6	11.6	1064.06
		25000 IU/5ml	5ml	Inj	21	320	45	7.1	611.12
7	Bivalirudin	250mg	1	Inj	6	16,360	5,428.90	3.01	201.35
8	Fondaparinux	2.5mg/0.5ml	0.5ml	Inj	6	900	680	1.32	32.35
		7.5mg/0.6ml	0.6ml	Inj	3	1589.5	1320	1.204	20.416

Table 3: Cost variation of different brands of fibrinolytics.

Sr. No	Drug	Strength (mg)	For	Dosage Form	Number of brands	Maximum cost (INR)	Minimum cost (INR)	Cost ratio	Cost variation (%)
1	Streptokinase	1.5e+006IU	1	Inj	16	3450	1680.08	2.05	105.34
		250000 IU	1	Inj	2	1257.14	544	2.3	131.09
		750000IU	1	Inj	10	1961	1141	1.71	71.866
		0.75MIU	1	Inj	6	2178	1250	1.74	74.24
		1.5MIU	1	Inj	7	3998	1900	2.05	105.15
2	Urokinase	250000 IU	1	Inj	6	2290	1850	1.23	23.78
		500000 IU	1	Inj	7	3650	3100	1.17	17.74
		750000 IU	1	Inj	4	4907	4300	1.141	14.11
		1e+006 IU	1	Inj	5	6527.78	2988.09	2.18	118.45
3	Tenecteplase	30mg	1	Inj	2	33000	28641.9	1.15	15.21
		40mg	1	Inj	3	43900	41688	1.05	5.3
4	Retepase	18mg	1	Inj	5	35,937.30	21,931.25	1.63	63.86

Table 4: Cost variation of various fixed dose combinations.

Sr. No	Drug	Strength (mg)	For	Dosage Form	Number of brands	Maximum cost (INR)	Minimum cost (INR)	Cost ratio	Cost variation (%)
1	Aspirin + Clopidogrel	75+75 Mg	10	Cap	19	89	3.1	28.7	2770.96
			10	Tab	42	105	24.2	4.33	333.88
2	Aspirin+ Clopidogrel	150+75 Mg	10	Cap	13	83	19.3	4.3	330.05
			10	Tab	31	157.8	22	7017	617.2
3	Aspirin+ Prasugrel	10+75 Mg	10	Cap	2	245	225.75	1.08	8.52

4. Discussion

Higher costs of medicine have been found to be a reason for medication non-adherence and have been found to be related to adverse health outcomes. Medication non-compliance can be the single most common reason for treatment failure. Non-compliance of the treatment results in progression of the disease, which increases the overall medical care costs. Treatment with generic drugs has been found to have fewer adverse clinical outcomes and improved treatment adherence than treatment with brand name versions. The costly brand of same generic drug is scientifically proved to be in no way superior to its economically cheaper counterpart. [15]

Ultimately, this leads to poor patient compliance, especially in case of drugs such as anticoagulants and antiplatelets which needs prolonged therapy. Poor patient compliance is a worldwide problem and can result in patients receiving inadequate doses of medication. [16]

The limitation of the study is that sources of information were limited to CIMS, but there are few other brands which are marketed in India but not published in the above-mentioned source. Less drug combinations are included which are another drawback of this study.

5. Conclusion:

This study finding showed a high percentage price variation in the minimum and maximum price of brands of the same anticoagulants, fibrinolytics, and antiplatelets drugs manufactured by pharmaceuticals market in India. In order to increase the adherence to treatment, we can achieve it by decreasing expensive treatment strategy and switching towards cost-effective treatment. To overcome this disadvantage of cost variation of the drugs, generic prescribing should be encouraged. Physicians should be made aware of the prices of various drugs while encouraging them to prescribe generic medicines & alternative cheaper brand medicine to ensure better compliance and reduce total health-care cost. Only a collective effort would propel us towards the goal of "Health for All."

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