Antihypertensive Drugs: Are they Cost-Effective?

Neeta Sharma[1], Meenu Mehta[2], Harish Dureja[3], Amrish Chandra[1]

[1]Department of Pharmacy, Amity Institute of Pharmacy, Amity University, Noida, Uttar Pradesh, India,
[2]Department of Pharmaceutical Sciences, Lovely Professional University, Punjab, India, [3]Department of
Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, Haryana, India

Abstract

Context: Hypertension, also termed as high blood pressure, is long-term medical condition which is major cause of morbidity, mortality and needs lifelong treatment, also leads to complications such as stroke, myocardial infarction, and chronic kidney disease. A significant difference in cost of antihypertensive drugs is available in regulated (India) and less regulated market (United States). **Objective:** The objective of the study was to analyze price variation of unit dosage form manufactured by different companies for the same formulation with the same strength in both markets by calculation percentage price variation among the market. **Materials and Methods:** Cost of particular unit drug manufactured by different companies, in same strength was obtained from "Current Index of Medical Specialties" and "Indian Drug Review" for regulated market and from "GoodRX" and "Online Pharmacies" for less regulated market in both INR and USD. **Results:** Percentage price variation is less in the US than in India, but prices are extremely high. In India, the price of ACE inhibitor (Enalapril 2.5 mg) was found to be INR 0.60 (USD 0.009) whereas in the US market it was INR 178.81 (USD 2.7501). **Conclusions:** This wide price variation is due to payers, more labor cost, and less regulation schemes in less regulated market. Revision in price regulation is required to equalize prices in both markets.

Key words: Antihypertensive, drug price control order, less regulated market, price variation, regulated market

INTRODUCTION

Hypertension is the attributable risk factor for stroke, myocardial infarction, vascular disease, and chronic kidney disease.[1] It is estimated that it affects one-third of the adult population of the western world.[2] As per National Health and Nutrition Examination Survey, 2011–2012, 82.8% of adults were aware of their hypertension, 75.5% were currently taking the medication to treat it, and 51.9% had their controlled blood pressure (BP) to <140/90 mmHg.[1,3] Furthermore, it is reported to be the fourth contributor to premature death in developed countries and the 7th in developing countries.[4] It is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease.[5] Complications from hypertension account for 9.4 million deaths worldwide every year.[6] It has been estimated that it will affect 1.5 billion people by the year 2025.[7] About 75 million American adults (32%) have higher BP due to this lifelong threatening disorder. Only half (54%) of people with high BP have their condition under control. Overall, the prevalence is higher in individuals who are 60 years and older as compared with younger adults.[1] High BP costs the nation $48.6 billion each year. This total includes the cost of health-care services, medication to treat it.[8] It is a symptom, not a disease. This serious medical condition happens when the force of blood pumping through the arteries is too strong.[9] Normal adult BP is defined as BP of 120 mmHg during contraction (systolic) and BP of 80 mmHg during relaxation (diastolic). When systolic BP is ≥140 mmHg or diastolic BP ≥90 mmHg, then BP is considered to be elevated or high as per medical guidelines.[10]

Etiology is basically classified into two categories: Primary (essential) and secondary. The primary cause is multifactorial includes increased peripheral resistance, stress, hormonal, neural, genetic familial, and lifestyle. On the other hand, the secondary cause is known as abnormal control includes renal

disorders - renin-angiotensin, sodium retention, antidiuretic hormone, aldosterone, and pheochromocytoma.[11] As per the WHO, most people with hypertension have no symptoms at all; that is why it is known as "silent killer."[12,13] Sometimes it causes symptoms such as headache, shortness of breath, dizziness, chest pain, and palpitations of the heart, but not always. Lifestyle changes, such as stopping tobacco use, eating healthily, exercising regularly and avoiding the harmful use of alcohol, are sufficient to control it.[14]

It can be classified in various ways: (1) Type of arterial pressure elevation: Systolic, diastolic, or mixed, (2) character of the elevation: Labile or sustained, (3) severity of the associated vascular disease - mild, moderate, severe, or malignant, (4) renin based: High renin (e.g., reninoma and renal artery stenosis) and low renin (e.g., liddle symptoms and salt-dependent hypertension), (5) pathophysiological based: Increased peripheral vascular resistance (e.g., pheochromocytoma and hypercalcemia), (6) primary (essential) and secondary, (7) ambulatory monitoring based-masked hypertension, white coat hypertension and dipper versus nondipper, (8) pregnancy associated-chronic hypertension, pre-eclampsia, pre-eclampsia superimposed on chronic hypertension and gestational hypertension, and (9) severity based-stable hypertension, hypertensive urgency, malignant hypertension, and resistant hypertension.[15]

Pharmaceuticals account for at least 10–30% of the total health-care expenses in every country.[16] The application of a pharmacoeconomic or cost-effectiveness standard requires extensive, high-quality clinical, economic, and health-care cost data, and well-defined methodologies for national costs and benefits. This ample level of expense initiates pharmacoeconomic to compare costs for pharmaceuticals to the lowest acceptable level.[17] Pharmacoeconomics deals with the cost of a particular drug in the same strength and dosage forms being manufactured by different pharmaceutical companies. However, the use of pharmacoeconomics has caused concern in some quarters, in part due to the sponsorship and use of studies by pharmaceutical manufacturers for promotional purposes.[18]

The objective of pharmacoeconomics is to determine pharmaceutical prices to ensure consistently high level of public health, ensure that a sufficient range of pharmaceutical products is available at reasonable prices, support efficient production of pharmaceuticals and encourage research and development of new pharmaceuticals.[19] There are five principle tools of pharmacoeconomic science that is: Cost identification, cost minimization, cost-benefit, cost-effectiveness, and cost utility.[20] In India, >3.1 million people are unaffordable for private health care. The main reasons for increasing cost of medicines are due to new marketed medicines, under patent law, and irrational drug prescription. Most of the people below poverty line face a choice between buying medicines or buying food due to high pricing of drugs. The United States spends more money on prescription drugs than any other country. It plays a pivotal role in formulary decision-making and has value when accessing biotechnology drugs, therapeutic drug monitoring, and disease management.[21]

SUBJECTS AND METHODS

The authors searched "Current Index of Medical Specialities" and "Indian Drug Review" for the current prices of prescription drugs in the same strength and dosage form being manufactured by different companies.[22] Furthermore, sorted PubMed, ScienceDirect, Google Scholar from January 2010 to October 2017, in brief, the search strategies included cost of a particular drug (cost per tablet) was obtained from MeSH terms (e.g., "orange book," "Pharma sahi daam," "pharmacoeconomics analysis," "pricing regulations," and "price regulated, and less regulated markets") and keywords (e.g., "hypertension" and "antihypertensive drugs"). The prescription drugs used for hypertension in the regulated market and less regulated market was gathered and then screened to get the maximum and minimum price for the same formulation.

Percentage cost variation within regulated and less regulated market was calculated using this formula:

$$\%\text{Cost variation} = \frac{\text{Max cost-Min cost}}{\text{Min cost}} \times 100$$

With the help of GraphPad Prism 7.0, the graphs were expressed. The price of less regulated market was in US dollars and for the comparison, the authors converted that in Indian rupees by multiplying with 65.02 (1 US dollar = 65.02 rupees). The data analysis was carried out using Microsoft office excel, 2017.

RESULTS

The prices of a total of 10 drugs available in 34 formulations were analyzed. These 34 pharmaceutical formulations are manufactured by different pharmaceutical companies. Figures 1-3 show the minimum and maximum price of antihypertensive drugs in the regulated and less regulated market. The maximum and minimum prices shown by ACE inhibitor (Enalapril 2.5 mg) in less regulated and regulated market are, respectively, INR 178.81 (USD 2.7501) and INR 0.60 (USD 0.009), angiotensin (AT1 receptor) blockers (Losartan 100 mg): INR 154.10 (USD 2.3700) and INR 4.98 (USD 0.07659), CCB's (Amlodipine 5 mg): INR 139.79 (USD 2.1499) and INR 0.65 (USD 0.0099), β adrenergic blockers (Propranolol 80 mg): INR 75.42 (USD 1.1599) and INR 2.20 (USD 0.0338), and β+α adrenergic blockers (Carvedilol 25 mg): INR 52.17 (USD 0.8024) and INR 4.20 (USD 0.0646). The percentage price variation in less regulated market is less than regulated market, but the prices are extremely high. These may be due to the quality provided by less regulated market (like US), payers role, more labor cost, and less regulation schemes.
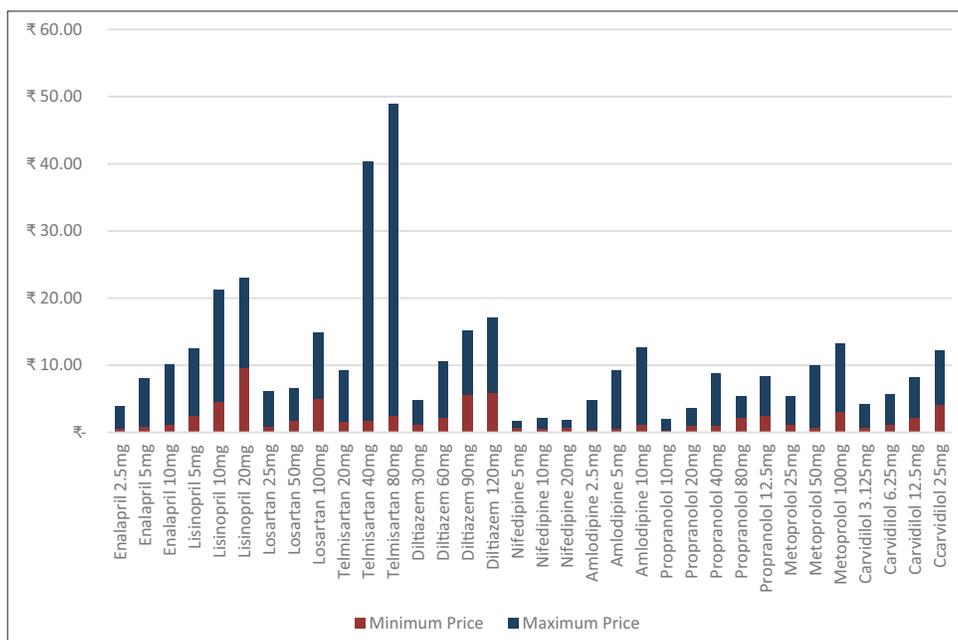
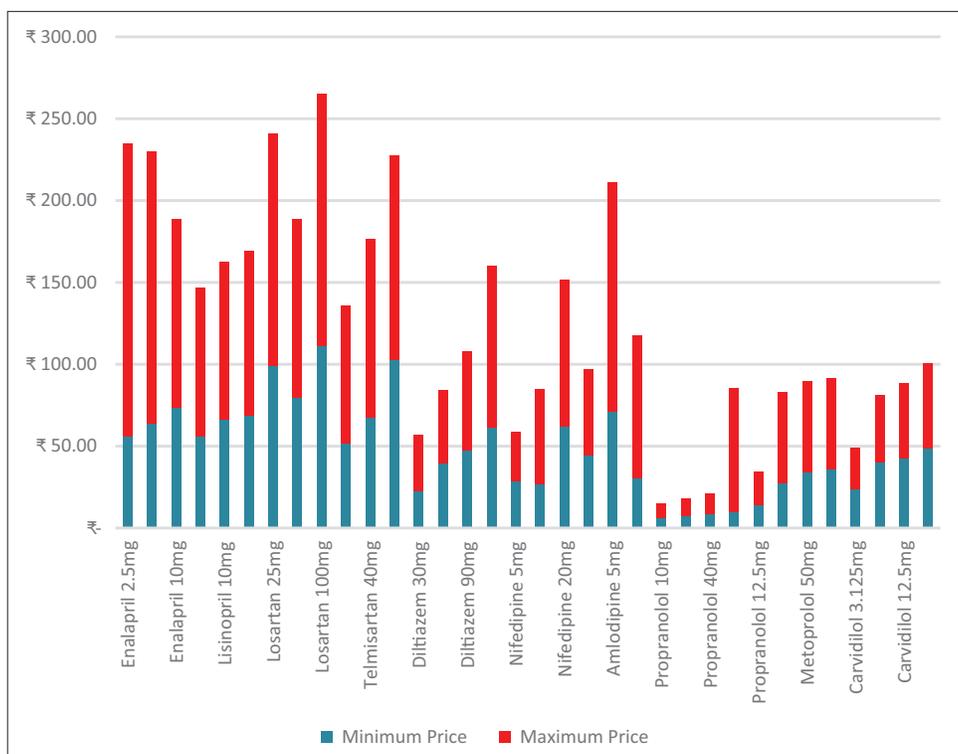**Figure 1:** Comparison of prices in highly regulated markets

Figure 2: Comparison of prices in less regulated markets

It is clear from Figure 3 that the prices in the less regulated area are too high than the regulated area.

DISCUSSION

The pharmaceutical market is flooded with huge number of branded and generic formulations across the world. Apart from the inventor, many pharmaceutical industries manufactured their own branded formulation of a particular drug which leads to huge price variation among the pharma sector.[23] The cost-effective analysis of antihypertensive drugs was studied of the same formulation with the same strengths. The common most drugs used as monotherapy for hypertension were taken for the study to compare the prices in regulated and less regulated markets.[23,24] The problem of higher prices
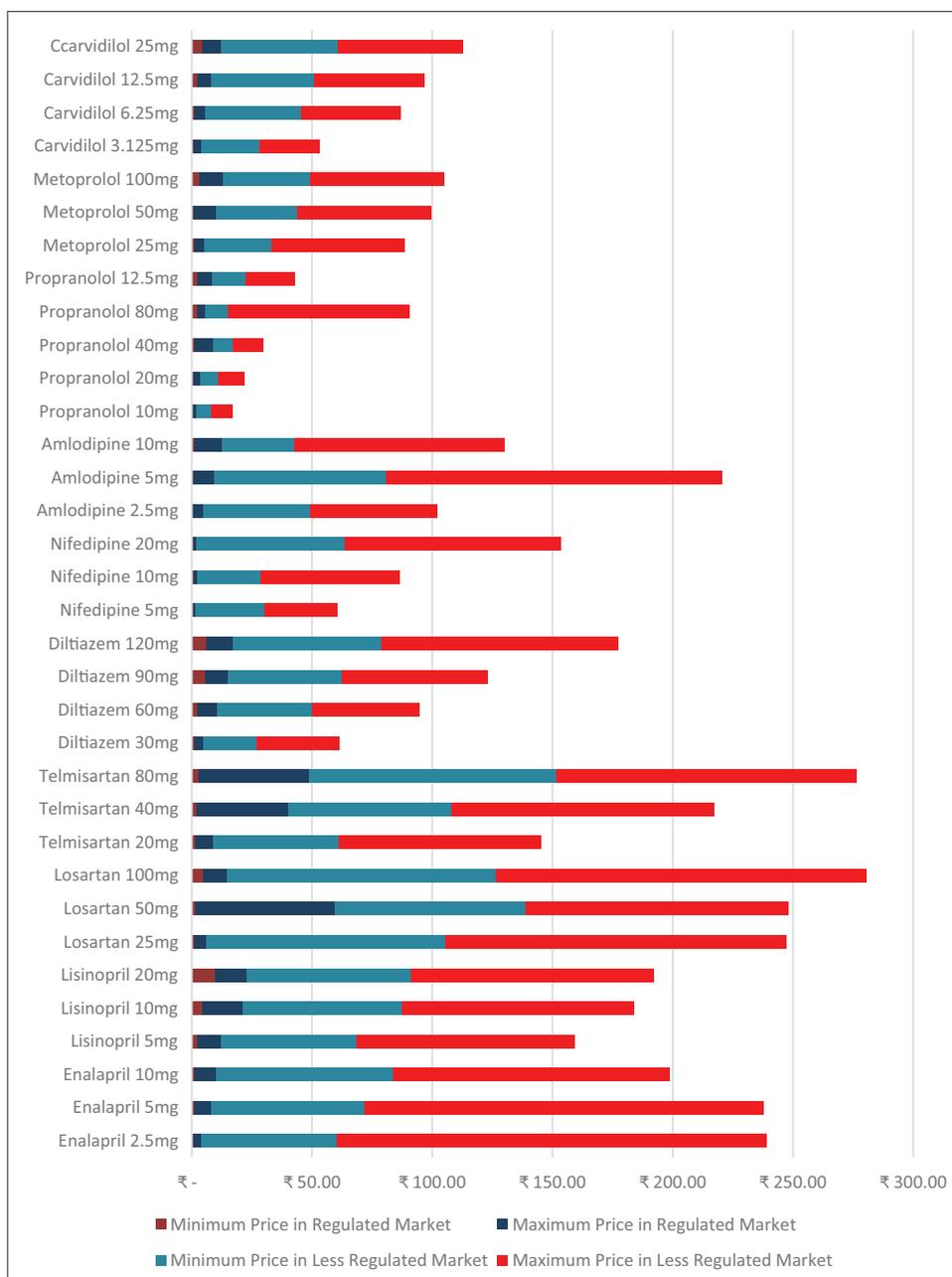
Figure 3: Comparison of prices between regulated and less regulated markets

of prescription drugs in less regulated market has deep and complicated roots and published the reasons in JAMA, the Journal of the American Medical Association.[26] The key findings in the journal for the higher price in U.S. is the price variation in overall manufacturing at a site located in US. High cost of active pharmaceutical ingredients, excipients and labor leads to this huge difference in price of finished product. As per Trading Economics, US is the developed country having the average wages of labor about 1444 INR/hour (22.22 USD/hour) whereas in the developing countries like India, average wage is 34.02 INR/hour (0.52 USD/hour).[27]

Implementation of Pharmaceutical Price Regulation Scheme (PPRS) and price control orders in regulated and less regulated

markets: As Indian pharmaceutical market is controlled by drug price control order (DPCO) and NPPA, so there is no direct control of prices by the manufacturer, however in the US, there is no regulation scheme, so it may be one of the leading causes of price variation. U.S. gives the better quality than India; this may be reason of higher prices also: As USFDA has strict norms related to the quality of the pharmaceutical products, so the US pays huge amount for the maintenance and production of drugs that is the reason of charging higher prices than India.

Role of public and private payers

During a drug's market exclusivity period, the primary counterbalance against extreme pricing is the negotiating

power of the payer. Every payer charges differently depending on the different locations that may be the reason of variation of prices in pharma markets. There may be some other factors that are responsible for the price variation among regulated and less regulated market that is as follow:

Economic factors

Presence of pharmaceutical markets based on their earlier structure existence. Drug manufacturers in less regulated market like U.S. set their own prices that are not the norm elsewhere in the world. The drug companies allow "government-protected monopolies" for certain drugs, preventing generics from coming to market to reduce prices.[25]

As in the case of regulated markets, the first price control order was issued under the Defense of India Act in 1963. After that price control order was issued under Essential Commodities Act, from 1970 onward. DPCO which is a Government Organization fix the price of the drugs in India. DPCO has introduced three parameters to ensure proper market conditions that include turnover, market monopoly, and market competition.[28]

The prices of 348 essential drugs in India reduce up to 80% with the emergence of 2013 DPCO. As a result, prices of medicines will now be selected by taking the average of all brands of drugs which have ≥1% of the market share instead of input costs.[29] Unfortunately, most of the hypertensive drugs do not come under that list. Hence, it becomes difficult for a common man to fulfill the required cost of the formulation according to their maximum retail price.[17] Price controls were initially established in 1957 through a voluntary price regulation scheme. In 1978, the scheme was renamed the PPRS and converted into a joint arrangement between the Department of Health (DOH) and individual firms to control excess profit-making. The DOH periodically reviews the terms of the PPRS and renegotiates health spending targets with the industry. Under the PPRS, the DOH sets company profit levels by evaluating a variety of factors, including long-term risk, UK investments, rate of return on capital, the company's relationship with the NHS, level of exports, and level of UK manufacturing.[30]

Whereas in case of less regulated market like USA, drug manufacturers fixed their own price in US and that is not the norm elsewhere in the world and some drugs are government protected monopoly so they prevent generics to come in market to reduce prices, the drugs prices are also not justified by R&D and the major cause of increasing prices is that FDA takes a long time to approve generic drugs.[26] There is lack of transparency in the margins of the pharmaceuticals to the researchers, health officials, and industries. Hence, the prices of drugs are like a black box.[31] There is a need to compare the prices of drugs of different brands present in the world. Therefore, the study was designed to cover the pharmacoeconomic of antihypertensive drugs in regulated

and less regulated markets. Drugs used in the management of hypertension were selected as it is one of the major causes of morbidity and mortality, and the treatment requires continuous prescription drug use. The data reveal that the prices of most of the antihypertensive brands which are used commonly show the percentage price variation >100%, which is not acceptable situation for patients. Of 10 drugs studied, most of which are commonly prescribed, percentage price variation is very large which leads to unfair burden on the consumer.[32,33]

CONCLUSION

Our study reveals the wide price variation among antihypertensive drugs available in regulated and less regulated markets. Hence, this variation should be controlled in an effective manner by regulating the less regulated markets. This will help in reducing the burden on both patient and health-care system.

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