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COST-EFFECTIVENESS STUDY OF ANTIHYPERTENSIVE DRUGS IN MUMBAI, INDIA

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ABSTRACT

Hypertension is a serious global public health problem. It accounts for 10% of all deaths in India and is the leading non-communicable disease. Recent studies have shown that the prevalence of hypertension is 25% in urban and 10% in rural people in India. It exerts a substantial public health burden on cardiovascular health status and health care systems in India. Antihypertensive treatment effectively reduces hypertension-related morbidity and mortality. The cost of medications has always been a barrier to effective treatment. The increasing prevalence of hypertension requires use of cost effective treatment for the effective management of the disease. The present study assesses the cost-effectiveness of antihypertensive drugs in patients with hypertension from Mumbai, India. A cross-sectional study was conducted to assess the cost-effectiveness of antihypertensive drugs. Face-to-face interviews were conducted by using a validated questionnaire in a total of 136 (66 males, 70 females) patients with hypertension from F-North Ward, Mumbai, India. Cost-effectiveness was determined on the basis of cost of antihypertensive drug/s, efficacy, adverse drug reactions, safety of administration, frequency of administration, and bioavailability. Atenolol was found to be the most cost-effective (INR 5.5/unit of effectiveness), followed by the amlodipine + losartan combination (INR 5.6), amlodipine (INR 6.3), captopril (INR 6.9), amlodipine + lisinopril (INR 9.6), losartan (INR 14.5) and lisinopril (INR 17.2) in the present study. Thirty-eight (28%) patients received combination therapy. Lisinopril prescribed to16 (11.8%) patients was the least cost-effective drug (INR: 17.2/unit of effectiveness). Prescriptions of cost-effective antihypertensive drugs (73.5%) were more common than less cost-effective antihypertensive drugs (26.5%) in hypertensive patients from Mumbai, India. Most of the patients (72%) were prescribed monotherapy in the treatment of hypertension.

KEYWORDS: *antihypertensive, cost-effectiveness, hypertension, Mumbai, India.*

INTRODUCTION

Hypertension is ranked as the third most important risk factor for attributable burden of disease in south Asia (2010)[1]. It exerts a substantial public health burden on cardiovascular health status and healthcare systems in India [2, 3]. HTN is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease (CHD) deaths in India [4]. This fact is significant as hypertension is a controllable disease and population-wide reduction in the blood pressure by 2mmHg can prevent 151,000 strokes and 153,000 coronary heart disease deaths in India[5]. The WHO rates HTN as one of the most important causes of premature death worldwide [6]. The Global and Regional Burden of Disease and Risk Factors study (2001), in a systematic analysis of population health data for attributable deaths and attributable disease burden, has ranked HTN in south Asia as second only to child underweight for age[7]. Hypertension accounts for 10% of worldwide healthcare expenditure underlining the considerable economic implications to resource constrained health systems[8]. Apart from health implications it has huge societal, developmental and economic costs. There is also noteworthy income loss to families affected by hypertension not only due to illness but also due to care giving and premature death[8]. In 2004, the annual income loss from NCDs among working adults in India was INR 251 billion (about US$ 50 billion) and that due to hypertension alone amounted to INR 43 billion[8]. It has been estimated that less than 20% of hypertensive patients have

adequate control of blood pressure[9]. Even though randomized clinical trials have determined the efficacy of antihypertensive treatment, the effective control of hypertension depends on case detection and adequate management by health professionals, followed by the long-term adhesion of patients to the treatment[10].Antihypertensive drug treatment often has elevated costs[11], a limitation that has not always been taken into account in clinical practice[12].Cost-effectiveness analysis is seldom available, particularly with regard to the individualization of costs.

Rationale

The developments of the last 50 years in the pharmaceutical armamentarium against hypertension have brought significant reductions in cardiovascular morbidity and mortality among hypertensive patients[13, 14]. Nevertheless, the current (and future) obligation of health care systems to operate under severe financial constraints necessitates the use of not only clinical effectiveness but also economical efficiency data associated with each treatment option. In this light, a large number of economic evaluations comparing the incremental costs and effects between different classes of drugs[15, 16], or among newer and older agents of the same therapeutic class[17], have been published. Almost all of the aforementioned studies have concluded that hypertension treatment represents an intervention that is associated with extremely favorable cost-effectiveness ratios[18]. In light of the above, and in order to contribute to this discussion; the purpose of the present study was to assess the cost-effectiveness of antihypertensive drugs in patients with hypertension from Mumbai, India.

Methods

Study design and participants

A cross sectional study was designed based on validated survey questionnaire. It was conducted in F-North ward of Mumbai, Maharashtra, India. Ethical approval was obtained from V.V. Hospital Independent Ethics Committee, Thane, India. Information about apartments and family members was acquired from the office of F-North ward, Mumbai Municipal Corporation. From their database, 1000 apartments having subjects within the age group of 30 – 75 were randomly selected. These apartments were visited by trained pharmacy students and a total of 200 subjects satisfying the inclusion criteria were identified from which 166 agreed to participate. The Inclusion criteria were age of 18 – 65 years, diagnosis of primary hypertension, a consultation and a blood pressure report from a physician within the period of 30 days prior to the interview date and written informed consent to participation in the study. Exclusion criteria were subjects with a recent cardiovascular episode (<1 year), known or suspected secondary hypertension, serious illness or pregnancy.

Study instrument

A survey questionnaire was designed in English after discussion with experts and a literature review of similar studies. The questionnaire was translated into Marathi and Hindi by experienced translator and back translated to English to ensure the content uniformity by another experienced translator. A pilot study was conducted in a sub sample of 30 subjects to ensure that the questionnaire would be appropriate, and understandable among the prospective respondents. The pilot testing allowed wording modifications in questions and also gave estimate of the average time required for interview and filling of the questionnaire. This population was not part of the final study.

Collection of data

Each selected apartment was visited by trained pharmacy student to collect the data. The purpose of the research was explained to the participant. Anonymity and confidentiality were guaranteed and maintained. The researchers complied with the international ethical guidelines for research. The information collected from each participant included the gender, age, occupation, marital status, religion, education, monthly family income per family member, waist / hip ratio, date since hypertensive, Systolic and diastolic blood pressure report from physician (in last 30 days), name, formulation, strength, price of antihypertensive/s medication, side effects if any and health insurance. The three reading of Supine blood pressure were taken by trained pharmacy student using a digital sphygmomanometer and the mean of these readings was considered for final calculation. Waist and hip circumferences (cm) were measured in duplicate with an anthropometric tape while the subjects were wearing light clothing. Waist circumference was measured at the minimum circumference between the iliac crest and the rib cage. Hip circumference was measured at the maximum protuberance of the buttocks, and the WHR was calculated. Data was recorded into predesigned case report form (CRF) by interviewers.

Data entry and analysis

Collected data from individual CRF was entered

into Microsoft excel and was verified by the authors other than interviewers. The data were analyzed by Microsoft excel for finding out relevant statistics. Qualitative variables were analyzed statistically, presented as frequencies and percentages.

Cost- effectiveness calculations

Cost effectiveness calculations were done by following method.

- Bioavailability: For every treatment bioavailability was determined from the standard pharmacology text book[19].
- Tolerability: Percentage Adverse drug reactions (ADR) were determined by following formula= (Number of adverse drug reactions/Number of patients on thetreatment) x 100.
    - Tolerability was calculated as = 100 - % ADR
- Efficacy: Efficacy calculations were done by following formulas
    - Systolic efficacy=100-(SBP-120)/1.2
    - Diastolic efficacy=100-(SBP-80)/0.8
    - Drug efficacy for single patient = (systolic efficacy + diastolic efficacy) / 2
    - Average efficacy for a treatment = total efficacy for treatment / number of patients on that treatment
- Safety of administration: For oral drugs was 100%
- Frequency of administration: ratings were as follows OD=100, BD=50, TID=33.3, QD=25
- Effectiveness of a treatment option = Sum of all criterion rating,
    - Where Criterion Rating = Criterion Value x Assigned Weight.
    - Assigned weights were based on the earlier study done by Abdulganiyu G[20], and they were as follows - Efficacy = 0.4, Tolerability = 0.2, Safety of administration = 0.1, Frequency of administration = 0.1, Bioavailability = 0.2
- Cost effectiveness Analysis (CEA) was done by following method:
    - Anti-hypertensive therapy is a lifelong management but follow up visit to physician is every 2-3 months. So for all treatments, the duration of therapy was considered as 3 months for calculations of cost effectiveness.
    - CEA = (Total cost for a treatment option for 3 months/ Effectiveness of the treatment option)
    - Cost is represented in Indian Rupees (INR)
- This was done and compared for each antihypertensive treatment option presently prescribed for the respondents in this study.
- Sensitivity analysis was performed to test whether the decisions change when specific variable (e.g. cost, effectiveness) were altered within reasonable range (10-25%) in favor of less cost-effective option in the management of hypertension.

RESULTS

Table 1 shows the socio-demographic parameters of participants from Mumbai under study. A total of 136 participants, with 66 (48.5 %) males and 70 (51.5 %) females were studied. The mean age was 52±9 years. Marital status, occupation, income and education of the participants is as shown in Table 1. Based on waist to hip ratio measurements, central obesity was seen in 25 (37.9%) males and 60 (85.7%) female participants. Out of total 136 respondents, maximum were treated with Amlodipine 36(26.5%), followed by Losartan 22(16.2%), Amlodipine + Losartan 20(14.7%), Atenolol as well as Amlodipine + Lisinopril combination 18(13.2%) each, Lisinopril 16(11.8%) and Captopril 6(4.4%). As shown in Table 2, when effectiveness alone was considered as the criteria rating for Amlodipine (85) was higher than Atenolol (82), Amlodipine + Losartan (80), Captopril (79), Amlodipine + Lisinopril (75), Losartan (74) and Lisinopril (73) in participants.

Table 1
Socio-demographic parameters of study participants from Mumbai.

Parameter N = 136	Frequency	Percentage
Gender		
Male	66	48.5
Female	70	51.5
Religion		
Hindu	136	100
Marital status		
With partner	130	95.6
Single	6	4.4
Occupation		
Employed	67	49.3
Business	27	19.9
Housewife	31	22.8
Retired	11	8
Monthly income / person		
Upper high class (> 10,000 INR)	113	83
High class (5000 to 9999 INR)	18	13.3
Upper middle class (3000 to 4999 INR)	2	1.5
Lower middle class (1500 to 2999 INR)	3	2.2
Education		
Graduate	118	86.7
Non graduate	18	13.3

Table 2
Effectiveness of treatment options used in the study.

		Atenolol n=18		Amlodipine + Losartan n=20		Amlodipine n=36		Captopril n=6		Amlodipine +Lisinopril n=18		Losartan n=22		Lisinopril n=16	
Criteria	**assigned weight**	**value**	**criteria rating**	**value**	**criteria rating**	**value**	**criteria rating**	**value**	**criteria rating**	**value**	**criteria rating**	**value**	**criteria rating**	**value**	**criteria rating**
Efficacy	0.4	85	34	75	30	81	32	82	33	65	26	81	32	83	33
Tolerability	0.2	100	20	100	20	100	20	90	18	100	20	100	20	100	20
Safety	0.1	100	10	100	10	100	10	100	10	100	10	100	10	100	10
Frequency	0.1	100	10	100	10	100	10	50	5	100	10	50	5	50	5
Bioavailability	0.2	40	8	50	10	65	13	65	13	45	9	35	7	25	5
Sum	**1**		**82**		**80**		**85**		**79**		**75**		**74**		**73**

As shown in Table 3, for treatment of hypertension in study participants, atenolol costed least (INR 5.5) per unit of effectiveness followed by amlodipine + losartan (INR 5.6), amlodipine (INR 6.3), captopril (INR 6.9), amlodipine + lisinopril (INR 9.6), losartan (INR 14.5) and lisinopril (INR 17.2). Sensitivity analysis done by assuming 25% increase in the cost and 25% decrease in the cost, indicated that the decision remains valid, confirming Atenolol was most cost effective treatment for study participants.

Table 3

Cost effectiveness analysis (CEA) and sensitivity analysis of treatment options used in the study.

Treatment option	frequency per day	cost of one tablet INR	daily cost INR	cost for 3 months INR	criteria value	CEA	increase 25 % cost	decrease 25% cost	criteria value	CEA with 25% more	CEA with 25% less
Atenolol	1	5	5	450	82	5.5	563	338	82	7	4
Amlodipine + Losartan	1	5	5	450	80	5.6	563	338	80	7	4
Amlodipine	1	6	6	540	85	6.3	675	405	85	8	5
Captopril	2	3	6	540	79	6.9	675	405	79	9	5
Amlodipine + Lisinopril	1	8	8	720	75	9.6	900	540	75	12	7
Losartan	2	6	12	1080	74	14.5	1350	810	74	18	11
Lisinopril	2	7	14	1260	73	17.2	1575	945	73	22	13

INR= Indian Rupee

DISCUSSION

Economic evaluation evidence for major health policy and public health interventions, such as hypertension treatment, is extremely valuable for demonstrating whether expenditure by organized health systems on these interventions represents "money well spent." It can also help to justify whether more or fewer of the scarce healthcare resources should be allocated for this purpose. In principal, for a chronic disease like hypertension, economic evaluations are nowadays performed by adopting a wide timeframe for the analysis, in order to include all future aspects (costs and outcomes) of the disease/intervention under survey. However, to complete the economic evaluation data surrounding treatment, short term economic evaluations with clinical endpoints are necessary[21,22] although sparsely reported in the literature. Following this line of thought, we conducted a cost-effectiveness study of hypertension treatment observed over the period of 3 months for the purpose of analysis. Effectiveness for Amlodipine (85) was higher than Atenolol (82), Amlodipine + Losartan (80), Captopril (79), Amlodipine + Lisinopril (75), Losartan (74) and Lisinopril (73) in participants. This was reflected in clinical practice, as out of total 136 respondents, maximum were treated with Amlodipine 36(26.5%), followed by Losartan 22(16.2%), Amlodipine + Losartan 20(14.7%), Atenolol as well as Amlodipine + Lisinopril combination 18(13.2%) each, Lisinopril 16(11.8%) and Captopril 6(4.4%). Cost effective analysis showed Atenolol was most effective as it costed least (INR 5.5) per unit of effectiveness. These result are similar to those reported by Jamali S[23] which showed that Atenolol was most cost-effective for the treatment of essential hypertension in comparison to conventional anti-hypertensive treatment. This study was able to describe the cost of the treatment and control of hypertension for patients taking blood pressure-lowering drugs. The selection of a population-based sample has the advantage of including a representative sample of the entire population and allows the cost-effectiveness of treatment based on drugs actually in use to be assessed, thereby differing from indirect estimates based upon data from production and sales of drugs, medical records or participants in randomized clinical trials[10]. Economic evaluation cannot provide a solution to all health care policy issues. However it does represent a significant input to the decision making process[24], the latter including a series of health-related and societal values that should be taken into account in the context of resource allocation. Hypertension given its chronicity and associated morbidity and mortality, constitutes a significant disease burden to the society, both in terms of the health-related repercussions as well as financial costs incurred due to morbidity and the cumulative cost of drug therapy[25]. As neither the symptoms of hypertension nor the beneficial effects of lowering blood pressure are readily apparent to patients, it is important to administer drugs that are cost-effective and have minimal adverse effects. This is particularly important in a developing country like India[25], where, the accretive cost of long-term therapy is often a significant deterrent to patient compliance. The results of this study contribute towards decision making involved in formulary management and by clinicians treating patients with hypertension.

CONCLUSION

Prescriptions of cost-effective antihypertensive drugs (73.5%) were more common than less cost-effective antihypertensive drugs (26.5%) in hypertensive patients from Mumbai, India. Most of the patients (72%) were prescribed monotherapy in the treatment of hypertension.

CONFLICT OF INTEREST

Conflict of interest declared none.

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