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RESEARCH ARTICLE

Prescribing Patterns of Anti Hypertensive Medications and Cost Effective Analysis of Anti Hypertensives in a Tertiary Care Hospital

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ABSTRACT

Hypertension means increased pressure of flowing blood on the lateral walls of arteries and veins. It is the best modifiable risk factor in case of CVS and Renal disorders, also strongest cause of morbidity and mortality. Due to increase in the prevalence of hypertension with the continuous increasing investment of treatment, factors that affect prescribing trends could have a significant impact on health economics. By 2000, it was estimated that over 1 billion individuals will be suffering with hypertension globally and by 2025, approximately 60% of increase shall be observed globally is estimated from hypertension. Drug utilisation review (DUR) programs have been defined as “structured, ongoing initiatives that interpret trends of drug utilisation in relation to predetermined criteria and attempt to prevent or minimise inappropriate prescribing.” According to WHO, Drug utilisation is defined as “the marketing, distribution, prescription and use of drugs in society with special emphasis on the resulting medical, social and economic consequences”.

Keywords: Hypertension, Renal disorders, Drug utilisation review

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1. Introduction

- Hypertension means increased pressure of flowing blood on the lateral walls of arteries and veins.
- It is the best modifiable risk factor in case of CVS and Renal disorders, also strongest cause of morbidity and mortality.
- Due to increase in the prevalence of hypertension with the continuous increasing investment of treatment, factors that affect prescribing trends could have a significant impact on health economics.

- By 2000, it was estimated that over 1 billion individuals will be suffering with hypertension globally and by 2025, approximately 60% of increase shall be observed globally is estimated from hypertension.
- Drug utilisation review (DUR) programs have been defined as “structured, ongoing initiatives that interpret trends of drug utilisation in relation to predetermined criteria and attempt to prevent or minimise inappropriate prescribing.”
- According to WHO, Drug utilisation is defined as “the marketing, distribution, prescription and use of drugs in society with special emphasis on the resulting medical, social and economic consequences”.
- Simply drug utilisation is defined as “the prescribing, dispensing, administering and ingesting of drugs

Possible outcomes of the study:

- Anti-hypertensive prescribing pattern can be uncovered by conducting the study. Prescribing pattern of anti-hypertensives in patients with hypertension and in patients with hypertension and Comorbidity can be studied.
- Through the study, it will be possible for the development of guidelines for the rural setup in the treatment of hypertension and cost effective analysis can be performed.
- Justification of the study:
- No guidelines for prescribing hypertension medication in rural setup or resource limited settings.
- Guidelines in prescribing for anti-hypertensives in hypertension with comorbidities.
- No study of compliances in rural setup.
- No cost-effective analysis in rural setup.
- Hence present study was selected and designed.

2. Materials and Methods

- **Study Design:**
- **Study Duration:**
- **Study Criteria:**
- **a) Inclusion criteria:** All primary hypertensive patients and hypertensive patients with comorbidities.

b) Exclusion Criteria: Subjects who are not willing to join the study.

Subjects under 18 years

- **Study size:** 100 subjects who are on antihypertensive medication for a period more than 2 months
- **Study Procedure:**
- The study includes 100 subjects and 192 prescriptions of 100 subjects were analyzed from time to time. All the subjects who were diagnosed with hypertension and along with comorbidities were studied and report was observed using data collection form.
- The prescription pattern of anti hypertensive's and the drug utilisation data shall be collected from the

prescription of patients regularly. Demographic profile of patients was also recorded from the same prescription itself.

- Depending on age, patients were divided in to following class intervals – 10-20, 20-30, 30-40, 40-50, 50-60, 60-70, 70-80 and above 80. Anti hypertensive medications were classified as ACEIs, ARBs, CCBs, BBs, diuretics and non selective beta and alpha 1 blockers (NS / ¹Bs).
- The average drug acquisition costs (ADAC, the costs of buying the drugs) were calculated on annual basis for each drug and the percentage expenditure cost (%EC) was calculated, using the following equations:

ADAC (daily)³⁹ = Total daily cost of drug class / Number of Prescriptions of the drug

Class (multiplied by 365 for the annual basis).

% EC = (Expenditure cost (EC) of the class / Total expenditure of all prescriptions) X 100

Sources of Data:

1st and last recorded blood pressure for each patient at each visit during the study period.

- Name and frequency regimen of each anti hypertensive medication from the prescription of each patient.
- Total cost of anti hypertensive medications for each prescription.

Follow Up: Out of 100 study subjects diagnosed with hypertension, 50 were males and 50 were females. Out of which 45 female and 47 male subjects were followed up during their subsequent visit and the remaining 5 female and 3 male subjects was considered as follow up failures.

Statistical analysis

The data shall be processed and presented using *In Stat* graph pad prism statistical program software. Data shall be subjected to *ANOVA* to determine t-test

3. Results and Discussion

Precision

Intraday Precision:

Intraday precision was determined by analyzing same concentration (60µg/ml) of Ciprofloxacin and Dexamethasone for six times in the same day.

Inter-day Precision: Inter-day precision was determined by analyzing the same concentration (60µg/ml) of Ciprofloxacin and Dexamethasone on different days.

Acceptance Criteria:

The Relative standard deviation of individual area of Ciprofloxacin and Dexamethasone from six standard preparations should be not more than 2.0%.

Observation:

The Relative standard deviation of individual area of Ciprofloxacin and Dexamethasone were found to be within limits.

Specificity

The specificity of the method is performed by separately injecting the blank, standard sample containing Ciprofloxacin and Dexamethasone. The interference observed (if any) at the retention times of each analyte in the chromatogram is evaluated.

Acceptance Criteria:

No Interference should be observed at the retention time of standard peaks in the blank.

Observation:

Interference was not observed with the standard peaks and the chromatograms of Standard and Sample were identical with same retention time.

Accuracy:**Acceptance Criteria:**

- The mean % Recovery of Ciprofloxacin and Dexamethasone at each level should be not less than 95.0% and not more than 105.0%.
- The %RSD of recovery of Ciprofloxacin and Dexamethasone from the three sample preparations at 50% and 150% levels should not be more than 5.0%.

Observation:

- The mean % Recovery of Ciprofloxacin and Dexamethasone were found to be within limits at each level.
- The % RSD of recovery of Ciprofloxacin and Dexamethasone from the three sample preparations was found to be 0.40 and 1.22 at 50% level and 0.39 and 0.54 at 150% level respectively.

Acceptance criteria:

%RSD should not be more than 2%

Theoretical plates should not less than 2000

Tailing factor should not more than 2.0

Observation: From the obtained values %RSD was found to be within the range of 0.5%-1.6% which states the method is acceptable.

Acceptance criteria:

%RSD should not be more than 2%

Theoretical plates should not less than 2000

Tailing factor should not more than 2.0

Observation:

From the obtained values %RSD was found to be within the range of 0.4%-1.5% which states the method is acceptable.

Ruggedness: Ruggedness of the method was performed by two different analysts using same experimental environmental conditions. It was performed by injecting the 60µg/ml of Ciprofloxacin and Dexamethasone, respectively. It was found to be rugged and %RSD (less than 2) indicating ruggedness of the method

Limit of detection and limit of quantization:

The Limit of detection of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated.

The Limit of quantification is an analytical procedure is the lowest amount of analyte in a sample, which can be quantitatively determined with suitable precision and accuracy. They can be calculated as

$$\text{Ciprofloxacin: LOD} = \frac{3.3 \sigma}{S}$$

SD = the Standard deviation of Y-intercept 5 calibrations

Slope = the mean slope of the 5 calibrations

Table 1: Age group distribution of patients

Age Groups (years)																
Category	10-20		20-30		30-40		40-50		50-60		60-70		70-80		80-90	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Male	0	0	1	1%	9	9%	9	9%	16	16%	12	12%	2	2%	1	1%
Female	0	0	2	2%	15	15%	15	15%	11	11%	7	7%	0	0%	0	0%

- Our study includes 100 subjects with hypertension and hypertension with Comorbidities, out of which 50 were male and 50 were female.
- Results in the present study showed a higher incidence of hypertension in male patients with age group of 50-60 years (16%) and female patients with age group of 30-50 years (15%) suggesting an earlier onset of hypertension in female population

Table 2: Frequency of drugs prescription in different age groups

Age Group (years)	ACEIs	ARBs	CCBs	BB	DU	NS / 1B
20 – 30	1(0.36)	--	17(6.22)	3(1.09)	8(2.93)	--
30 – 40	29(10.62)	1(0.36)	16(5.86)	--	1(0.36)	--
40 – 50	1(0.36)	13(4.76)	34(12.45)	2(0.73)	1(0.36)	--
50 – 60	--	18(6.59)	66(24.17)	19(6.95)	7(2.56)	--
60 – 70	7(2.56)	8(2.93)	8(2.93)	--	6(2.19)	2(0.73)
70 – 80	--	3(1.09)	--	--	2(0.73)	--
80 – 90	--	--	--	--	--	--

CCBs (amlodipine) are the most commonly prescribed group of antihypertensive drugs in the age groups 20-30, 40-50, 50-60years. In the age group of 30-40years, ACEIs was prescribed more commonly followed by CCBs (amlodipine).

Table 3: Comorbidities of the patients

S.no	Comorbidity	Number		Total	Percentile of comorbidity
		Male	Female		
1	Dengue	-	1	1	1.02
2	Thrombocytopenia	-	1	1	1.02
3	Diabetes Mellitus	6	25	31	31.63
4	COPD	1	-	1	1.02
5	CHF	1	6	7	7.14
6	IHD	15	-	15	15.30
7	Stable Angina	1	-	1	1.02
8	Epilepsy	1	-	1	1.02
9	Thyroid	-	9	9	9.18
10	TB	1	-	1	1.02
11	Pedal oedema	1	6	7	7.14
12	Cardiomegaly	-	1	1	1.02
13	LVH	8	-	8	8.16
14	PC Stroke	4	-	4	4.08
15	Right temporal Infarct	4	-	4	4.08
16	Asthma	1	-	1	1.02
17	Multiple joint pains	1	-	1	1.02
18	Dilated LV, LA	2	-	2	2.04
19	Severe LV dysfunction	2	-	2	2.04
Total		49 (49%)	44 (44%)	98 (98%)	

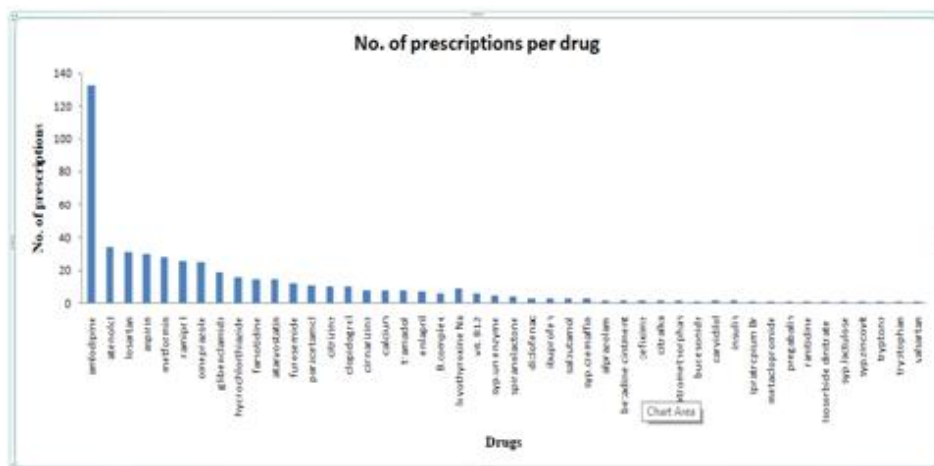


Figure 1: Number of Prescriptions per drug

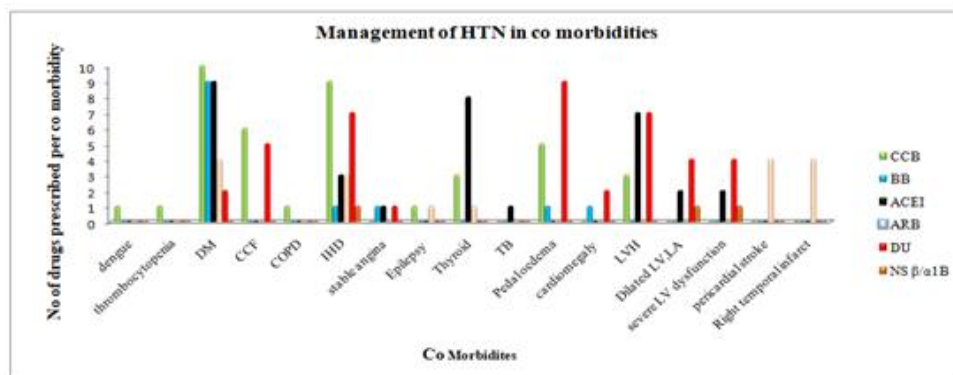


Figure 2: Management of Hypertension in comorbidities

Table 4: Monthly, Annual Drug Acquisition Costs and Total Expenditure of Anti-Hypertensive's

S.No	Drug	WHO Defined Daily Dose (mg)	Brand name	Cost/10 tab (Ks)	Generic name	Cost/ 10 tab(Ks)	Economic difference (%)	%Expenditure cost (Ks)	ADAC (Ks)
1	Ramipril	2.5 mg	Ramgee	45.00	Ramipril	13.00	71.1	9.39	63.17
2	Amlodipine	5 mg	Amlong	55.00	Amlodipine	6.00	92.30	69.39	17.83
3	Furosemide	40 mg	Lasix	5.71	Furosemide	5.00	25.48	0.64	20.40
4	Losartan	50 mg	Losarb	45.00	Losartan	18.00	60	11.19	52.98
5	Atenolol	50 mg	Cadpacas	15.90	Atenolol	7.00	55.97	4.33	17.06
6	Carvedilol	6.25 mg	Cardifine	13.00	Carvedilol	27.00	37.20	0.69	781.75
7	Enalapril	5 mg	Eipril	30.00	Enalapril	6.00	80	1.68	156.42
8	Hydrochlorothiazide	25 mg	Epzide	11.00	Hydrochlorothiazide	3.75	79.54	1.50	23.61
9	Spiranolactone	25 mg	Aldactone	18.50	Spiranolactone	11.22	728	0.59	168.81
10	Valsartan	80 mg	Starval	59.00	Valsartan			0.55	2518.5
	Total							100	3823.58

% ED (Economic difference) = (ED/maximum value) X 100

%EC (Expenditure Cost) = (EC of drug class / total expenditure of all prescriptions) X 100

ADAC (Average daily acquisition cost) = (Total daily cost of the drug class / number of prescriptions of drug class) X 365

Cost effective analysis of present study, by taking 100 patients with hypertension and along with Comorbidities, a total expenditure of Rs.3823.58 was invested in 1 year. Among the prescribed antihypertensives, the most costliest drug was Valsartan followed by amlodipine and least expensive drugs was found to be Furosemide followed by Hydrochlorothiazide.

Discussion

Hypertension is a global problem and the risk of hypertension depends on large number of factors like genetic, race, ethnic, environmental and psycho social factors. In India, surveys on hypertension explains that 25-30% of urban adults and 10-15% of rural adults have hypertension (Bp 140/90 mm Hg) (stage-I), 12-15% of urban adults and 5-7% of rural adults have stage - II and high levels of hypertension.

The study was based on a sample of 100 subjects diagnosed with hypertension and along with comorbidities. The present study gives information on drug utilization or prescription pattern and cost effectiveness of anti-hypertensives. A total of 192 prescriptions of 100 subjects were studied. It was observed that equal number of men and women encountered over the period of study indicating that both men and women have equal risk of hypertension in rural setup. In black hypertensive population, including those with diabetes, a CCB or Thiazide type diuretic is recommended as initial therapy according to JNC- 8 guidelines and our study also supports these results, in which CCB (Amlodipine) are prescribed with high frequency as initial therapy followed by BB.

The patients with Comorbidity mainly were prescribed with 1 or 2 antihypertensive medications along with other drugs to treat their associated Comorbidities like diabetes mellitus, IHD, CCF, Thyroid disorder, pedal oedema, LVH etc. However, a case of hypertension with associated Comorbidity DM and already a known case of TB on medication was put on Ramipril (ACEI) and appropriate oral hypoglycemics. A severe case of hypertension with IHD, dilated LV, LA, severe LV dysfunction was treated with Furosemide (LD), Spiranolactone (KSD), Ramipril (ACEI) and Carvedilol (NS / 1B).

In our study, the most prevalent coexisting disease DM was prescribed with CCBs, BBs, ACEIs, ARBs where as in the study conducted by Mirza Atif Beg, et al (38) ARBs, ACEIs were commonly prescribed. Major drawback of drug utilisation studies is lack of detailed. The cost effectiveness was determined by relationship between the profits obtained for the investment. Main determinants for cost effective analysis are investment of drug therapy and the initial risk of hypertension to the patients. A total of Rs.3823.58 was invested in 1 year on drug acquisition for 100 patients of hypertension and along with Comorbidities. Furosemide (Rs 0.67/tab), Hydrochlorothiazide (Rs 1.01/tab) were the least costly drugs followed by Atenolol (Rs 1.59/tab), Aldactone (Rs 1.85/tab). Valsartan (Rs 6.9/tab), Amlodipine (Rs 6.5/tab), Losartan (Rs 4.5/tab), Carvedilol (Rs 4.3/tab) were the expensive drugs used. In the study cost of brand drugs like Valsartan, amlodipine are higher compare to their generic one. Amlodipine (CCB) accounted for 69.4% of annual drug expenditure which mostly prescribed even though, it is highly expensive. This may be due to good compliance, better relief from illness, less incidence of ADRs. Furosemide used in 4.49 % of prescriptions accounted for 0.64 % (least % EC), Carvedilol accounted 0.69 % for 0.74 % prescriptions. Diuretics accounted 0.64 %, 0.59 % and 1.50 % of annual expenditure for 12.35 % prescriptions.

An overview of totality of evidences recommends that the major groups of drugs used in hypertension are approximately equivalent in safety and efficacy except the drug amlodipine (CCB) which is majorly prescribed is highly expensive even though there is safety and efficacy. At the same time, the generic drugs are least expensive compare to branded one. Hence, our study suggests that use of generic drugs leads to most cost effective and better pharmacologic therapy with accurate safety and efficacy.

4. Conclusion

The drug use pattern in hypertension was found to be standard guideline's based and majority of the cost was borne by the patient. The total cost increased was due to administration of drugs to treat the adverse drug reaction. Majority of the drugs prescribed were by their brand names so generics should be made available which can reduce the cost of treatment. Considering the polypharmacy, use of brand names and inappropriate selection of drugs which increased the total cost of treatment, following measures are recommended:

- Revise hospital schedule formulary
- Drugs on schedule should be made available throughout the year
- Prescription auditing should be done on regular basis
- Prospective, randomised, cohort studies should be planned in a larger sample size, so that policy makers will get the better insight in to present scenario and can provide ways to optimize the treatment of patients with hypertension.

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