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Original Research Article

A Comparative Study on the Impact of Side effects of Antihypertensive Drug Classes on Adherence to Medication

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Abstract

Background: Hypertension is the most common chronic illness and one of the most important risk factors for cardiovascular disease. Medication nonadherence is the leading cause of uncontrolled hypertension, which has become a significant concern in developed countries. The side effects of first-line drugs such as Diuretics, Calcium channel blockers and Angiotensin receptor blockers could be accounted for the non-adherence.

Aim and Objectives: The study was focused on determining the impact of the first-line antihypertensive class side effects on drug adherence.

Materials and Methods: The study compared the adverse effects of Diuretics, Calcium channel blockers and Angiotensin receptor blockers using structured questionnaires. The side effects, severity and adherence were calculated by assessing the Physical symptom distress index (PSD), Overall symptom distress index (OSD) and pill count adherence ratio (PCAR).

Results: In total 39.3% (22 out of 56 patients) at the end of 4 weeks and 41.1% (23 out of 56 patients) at the end of 8 weeks experienced side effects. Diuretics had a higher mean OSD (3.56) than the Calcium channel blocker (1.75) and Angiotensin receptor blocker (0.60). Angiotensin receptor blocker produced side effects in 25% of people consuming it and medication adherence of 70%. Following that, the Calcium channel blocker produced side effects in 45% and medication adherence in 60% of the patients. However, Diuretics have side effects of 56.3% and medication adherence of 62.5%.

Conclusion: The above study proved that Angiotensin receptor blockers produced fewer side effects and more drug adherence than CCB and diuretics. This suggested that side effects might substantially affect antihypertensive drug adherence.

Keywords: Antihypertensive drug, Side effects, medication adherence.

Introduction

The most prevalent chronic ailment in developed nations is hypertension, which is also one of the main risk factors for cardiovascular disease [1]. Antihypertensive medications can successfully manage hypertension and the consequences that it causes [2]. There would be a tiny percentage of patients with uncontrolled hypertension and associated problems if patients took their medications as directed and adhered to therapeutic lifestyle adjustments like physical activity and calorie and salt limitations [3]. Several classes of antihypertensives are administered, including Beta blockers, Diuretics, Angiotensin-converting enzyme (ACE) inhibitors, Calcium channel blockers (CCB), and Angiotensin II

receptor blockers (ARB). ACE/ARB and CCB/diuretics are the first-line medications used in the younger (less than 55) and older (greater than 55) age groups, respectively, according to Indian hypertension guidelines. Side effects and

education compliance are crucial aspects in the management of hypertension. According to the World Health Organization, "the degree to which the person's behaviour conforms with the approved advice from a health care provider" [4] is the definition of medical adherence. Medication nonadherence, defined as taking fewer than 80% of the recommended dosage of pills [5] has been noted as the primary contributor to uncontrolled hypertension [6]. The risk of uncontrolled hypertension increases by five times with nonadherence, as do general mortality rates, hospitalisation rates, and healthcare costs [6,7].

According to several researchers, side effects are a significant factor in patients' poor compliance with antihypertensive medication [8]. However, these cross-sectional investigations were vulnerable to reverse causality bias. At regular dosages, 20 to 97 percent of individuals using antihypertensive medications experience adverse pharmacological effects [9].

According to Lin *et al*, 's research, people with hypertension who had any side effects from their medication were 77% less likely to stick with it than those who did not [10]. Most of the side effects caused by diuretics, calcium channel blockers, and angiotensin receptor blockers might be the important cause of medication- nonadherence. The most common side effects are frequent urination, ankle oedema, headache, excessive urination, fatigue, muscle cramps, and dizziness (diuretics), as ankle oedema, giddiness, palpitations, and headache (CCB) and fatigue, dizziness, and headache (ARB). The three that stood out for everyone were headaches, decreased libido, and increased micturition [11]. This study clarifies the adverse effects of the three antihypertensive drug classes (diuretics, CCB, and ARB) and how they impact patient adherence to individual drug class regimens.

Aim

The above study aimed to evaluate the association between antihypertensive drug classes side effects and medication adherence.

Material and Methods

This questionnaire-based observational study was conducted among hypertensive patients visiting Medicine- Hypertensive clinic of Sree Balaji Medical College and hospital for a duration of six months (April 2019 to September 2019). Institutional ethics committee clearance was obtained.

Inclusion criteria: Individuals between the age of 18 to 80 with newly diagnosed essential hypertension- stage 1 hypertension (systolic/diastolic BP >140-149/90-99 mmHg, on the average of 2 or more readings, according to JNC 8 guidelines) were included in the study.

Exclusion criteria: Patients who were already on medications for other co-morbid conditions like diabetes mellitus, epilepsy, bronchial asthma, Chronic diseases like tuberculosis, chronic kidney disease or patients with history of any cancer, Pregnant and lactating mothers, and Patients who are either below 18 or above 80 years of age were excluded from the study.

Data Collection Instruments: Open and closed-ended structured questionnaires, tablet counter.

Methodology

The hypertensive patients attended the hypertensive clinic-Hospital during the study period and prescribed Amlodipine 5mg (CCB), Hydrochlorothiazide 25mg (Diuretics), and Telmisartan 20mg (ARB) were selected. Those, who were willing and fulfilled the criteria, were included in the study. Seventy-five hypertensive

patients who were started on three different classes of drugs Hydrochlorothiazide (Diuretics-25), Amlodipine (Calcium channel blockers-25), Telmisartan (Angiotensin receptor blockers-25) were recruited. The written consent was obtained from the patients after explaining the study procedure in their local language. Five patients in CCB and ARB group did not visit for follow-up. In the diuretics group, nine patients were lost for follow-up. Side effect symptoms of specific drug classes and the other factors influencing drug adherence were assessed by using structured questionnaires, and pills were counted as well to strengthen the results (Physical symptom- distress index (PSD), overall symptom distress (OSD), and pill count adherence ratio (PCAR). Data collection was done for about a period of six months. The data regarding the dose and frequency of the antihypertensive drugs, along with the other necessary particulars of the patient like name, age,sex, contact details, and blood pressure readings were collected at the time of recruitment. During the follow-up visits (at end of the fourth and eighth week), data were collected on the side effects of each drug class separately. The other factors that influence medication adherence were assessed using structured questionnaires.

Drug side effects were assessed using the PSD - Physical symptom- distress index [12]. It was calculated in the following manner. First, the presence of side effects is ascertained.

Then the frequency of the symptom is noted as:

1 One to two times a month
2 One to two times a week
3 Each week
4 Daily

Next the severity of the side effects is taken as:

0 Not at all bothered

1 Not very bothered
2 Somewhat bothered
3 Very bothered
4 Extremely bothered

Then the presence of a symptom, their frequency. and severities have multiplied by the sum of all symptoms together, giving the overall symptom distress -OSD [13]. Adherence was calculated using pill count adherence ratio PACR= Pills consumed out of the number of pills prescribed X100. If the PCAR is less than 80%, then the patient is non- adherent to the prescribed medication.

Statistical Analysis

After collecting the data, it was processed using the statistical package of social service (SPSS). Chi-square (p-value) test, post-hoc test and Kruskal-Wallis test were used todetermine the level of significance.

Results

Table 1: Side effects among different drug class of Anti-hypertensive Medication

Anti -Hypertensive Medication	Side Effects Present Absent		P Value (Chi-square)
4 Weeks	Total (22)	Total (34)	
Calcium channel blockers	8(40%)	12(60%)	
Angiotensin receptor blockers	5(25%)	15(75%)	
Diuretics	9(56.3%)	7(43.8%)	0.162
8 weeks	Total (23)	Total (33)	
Calcium channel blockers	9 (45%)	11(55%)	
Angiotensin receptor blockers	5 (25%)	15 (75%)	0.151
Diuretics	9 (56.3%)	7 (43.8%)	

Table 1: Depicts that in total 39.3% (22 out of 56 patients) at the end of 4 weeks and 41.1% (23 out of 56 patients) at the end of 8 weeks experienced side effects to the prescribed anti-hypertensive medication. Out of these,40% (8 out of 20) at the end of 4weeks & 45% (9 out of 20) at the end of 8 weeks of patients consuming Calcium channel blockers, 25% (5 out of 20) of patients consuming Angiotensin II receptor blockers at the end of 4th and 8th weeks and 56.3% (9 out of 16) of patients consuming diuretics at the end of 4th and 8th weeks experienced side effects. They had no statistical significance.

Table 2: Overall Symptom Distress score of Anti-hypertensive medications

Anti-Hypertensive Medication	OSD score Mean±SD	Mean CI	Mean Rank (Kruskal-Wallis test)	P value (Chi-square)	P value (ANOVA)
Calcium channel blockers	1.75 ±2.0	(0.822.68)	29.23	0.033	0.005
Angiotensin receptor blockers	0.6 ±1.3	(0-1.2)	22.50		
Diuretics	3.56 ± 4.1	(1.39-5.74)	35.09		

Table 2: Total mean OSD (overall symptom distress) of all three drug classes combined is 1.38. However, Diuretics has the highest mean OSD of 3.56 followed by Calcium channel blockers which has a mean OSD of 1.75 followed closely by Angiotensin II receptor blockers with a mean OSD of 0.60. By Kruskal-Wallis test in Table 2 shows that mean OSD difference of all 3 drug classes have a significance of 0.033.

Table 3: Pill Count Adherence Ratio (PCAR) for drug classes of Anti-hypertensive medication

Anti -Hypertensive Medication	PCAR<80	≥80%	P Value (Chi-square)
Calcium channel blockers (20)	8 (40%)	12 (60%)	0.79
Angiotensin receptor blockers (20)	6 (30%)	14 (70%)	
Diuretics (16)	6 (37.5%)	10 (62.5%)	

Table 3: Out of 56, 20 (35.7%) turned out to be non-adherent since their PCAR (Pill count adherence ratio) was less than 80% (Table 3). Of the 20 non-adherent cases, 8 cases (40%) were reported by patients taking Calcium channel blockers, 6 cases (30%) by patients taking Angiotensin II receptor blocker and 6 cases (37.5%) by patients taking Diuretics. As far the specific drug classes are concerned Calcium channel blockers report of producing side effects in 45 out of 100 people (45%) with a mean OSD of 1.75 and a medication adherence of 60%. Angiotensin receptor blockers produce side effects in 25% people consuming it with a mean OSD of 0.60 and a medication adherence of 70%. Diuretics produce side effects in 56.3% with a mean OSD of 3.56 and a medication adherence of 62.5%.

Discussion

The overall symptom distress (OSD) scale was utilised to evaluate the patients' adverse effects. A high OSD denotes serious side effects, and a low OSD denotes less serious side effects. Diuretics had a higher mean OSD than the other two drug classes, which indicates that they experienced more side effects, more frequently and with greater severity. A few of were giddiness, muscle soreness, increased urination, and fatigue. Ankle oedema, giddiness, and headache were the most common side effects that calcium channel blocker users reported. Patients on an ARB noted fatigue and giddiness. However, the classification of these adverse effects into their respective systems (genitourinary, central nervous system, etc.) was not done, as it was in one study [13]. The three drugs did not have any other recent side effects to report.

ARB has a mean OSD of 0.60, while diuretics have a mean OSD of 3.56. The mean OSD difference between diuretics and ARB was 0.005 (p=0.005) on repeated comparisons, indicating its importance. Moreover, using the Kruskal-Walli's method, the overall comparison of the mean OSD across all three medication classes had a significant level of 0.033. The greater disparity between the mean OSD values of the various medication groups gives rise to this relevance.

Utilizing the PCAR-pill count adherence ratio, the medication adherence was computed. PCAR is the percentage of the number of tablets consumed from the prescribed tablets. The patient is non-adherent if the ratio is less than 80% to the prescribed medicine. Here, 20 out of 60 instances, or 35.7%, were non-adherent, meaning they consumed less than 48 of the 60 prescribed pills (80%).

According to the data gathered from the questionnaire, side effects, forgetfulness, and the patient's ignorance of the consequences of non-adherence were some reasons for non-adherence. Angiotensin receptor blockers had higher adherence because of their fewer side effects (70 percent). Calcium channel blockers are slightly better than diuretics in drug adherence (2.5 percent difference), even though diuretics experienced more significant adverse effects (11.3 percent difference) than CCB.

These might be due to the specific side effects of calcium channel blockers [14]. However, diuretics and beta blockers, had the lowest rates of adherence, according to one study [15]. Furthermore, social demographic factors and patient factors play vital roles in drug adherence. So, the above findings suggested that side effects are among the main factors affecting medication adherence.

Limitations

In our study, patients who had attended the hypertensive clinic during the study period and fulfilled the criteria were taken. However, a multicentric study with more sample size will be needed for more reliable conclusion.

Conclusion

The anti-hypertensive drug class with the minor side effects and most adherence is Angiotensin receptor blockers proving that side effects impact medication adherence. Further studies analyzing factors affecting adherence to anti-hypertensive drug classes are needed. However, patient motivation and awareness improve drug adherence and effective control of hypertension.

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