Association between medication adherence and blood pressure control in urban hypertensive patients in central India

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ABSTRACT

Introduction: Cardiovascular and renal complications associated with hypertension (HTN) can be reduced if blood pressure (BP) is well controlled. However, a large percentage of patients fail to achieve target BPs, largely due to poor medication adherence. We conducted a cross-sectional study of patients of HTN to assess patient adherence to treatment and the association between medication adherence and BP control.

Methodology: The study was a cross-sectional survey of adult hypertensive patients of either sex who had been on antihypertensive therapy for the past 3 months. Medication adherence was measured using the 8-item Morisky Medication Adherence Scale (MMAS-8). Level of control of BP was evaluated using the BP goals recommended by the Eighth Joint National Committee (JNC-8).

Results: Out of a total of 200 patients, only 29.5% of patients had achieved their target BP as per JNC-8 recommendations after a minimum of 3 months of antihypertensive therapy. The average adherence score on the MMAS-8 was 6.47 (±1.8). A high adherence was found in 39% of patients, while 32.5% of HTN patients had a medium score and 28.5% had low adherence scores. There was a significant correlation between medication adherence and BP control. Only 1.5% of patients with low adherence score and 11.5% with medium score had achieved their target BP while 16.5% with high had done so.

Conclusion: Higher medication adherence scores were associated with better BP control. However, the percentage of patients with controlled HTN on treatment was low as was the proportion of patients with a high medication adherence score.

Keywords: Blood pressure control, hypertension, medication adherence

Introduction

Hypertension (HTN) is one of the most important causes of premature death worldwide and the third most important risk factor for attributable burden of disease in South Asia.[1] Recent systematic reviews and meta-analyses show that on an average, about 1 in 3 adults in the developing world is hypertensive.[2] In India, about 33% of the urban and 25% of the rural population has HTN.[3]

Raised blood pressure (BP) is a powerful and independent risk factor for cardiovascular and renal disease. The higher the BP, the higher is the risk of stroke, coronary heart disease, renal disease, heart failure, and death. Data from many observational epidemiological studies provide evidence of the direct relationship between BP and cardiovascular disease. In a recent meta-analysis of data from 61 prospective observational studies that together enrolled 9,58,074 adults, there were strong direct relationships between average BP and vascular mortality.[4] In the past decade, age-adjusted rates of stroke, end-stage renal disease, and the prevalence of heart failure have increased. An important factor responsible for these
trends is inadequate control of BP in the hypertensive population.\(^5\) Despite the availability of a number of effective antihypertensive agents, a 2003–2004 survey revealed that only 54%–59% of treated hypertensive patients were reported to have their BP controlled.\(^6\)

Inability to achieve target BPs deprives the patient of the full benefit of antihypertensive therapy in reducing their cardiovascular risk. On the other hand, hypertensive patients in whom BP is well controlled and recommended BP goals are achieved, have a reduced cardiovascular risk.\(^7\)

A major contributor toward inadequate BP control is poor medication adherence.\(^8,9\) The present study was, therefore, planned as a small cross-sectional study of patients of HTN to assess patient adherence to treatment prescribed for HTN and to explore if there is any association between treatment adherence and the level of BP control. Association of adherence with demographic and other factors such as number of drugs, duration of therapy, and cost of drugs was also assessed.

**Methodology**

The study was carried out as a cross-sectional survey of adult hypertensive patients who visited the internal medicine outpatient department of a tertiary care center in Bhopal (Madhya Pradesh). At present, there is no separate HTN clinic at the study site.

Sampling method was convenience sampling. All adult patients of either sex, over 18 years old, who had been on antihypertensive therapy for the past 3 months or more and who were willing to participate were included in the study.

Medication adherence was measured using the 8-item Morisky Medication Adherence Scale (MMAS-8)\.\(^{10}\) The MMAS-8 is an adherence scale consisting of 8 items each of which measures a specific medication-taking behavior. Response categories are yes/no for 7 items and a 5-point Likert response for the last item. Scores of the MMAS-8 range from 0 to 8. A score below 6 indicates low adherence, a score between 6 and <8 indicates medium adherence, and a score of 8 indicates high adherence. The questionnaire was administered by one of the investigators.

BP was measured twice at 5 min interval using a mercury sphygmomanometer, and the mean of the two BP measurements was taken as current reading. The level of control of BP achieved with antihypertensives was evaluated using the BP goals recommended by the Eighth Joint National Committee (JNC-8). BP was considered to be uncontrolled if either the systolic or diastolic pressure was found to be above the recommended BP goal 3 months or more after being prescribed an antihypertensive drug. Recommended target BPs as per JNC-8 include BP at <150/90 mmHg for a person 60 years or older who is not suffering from diabetes mellitus or chronic kidney disease and a BP at <140/90 mmHg for all others.

Sample size calculations were done to estimate proportion of patients with optimal drug adherence. To estimate 50% optimal adherence with 95% confidence interval (CI) of 42.5–57.5, required sample size would be 177. Considering a nonresponse rate of 20%, a sample size of 215 was taken.

Data were collected from eligible patients using a standard case record form and the MMAS-8.

The current BP value and information regarding drug treatment for HTN or any other diseases for which the patient was being treated at the study site was collected at the time of interview from the patients and from the outpatient file which is maintained with the patient.

Cost of drugs was estimated using the discounted prices at which drugs are sold to the OPD patients at the in-house pharmacy shop. Cost of drugs which were not available at the in-house pharmacy (33.1% of total antihypertensive drugs prescribed) was determined using www.mims.com/india or www.medlineindia.com. In case of generics, cost of the cheapest brand available was included in the study.

Data were entered and analyzed using the IBM-SPSS version 21 (IBM Corp. Released 2012. Armonk, NY, USA). Categorical data were summarized as count and percentage while numerical data were taken as mean and standard deviation. Chi-square test was used for testing association of BP control with drug adherence and other categorical variables. Mann–Whitney test was used to test difference between nonnormally distributed variables such as number of drugs, number of antihypertensive drugs, and cost of drugs with respect to their control status. Binary logistic regression analysis was used to identify independent predictors of BP control status. BP control status was the outcome-dependent variable. Independent variables were age, gender, education, occupation, duration of disease, treatment duration, combination therapy, cost of treatment, and systolic and diastolic BP at
the time of diagnosis. Hosmer–Lemeshow test was used as goodness of fit test and Omnibus test of model coefficient was used to test significance of model. Odds ratio (OR) and 95% CI of OR were calculated for all independent variables.

Informed consent was taken from all patients before being included in the study. Clearance from the Institutional Human Ethics Committee was taken before starting data collection.

Results

A total of 215 patients were invited to enroll in the study, of which 200 consented to participate. The mean age of participants was 57.1 years (±12.0), with a minimum age of 18 years and maximum of 90 years. Out of a total 200 patients, 109 (54.5) were below 60 years of age. The number of women (110 or 55%) was slightly but not significantly higher as compared to men. Only 82 (41.0%) of the participants were educated up to graduate level or above. Similarly, 80 (40.0%) of the patients were employed, the rest being unemployed, retired, or homemakers.

Among the total, 71 patients had a concomitant disease, with diabetes mellitus being the most common (28%). Average duration of diagnosis of HTN was 6.9 years (±6.42) and the average duration of antihypertensive medication intake was 6.3 years (±6.02). Mean BP at the time of diagnosis was 167.2/94.2 mmHg. The average number of pills prescribed per patient was 2.25 (counting an FDC as one drug). The mean number of antihypertensive pills prescribed (each pill could contain more than one antihypertensive drug) per patient was 1.44. While 132 patients were on a single antihypertensive medication, 54 were taking two antihypertensive drugs and 14 were using three to four drugs. The most frequently prescribed antihypertensive medications were telmisartan (57.5% of patients), amlodipine (33.5%), and metoprolol (18.0%), [Table 1].

Only 59 (29.5%) of patients had achieved their target BP as per JNC-8 recommendations after a minimum of 3 months of antihypertensive therapy, and their disease status was labeled as “controlled.” Those who failed to achieve their target BP targets after 3 months of therapy (141, 70.5%) were labeled as “uncontrolled.” Using Pearson’s Chi-square test, we found no association between demographic factors such as age, gender, and occupation on control status. However, education did appear to have an impact on BP control as only 46 (23%) patients who had completed graduation failed to achieve their target BPs compared to 95 (47.5%) of those who were less educated [Table 2]. Disease and drug-related factors such as duration of HTN, duration of drug treatment, number of drugs, or cost of drugs also did not show any association with BP control. Average cost of antihypertensive drugs was Rupees 7.72 per day.

Table 1: Frequency of various antihypertensive drugs prescribed

| Drug name                        | Number of prescriptions | Percentage of prescriptions (n=200) | Percentage of antihypertensive drugs (n=345)* |
|----------------------------------|-------------------------|-----------------------------------|-----------------------------------------------|
| Drugs acting at renin-angiotensin system |
| Angiotensin receptor blockers    | 144                     | 72.0                              | 41.7                                          |
| Telmisartan                     | 115                     | 57.5                              | 33.3                                          |
| Losartan                        | 18                      | 9.0                               | 5.2                                           |
| Olmesartan                      | 11                      | 5.5                               | 3.2                                           |
| Angiotensin-converting-enzyme inhibitors | 13                  | 6.5                               | 3.8                                           |
| Ramipril                        | 12                      | 6.0                               | 1.7                                           |
| Enalapril                       | 1                       | 0.5                               | 0.3                                           |
| CCBs                             | 72                      | 36.0                              | 20.9                                          |
| Amlodipine                      | 67                      | 33.5                              | 19.4                                          |
| Other CCBs*                     | 5                       | 2.5                               | 1.4                                           |
| Diuretics                       | 59                      | 29.5                              | 17.1                                          |
| Hydrochlorothiazide             | 42                      | 21                                | 12.2                                          |
| Chlorthalidone                  | 16                      | 8.0                               | 5.2                                           |
| Furosemide                      | 1                       | 0.5                               | 0.3                                           |
| Beta adrenergic blockers        | 56                      | 28.0                              | 16.2                                          |
| Metoprolol                      | 36                      | 18.0                              | 10.4                                          |
| Atenolol                        | 17                      | 8.5                               | 4.9                                           |
| Other beta blockers**           | 3                       | 1.5                               | 0.9                                           |
| Prazosin                        | 1                       | 0.5                               | 0.3                                           |
| Total                           | 345                     |                                    |                                               |

*One patient may be receiving more than one antihypertensive medication, *Cilnidipine, diltiazem, nifedipine, **Betalol, carvedilol, nebivolol. CCBs - Calcium channel blockers.
The average adherence score on the MMAS-8 was 6.47 (±1.8). A high adherence (MMAS-8 score = 8) was found in 78 (39%) patients while 65 (32.5%) HTN patients had a medium (6 to <8) score and 57 (28.5%) had low adherence scores (<6). Again, there was a significant association between medication adherence and education.
status, with patients who were more educated having higher MMAS scores [Table 3] while age, gender, and occupation had no influence on adherence. There was no association between duration of HTN, duration of drug treatment, number of drugs, or cost of drugs on BP control.

There was a significant association between medication adherence and BP control. Only 3 (1.5%) patients with low adherence score and 23 (11.5%) with medium score had achieved their target BP while 33 (16.5%) with high had done so. Although the number of patients with uncontrolled BP was higher in all adherence groups, this gap kept decreasing as we approached a high MMAS-8 score [Table 2] which shows that better compliance did lead to better BP control.

Binary logistic regression analysis was carried out to identify independent predictors of BP control status [Table 4]. Data were fit for model ($P > 0.01$ for Hosmer–Lemeshow and $P < 0.01$ for Omnibus test) and 35% variation in outcome could be explained with the model ($R^2 = 0.353$). Patients with a high adherence score [OR 13 [3.31–51.7]], medium adherence score [OR 9.9 [2.5–37.8]], and those with education up to graduate level or above [OR 2.8 [1.23–6.51]] were more likely to have their BP controlled and these were independent predictors. Furthermore, lower BP readings at the time of diagnosis were independent predictor for optimal BP control.

**Discussion**

The World Health Organization (WHO) defines adherence as “the extent to which a person’s behaviour — taking medication, following a diet, and/or executing lifestyle changes — corresponds with agreed recommendations from a health care provider.” A meta-analysis of studies spread over five decades has estimated the average nonadherence rate to be 24.8%.[11] Adherence is especially an issue in chronic asymptomatic disorders. According to the WHO, nonadherence of patients with chronic diseases is around 50% in developed countries and probably higher in developing countries. Studies of medication adherence and persistence specifically in HTN have revealed that only 50% of patients for whom drug treatment is initiated persist on treatment 1 year later.[12]

In our study, we found a high adherence in 39% of patients while 32.5% of patients had a medium score and 28.5% had low adherence scores. These findings are comparable to the 35.6%, 36.0%, and 28.4% good, medium, and poor medication adherence scores, respectively, reported by Hyre et al.[13] Low adherence to antihypertensives contributes to poor blood pressure control. In fact, up to 75% of hypertensive patients do not achieve target BP, mainly due to poor adherence.[8,9,14] Uncontrolled BP, in turn, increases the risk of adverse cardiovascular and renal complications.[8,14] The relative risk of myocardial infarction, angina, and stroke may be nearly double in patients with HTN and hyperlipidemia who are nonadherent as compared to those who show ideal adherence.[13]

Only 29.5% of the patients among our study participants had their BP under control as per the JNC-8 recommendations. This is lower than the reported figure of 54%–59% by Ong et al. or 33% (as per JNC 7) by Morgado et al.[14] There was a significant positive association between a high adherence score and BP control. A significantly higher percentage (16.5%) of patients with high adherence scores had achieved target BPs compared to those with low (1.5%) or medium (11.5%) adherence scores.

We also carried out a post hoc analysis to assess the association of demographic factors, duration of disease, duration of drug therapy, number of drugs, and cost of drugs with BP control as well as medication adherence levels. Factors contributing to low medication adherence include number of drugs, cost of drugs, treatment side effects, asymptomatic disease, and knowledge regarding HTN.[16,17] We found a positive correlation between education status and BP control as well as adherence. BP control was better in those with a graduate degree.
Adherence scores were also better in graduates, so it can be assumed that the improvement in BP control was a result of better compliance. Illiteracy has been recognized as a cause for poor adherence.[9] We found no association between other demographic characteristics such as gender, age, socioeconomic status, and medication adherence or disease control. This is in keeping with several other studies, which found adherence has no apparent association with demographic characteristics or disease severity,[11] although some studies have reported lower adherence reported among younger individuals and men.[12] We also found no association between the number of drugs, cost of drugs, duration of disease, or duration of drug therapy with treatment adherence or BP control.

Conclusion

Patient nonadherence to antihypertensive treatment recommendations remains a global problem, and promoting patient adherence is a major clinical hurdle that is necessary to decrease cardiovascular morbidity and mortality. In our study, although the adherence rates were comparable to the globally reported rates, the BP control rates were lower. Therefore, there is a need to look for additional reasons for poor BP control as well as monitoring antihypertensive therapy to ensure that adequate control over BP is obtained. Since there seems to be a positive association between medication adherence and BP control, measures to improve patient compliance need to become a priority to ensure that patients with HTN gain full benefit of the available medications for the control of their disease.

Limitation of the study

Additional factors such as regular physical activity, alcohol consumption, smoking, psychological factors, and knowledge about HTN, which could impact BP control and/or medication adherence, were not considered in our study.

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Conflicts of interest

There are no conflicts of interest.

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