Print ISSN 2319-2003 | Online ISSN 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

doi: 10.5455/2319-2003.ijbcp20150222

Research Article

Comparative evaluation of beta-blockers with or without statins in the treatment of essential hypertension at a tertiary health care setup

Shalu Bawa[1], Shakti B. Dutta[1], Hitender Kumar[1], Mirza Atif Beg[1]*, Amit Varma[2], Mohammad Anjoom[1]

[1]Department of Pharmacology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun, Uttarakhand, India, [2]Department of Medicine, Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun, Uttarakhand, India

Received: 10 December 2014
Accepted: 2 January 2015

***Correspondence to:**
Mirza Atif Beg,
Email: mabeg1997@gmail.com

ABSTRACT

Background: The effects of statins apart from their role as cholesterol lowering agents have prompted this study to evaluate their antihypertensive role. Beta-blockers (BB) are one of the most effective drugs in hypertension. The present study was designed for comparative evaluation of BB with or without statins in the treatment of essential hypertension in a tertiary health care setup.

Methods: This study was conducted in 20 hypertensive patients by Pharmacology Department in Medicine outpatient department at SGRRIM and HS Dehradun for 1 year. Initially, patients were stabilized for 4 weeks by BB and then subdivided into 2 groups. Group I: BB (n=10) and Group II: BB+statins (n=10). Patients were followed up every 4 weeks for 16 weeks. Systolic blood pressure (SBP) and diastolic blood pressure (DBP), waist hip ratio (WHR), body mass index (BMI) were done every visit. Lipid profile was done at 4 and 16 weeks. Analysis was performed using t test. $p \leq 0.05$ was significant.

Results: At 4 and 16 weeks, SBP in Group I was 133.6±3.7 and 127±1.61 mmHg ($p>0.05$) and in Group II was 141.2±2.97 and 130.6±0.71 mmHg ($p<0.01$). At 4 and 16 weeks DBP in Group I was 79.6±2.37 and 81±0.54 mmHg ($p>0.05$) and in Group II was 84.6±1.39 and 83.8±1.45 mmHg ($p>0.05$), respectively. At 16 weeks intergroup SBP and DBP comparison was done, which was not significant ($p>0.05$). At 4 and 16 weeks improvement in lipid profile in Group I ($p>0.05$) was not significant, but a significant improvement in Group II ($p<0.05$) have been observed and no significant changes in BMI and WHR in Groups I and II ($p>0.05$), respectively.

Conclusions: Both groups showed significant improvement in BP. However, no significant difference was seen on intergroup comparison. Larger studies with more patients are needed to establish the role of statins in hypertension.

Keywords: Beta-blockers, Blood pressure, Essential hypertension, Lipid profile, Statins

INTRODUCTION

Hypertension is an increasingly prevalent chronic condition that is associated with serious morbidity and mortality. It is an important risk factor for the development and progression of cardiovascular disease, which is predicted to become the leading cause of death and disability worldwide by 2020.[1] In India, 23.10% men and 22.60% women over the age of 25 years suffer from hypertension.[2] There is considerable evidence that hypertension and dyslipidemia are interrelated metabolically, epidemiologically, and clinically.[3] Owing to this correlation, statins have been used in patients with hypertension with an attempt to counter dyslipidemia, which is itself an independent risk factor for cardiovascular and cerebrovascular diseases.[4] The remarkable benefit achieved with statin treatment in patients with a wide range of cholesterol levels cannot be attributed only to their cholesterol lowering effect alone. The effectiveness and rapidity of statin induced decreases in coronary events have led to the assumption that these agents may possess some "cholesterol independent effects." Statins cause an improvement in endothelial function by activating endothelial nitric oxide synthase, down regulate angiotensin II Type 1 receptors, reduce levels of endothelin-1 and decrease the vascular production of reactive oxygen species.[5] The effect of statins, apart from their role as cholesterol lowering agents has prompted this study to evaluate if they can play a role as antihypertensives. β blockers (BB) have

received enormous clinical attention because of their efficacy in the treatment of hypertension, ischemic heart disease, congestive heart failure and certain arrhythmias. are among one of the safest and most effective antihypertensive drugs available.[6] Therefore, we have compared BB either alone or in combination with statins in essential hypertension in a tertiary health care health setup in Dehradun, Uttarakhand.

METHODS

This open-label study was conducted in the Department of Pharmacology and Medicine at SGRRIM&HS Patel Nagar Dehradun for 1 year from January 2012 to December 2012 and included patients diagnosed with essential hypertension attending Medicine outpatient department. Prior to the initiation of the study, approval was taken from Institutional Ethics Committee and written informed consent was obtained from all the patients. A total of 20 consecutive patients suffering from essential hypertension as per JNC VII guidelines were included in this study.[7] Inclusion criteria: The hypertensive patients of either sex, aged between 20 and 60 years were included in the study. Exclusion criteria: Patients aged < 20 years and > 60 years, secondary hypertension, having hypersensitivity to statins, pregnant and lactating women, myopathies, diabetes mellitus, liver diseases, kidney diseases, any other chronic systemic illness and acute emergencies.

Treatment protocol

A total of 20 hypertensive patients were included in the study as per JNC VII criteria.[7] The BP of patients was stabilized initially by giving Atenolol 50 mg once daily (OD) for a period of 4 weeks. After stabilization period of 4 weeks, patients were further subdivided into 2 groups. Group I: Atenolol 50 mg OD (n=10) and Group II: Atenolol 50 mg OD +Atorvastatin 10 mg OD (n=10). The patients were called for follow-up after every 4 weeks for a period 16 weeks. Measurement of systolic blood pressure (SBP) and diastolic blood pressure (DBP), waist hip ratio (WHR) and body mass index (BMI) was done at every visit. Lipid profile was done at 4 weeks and at the end of 16 weeks. Primary end points were change in SBP and DBP. Changes in WHR, BMI and lipid profile were secondary end points. The patients were examined thoroughly at each follow-up visit for any adverse drug reactions due to the drugs given. The treatment groups were compared and results were analyzed by paired and unpaired t test. $p<0.05$ was considered to be significant.

RESULTS

A total of 20 hypertensive patients had a mean age of 50.25±2.17 years. Men and women were in the ratio of 8:12 (40%, 60%). 8(40%) patients had a positive family history of hypertension. 7 (35%) patients were newly diagnosed hypertensive patients. The mean duration of hypertension was 3.08±0.46 years (Table 1). At the start of study, the SBP, DBP, BMI and WHR were 148.2±2.14 mm Hg, 90.1±1.56 mm Hg, 25.83 ±0.86 kg/m2 and 0.97±0.006 respectively (Table 2). The patients underwent a titration phase of 4 weeks during which the SBP and DBP showed significant improvement ($p<0.01$) (Table 3). At 4 weeks, comparison of SBP and DBP was done between Group-I and Group-II. The SBP of Group-I and Group-II were 133.6±3.7 mm Hg and 141.2±2.97 mm Hg respectively ($p>0.05$). The DBP of Group-I and Group-II were 79.6±2.37 mm Hg and 84.6±1.39 Hg ($p>0.05$). No significant difference was seen in SBP and DBP between the groups at 4 weeks. Patients were followed up every 4 weekly till the end of study period (16 weeks). At 16 weeks, the comparison of change in SBP and DBP was done between 4 weeks and 16 weeks in Group-I and Group-II. The SBP at 16 weeks in Group-I was 127±1.61 mmHg ($p>0.05$) and in Group-II was 130.6±0.75 mmHg ($p<0.01$) (Figure 2). The improvement was significant in the group that received BB + statins (Group-II) as compared to the group which received only BB (Group-I) (Figure 1). The diastolic BP at the end of 16 weeks in Group-I was 81±0.54 mm Hg ($p>0.05$) and in Group-II was 83.8±1.45 mm Hg ($p>0.05$). There was no significant change in DBP in both the groups (Figure 2). Both the study groups showed improvement in SBP and DBP in 16 week period. At 16 weeks the comparison of fall in SBP and DBP was done between Groups-I and Group-II. The SBP in Group-I was 127±1.56 mm Hg and in Group-II was 130.6±0.75 mm Hg ($p>0.05$). The DBP in Group-I was 81±0.54 mm Hg and in Group-II was 83.8±1.45 mm Hg ($p>0.05$). No significant difference was seen between the groups with respect to SBP and DBP at the end of 16 weeks (Figure 3).

There was a significant improvement in lipid profile at the end of study period in the group that received statins

Table 1: Demographic profile.

Parameters	Number (% age)
Total no of patients	20
Mean age (years)	50.25±2.17
Men:Women	8:12 (40% vs. 60%)
Positive family history of hypertension	8 (40%)
Newly diagnosed patients	7 (35%)
Mean duration of illness (years)	3.08±0.46

Table 2: Baseline characteristics of study group.

Parameters	BB
SBP (mm Hg)	148.2±2.14
DBP (mm Hg)	90.1±1.56
BMI (kg/m^2)	25.83±0.86
WHR	0.97±0.006

BB: Beta blockers, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, WHR: Waist hip ratio

Table 3: BP control during the titration phase.

SBP (mm Hg)		p value	DBP (mmHg)		p value
0 weeks	4 weeks		0 weeks	4 weeks	
148.2±2.14	137±2.41	<0.01	90.1±1.56	82.1±1.42	<0.001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BP: Blood pressure

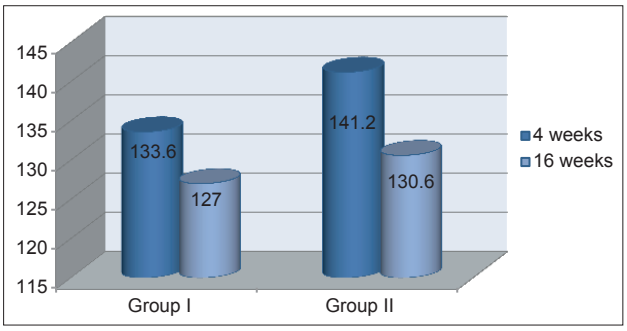

Figure 1: Systolic blood pressure comparison between 4 and 16 weeks, Group I: Beta blockers p>0.05 (not significant), Group II: Beta blockers+Statins p<0.01 (significant).

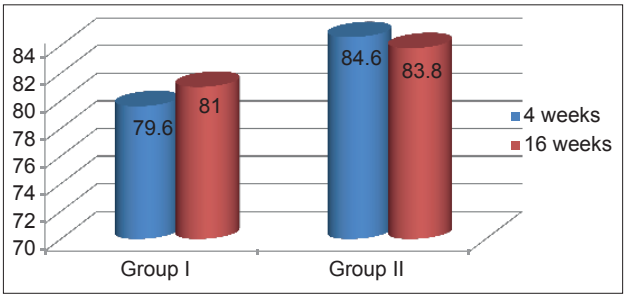

Figure 2: Diastolic blood pressure comparison between 4 and 16 weeks, Group I: Beta blockers p>0.05 (not significant), Group II: Beta blockers+statins p>0.05 (not significant).

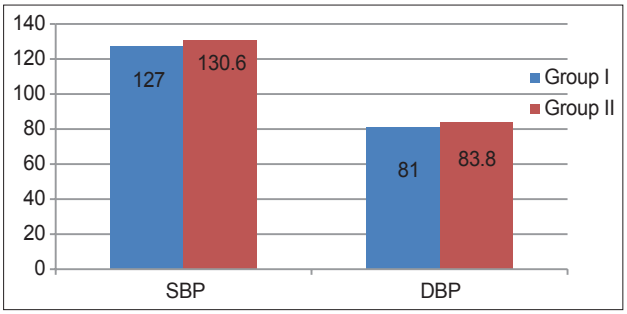

Figure 3: Intergroup blood pressure comparison at 16 weeks, Group I: Beta blockers p>0.05 (not significant), Group II: Beta blockers+Statins p>0.05 (not significant).

when compared to the group that did not receive statins (Table 4). There was no significant change in BMI and WHR between 4 weeks and 16 weeks in both the groups (Figures 4 and 5). Overall 7 adverse drug reactions were seen in the study period. 3 in Group-I and 4 in Group-II. Fatigability in 3 patients followed by generalized body

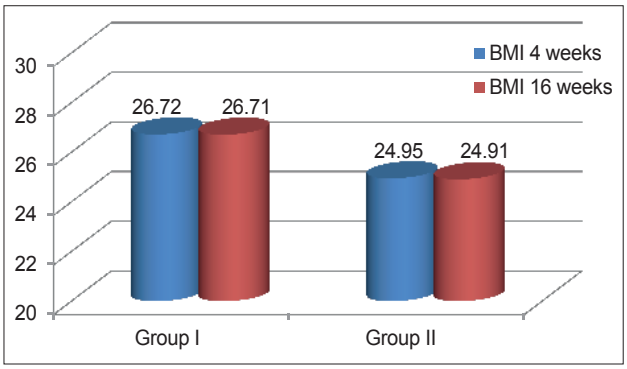

Figure 4: Body mass index at 4 and 16 weeks, Group I: Beta blockers p>0.05 (not significant), Group II: Beta blockers+Statins p>0.05 (not significant).

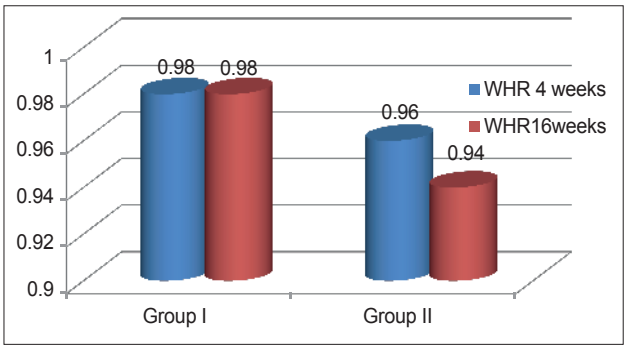

Figure 5: Waist hip ratio at 4 and 16 weeks, Group I: Beta blockers p>0.05 (not significant), Group II: Beta blockers+statins p>0.05 (not significant).

weakness in 2 patients and nausea and abdominal pain in 1 patient each. Adverse effects were mild and did not require any modification or withdrawal of study medications.

DISCUSSION

Essential hypertension is commonly seen in middle aged individuals; especially after 50 years of age.[8] The average age of patients in the present study was 50.25 years, reflecting the usual age group of disease manifestation. This was comparable to the age of the patients in previous studies where it was reported to be 52.3 years and 52.93 years.[9] Hypertension was more prevalent in females in our study, which was comparable to that observed in the previous study on hypertensive patients.[10] A positive family history was seen in 8 (40%) patients out of 20 in this study, because of the probable multi factorial inheritance, the familial association in hypertension has not been proven yet, but there are epidemiological evidences linking hypertension

Table 4: Change in lipid profile over the study period.

Groups (n=10)	S Chol 4 week (mg/dl)	S Chol 16 week (mg/dl)	TG 4 week (mg/dl)	TG 16 week (mg/dl)	HDL 4 week (mg/dl)	HDL 16 week (mg/dl)	LDL 4 week (mg/dl)	LDL 16 week (mg/dl)
I	180.5±9.39	186.7±9.3	118.6±6.8	113.2±6.7	48.6±3.9	45.8±3.51	90.5±8.23	98.3±8.3
II	188.1±6.58	168.7±5.98*	110.4±4.1	98±3.6*	47.5±1.8	50.4±1.83	89.7±2.1	82.3±2.3*

Group I: Beta blockers Group II: Beta blockers+Statins, *p<0.001, TG: Triglyceride, HDL: High density lipoprotein, LDL: Low density lipoprotein

to a positive family history (Table 1).[8] Hypertension though commonly associated with obesity in developed nations, is also associated with non-obese population especially in developing nations.[11] The average BMI and WHR of the patients in the present study were in the normal range and both these parameters remained constant throughout the study period, suggesting that they had no role to play in decrease in BP, seen with the study groups (Figures 4 and 5). This was comparable with the previous study by Radhika et al.[12]

The present study showed a significant improvement in BP in titration period. Earlier studies have shown that BB are highly effective in the treatment of essential hypertension in reducing both SBP and DBP.[13] In the present study, the group which received BBs + statins showed a more significant fall in SBP when compared to the groups, which received BBs alone (Figure 1) Our results were consistent with other studies in which also greater significant fall in SBP was seen in statin user than non-user groups. A retrospective study using antihypertensive drug database by Hashimoto et al. showed a greater reduction in SBP in hypertensive patients.[14] The statin treated group showed a greater reduction in BP. Ikeda et al. observed an additional lowering effect of pravastatin only on SBP in patients undergoing long-term treatment with antihypertensive agents.[15] A meta-analysis of antihypertensive effects of statins by Alexandros et al. also showed a significant reduction in SBP and DBP in patients taking statins.[16] However in the present study, such results were not observed with respect to DBP in either group (Figure 2). At 16 weeks, comparison was done between Group-I and Group-II. No intergroup difference was found between the groups (Figure 3). This result was consistent with previous study; the Plaque Hypertension Lipid Lowering Italian Study randomized double blind trial in which intergroup comparison was done between patients receiving antihypertensive treatment (hydrochlorthiazide or fosinopril) with or without addition of statin (pravastatin).[17]

A significant improvement in lipid profile was observed in all patients who received statins. These findings were consistent with many previous studies where lipid lowering effects of atorvastatin have been well proven (Table 4).[18] Few adverse effects were noted during the study period which were mild and did not require any alteration or discontinuation of study drugs. These adverse effects were mild and were comparable to those reported in other clinical studies.[5]

Study limitations

This study was an open label study. The patients and the doctor were aware of the prescribed drugs. Hence, there are more chances of errors. Second, the sample size was small. Third, the duration of follow-up was just 16 weeks. A longer follow up period with larger sample size may have yielded different results. Hence keeping these limitations in view, further studies with larger sample size and longer duration are needed to evaluate the magnitude of the antihypertensive effects of statins.

CONCLUSIONS

To conclude, the patients who received BB + statins had a more significant fall in SBP than the patients who received only BB. However, no intergroup difference was found on comparing the study groups at the end of study period. But further larger studies with more number of patients and longer duration are needed to establish the role of statins in hypertension.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Boos CJ, Beevers GD, Lip GY. Assessment of platelet activation indices using the ADVIATM 120 amongst 'high-risk' patients with hypertension. Ann Med. 2007;39(1):72-8.
2. Whitworth JA, World Health Organization, International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. J Hypertens. 2003;21(11):1983-92.
3. Kapoor S, Tyagi R, Saluja K, Chaturvedi A, Kapoor AK. Emerging health threats among a primitive tribal group of Central India. J Public Health Epidemiol. 2010;2:13-9.
4. Wilson PW, Kannel WB, Silbershatz H, D'Agostino RB. Clustering of metabolic factors and coronary heart disease. Arch Intern Med. 1999;159(10):1104-9.
5. Carlos A. Feldstein statins in hypertension. Are they a new class of antihypertensive agents. Rev Latino Am Hypertens. 2008;3(2):33-8.
6. Michel T, Hoffman BB. Treatment of myocardial Ischemia and hypertension. In: Brunton LL, Chabner B, Knollman BC,

editors. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 12th Edition. New York: McGraw-Hill; 2011: 745-88.
7. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Hypertension. 2003;42(6):1206-52.
8. Kotchen TA. Disorders of the cardiovascular system; Vascular disease. Hypertensive vascular disease. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 18th Edition, Section 5. New York: McGraw-Hill; 2012: 2042-59.
9. Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, et al. Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey, 1988-1991. Hypertension. 1995;25(3):305-13.
10. Awoke A, Awoke T, Alemu S, Megabiaw B. Prevalence and associated factors of hypertension among adults in Gondar, Northwest Ethiopia: a community based cross-sectional study. BMC Cardiovasc Disord. 2012;12:113.
11. Mgonda YM, Ramaiya KL, Swai AB, McLarty DG, Alberti KG. Insulin resistance and hypertension in non-obese Africans in Tanzania. Hypertension. 1998;31(1):114-8.
12. Radhika G, Sathya RM, Sudha V, Ganesan A, Mohan V. Dietary salt intake and hypertension in an urban south Indian population – [CURES - 53]. J Assoc Physicians India. 2007;55:405-11.
13. Ibrahim MM, Mossallam R. Clinical evaluation of atenolol in hypertensive patients. Circulation. 1981;64(2):368-74.
14. Hashimoto S, Urushihara H, Hinotsu S, Kosugi S, Kawakami K. Effect of HMG-CoA reductase inhibitors on blood pressure in hypertensive patients treated with blood pressure-lowering agents: retrospective study using an anti-hypertensive drug database. Eur Rev Med Pharmacol Sci. 2012;16(2):235-41.
15. Ikeda T, Sakurai J, Nakayama D, Takahashi Y, Matsuo K, Shibuya Y, et al. Pravastatin has an additional depressor effect in patients undergoing long-term treatment with antihypertensive drugs. Am J Hypertens. 2004;17(6):502-6.
16. Briasoulis A, Agarwal V, Valachis A, Messerli FH. Antihypertensive effects of statins: a meta-analysis of prospective controlled studies. J Clin Hypertens (Greenwich). 2013;15(5):310-20.
17. Mancia G, Parati G, Revera M, Bilo G, Giuliano A, Veglia F, et al. Statins, antihypertensive treatment, and blood pressure control in clinic and over 24 hours: evidence from PHYLLIS randomised double blind trial. BMJ. 2010;340:c1197.
18. Simons LA, Sullivan D, Simons J, Celermajer DS. Effects of atorvastatin monotherapy and simvastatin plus cholestyramine on arterial endothelial function in patients with severe primary hypercholesterolaemia. Atherosclerosis. 1998;137(1):197-203.

doi: 10.5455/2319-2003.ijbcp20150222
Cite this article as: Bawa S, Dutta SB, Kumar H, Beg MA, Varma A, Anjoom M.Comparative evaluation of beta-blockers with or without statins in the treatment of essential hypertension at a tertiary health care setup. Int J Basic Clin Pharmacol 2015;4:125-9.