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COMPARATIVE EVALUATION OF THERAPEUTIC EFFECT OF MOXONIDINE VERSUS AMLODIPINE ON BLOOD PRESSURE IN OBESE HYPERTENSIVES

General Medicine

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ABSTRACT

Background: High blood pressure is frequently associated with metabolic alterations such as insulin resistance, impaired glucose tolerance, dyslipidaemia and obesity. Moxonidine, a selective imidazoline receptor agonist, reduces activity of sympathetic nervous system and lowers blood pressure, and has been shown to have beneficial effects on lipid and carbohydrate metabolism. The present study has been conducted to evaluate antihypertensive efficacy of moxonidine and compare it with amlodipine in mild to moderate hypertension in obese patients.

Methods: This was an open-label randomized study. Patients were divided into two groups of 50 patients each, first group was given amlodipine 5 mg daily and the second group was given moxonidine 0.2 mg once daily. At the end of 8 weeks, the therapeutic effects of both regimes on blood pressure in obese patients with stage 1 and stage 2 hypertension were compared and also with lipid profile, fasting sugars and microalbuminuria.

Results: The study involved 100 participants with a mean age of 51.12±6.25 years and 48.88±5.15 years in moxonidine group and amlodipine group, respectively. Systolic and diastolic blood pressure reduction was significant in both groups at 8-weeks ($p<0.001$). The reduction in FBS ($p=0.008$), total cholesterol ($p=0.04$), serum triglycerides ($p<0.001$) and increase in HDL ($p=0.02$) were all significant in moxonidine group, but LDL reduction was not significant. In amlodipine group, change in FBS, total cholesterol, serum triglycerides, HDL and LDL levels were all insignificant. There was also significant reduction in microalbuminuria in moxonidine group.

Conclusion: Moxonidine and amlodipine are equally effective antihypertensives and safe in obese hypertensives. Moxondine has additional favourable effects on lipid profile (serum cholesterol, TGs and LDL), fasting blood glucose and microalbuminuria.

KEYWORDS

Moxonidine, Amlodipine, Obese, Hypertension, Lipid profile, Microalbuminuria.

INTRODUCTION

Hypertension is the leading behavioural and physiological risk factor causing 13% of global deaths. One in three adults worldwide has hypertension[1]. Epidemiological studies have shown that hypertension is present in 25% of urban and 10% of rural subjects in India. Hypertension increases the risk of cardiovascular disease attributable for around half of all deaths from stroke and heart disease[2]. In India hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths[3].The increasing prevalence of hypertension occurred in conjunction with a dramatic increase in the prevalence of overweight and obesity.

High blood pressure is frequently associated with metabolic alterations such as insulin resistance (IR), impaired glucose tolerance (IGT), dyslipidaemia and also with concomitant risk factors, obesity and left ventricular hypertrophy (LVH). These factors in the presence of high blood pressure can further increase the risk of cardiovascular diseases[4,5]. High prevalence of obesity and insulin resistance in urban Indian population is well known.

Among the calcium channel blockers (CCBs), amlodipine belongs to the 1,4 dihydropyridine class and has been shown to be an effective antihypertensive drug providing smooth 24-hour blood pressure control without orthostatic hypotension and is well tolerated as monotherapy and in combination with other antihypertensive drugs. But the decrease in blood pressure is not accompanied by any significant change in heart rate or plasma catecholamine levels. Moxonidine, a selective imidazoline receptor agonist, reduces the activity of the sympathetic nervous system and effectively lowers blood pressure, is well tolerated and has been shown to have beneficial effects on lipid and carbohydrate metabolism and insulin sensitivity[6]. The present study was conducted to evaluate antihypertensive efficacy of moxonidine and to compare it with a conventional drug amlodipine in mild to moderate hypertension in obese patients.

METHODS

It was open-label randomized study. A simple randomization method using a table of random numbers was followed. Patients attending the OPD of department of medicine of a tertiary care hospital of north India were recruited for the study. 100 overweight and obese patients with stage 1 and stage 2 hypertension (as per IHG III guidelines) were selected at random and were considered eligible. Patients were excluded from the study who had severe concomitant disorders affecting major organ systems (cardiovascular disease [other than hypertension], respiratory, digestive, endocrine, neurologic/psychiatric or immunologic disease), other relevant diseases as revealed by history, physical examination and/or laboratory assessments, or had undergone (or were scheduled to undergo) major surgery.

Patients were divided into two groups of 50 patients each, first group was given amlodipine 5 mg daily and the second group was given moxonidine 0.2 mg once daily. Dose of moxonidine was not increased from 0.2 mg during the study. Before the patients were enrolled in the trial, a washout period of 2 weeks was observed during which all medications were discontinued and due care was taken not to withdraw the earlier therapy abruptly. Blood pressure at the end of the washout period was taken as baseline and at the end of 8 weeks. Levels of fasting blood sugar, serum total cholesterol (TC), serum high density lipoprotein (HDL), serum low density lipoprotein (LDL), and serum triglycerides (TGs), weight, body mass index (BMI), microalbuminuria and electrocardiogram (ECG) were determined in the beginning of the study (ending with the washout period) and again at the end of 8 weeks.

At the end of 8 weeks, the therapeutic effects of both regimes on blood pressure in obese patients with stage 1 and stage 2 hypertension were compared and also with lipid profile, fasting sugars and microalbuminuria.

All the data were recorded on Microsoft Excel database and statistical analysis was performed using SPSS software (version 23.0, SPSS Inc., Illinois, USA). Categorical variables were presented as numbers and percentage, continuous variables as mean ± standard deviation (SD) or median and 95% confidence interval (95% CI). Categorical variables were compared by chi-squared analysis. Continuous variables were tested for lack of normality by the Kolmogorov–Smirnov test. The paired samples t-test was used for assessing the effect of treatment in

each group. Analysis of covariance (ANCOVA), adjusted for baseline values, was used for comparisons between treatment groups. A p-value of <0.05 was considered being statistically significant.

RESULTS

There were no differences in age between study groups. The baseline characteristics of patients are shown in Table 1. The mean age in moxonidine group was 51.12 ± 6.25 years and in amlodipine group was 48.88 ± 5.15 years. Patients having stage 1 hypertension were 12 in moxonidine group and 15 in amlodipine group and in stage 2 were, 38 and 35 patients, respectively. The baseline concentrations of FBS, total cholesterol, serum triglycerides, LDL, and HDL as well as those of microalbuminuria were similar in the both study groups.

Table 1. Baseline Characteristics Of All Study Participants.

	Group I (Moxonidine) N=50	Group II (Amlodipine) N=50	P-value
Age (years)	51.12 ± 6.25	48.88 ± 5.15	NS
Sex (Males:Females)	16:34	17:33	NS
Weight (kgs)	83.90 ± 9.27	83.94 ± 9.93	NS
BMI (kg/m^2)	32.88 ± 1.49	33.36 ± 1.32	NS
SBP (mm of Hg)	167.36 ± 14.46	162. 96 ± 13.82	NS
DBP (mm of Hg)	102.88 ± 7.57	100.88 ± 7.57	NS
HTN Stage 1: Stage 2	12:38	15:35	NS
FBS (mg/dl)	133.40 ± 52.72	130.04 ± 49.53	NS
S. Cholesterol (mg/dl)	204.66 ± 35.63	206.05 ± 26.76	NS
LDL (mg/dl)	127.86 ± 31.92	135.72 ± 26.17	NS
TGs (mg/dl)	205.40 ± 58.32	164.64 ± 31.06	NS
HDL (mg/dl)	35.96 ± 4.83	37.40 ± 4.32	NS
Microalbuminuria (%)	44 %	40 %	NS

All values are presented as Mean ± SD or number (%).

BMI-Body Mass Index; SBP-Systolic Blood Pressure; DBP-Diastolic Blood Pressure; HTN-Hypertension; FBS-Fasting Blood Sugar; LDL-Serum Low Density Lipoprotein; TGs-Serum Triglycerides; HDL-Serum High Density Lipoprotein

Table 2 shows systolic and diastolic blood pressures at 0 and 8 weeks both groups. BP was markedly decreased at 8 weeks with SBP and DBP showing highly significant differences ($p < 0.001$) at 8-weeks in both groups. There was insignificant difference in BMI in both the groups at the end of 8 weeks, 32.98 ± 1.49 kg/m^2 at 0-week and 32.86 ± 1.34 kg/m^2 at end of 8-weeks in moxonidine group (p=0.14) and 33.36 ± 1.32 kg/m^2 at 0-week and 33.44 ± 1.31 kg/m^2 at end of 8-weeks in amlodipine group (p=0.25). There was significant reduction in total serum cholesterol in moxonidine group, 204.66 ± 35.6 mg/dL at baseline and 201.68± 35.7 mg/dL at 8-weeks (p=0.04), whereas in amlodipine group there was nonsignificant change (p=0.13). Serum triglycerides also showed significant reduction in moxonidine group, 205.40 ± 58.3 mg/dL at baseline and 193.44 ± 55.1 mg/dL at 8-weeks (p<0.001), whereas in amlodipine group there was nonsignificant change (p=0.64). There was no significant difference noted in serum LDL at 8-weeks in both moxonidine and amlodipine groups. Serum HDL was significantly increased in moxonidine group at 8-weeks, but the change was not significant in amlodipine group. (Table 3) Fasting blood sugar (p=0.008) and microalbuminuria (p=0.03) were also significantly reduced in moxonidine group at 8-weeks and non-significant in amlodipine group. (Figure 1)

Table 2. Systolic And Diastolic Blood Pressure At 0-week And 8-weeks In Both Groups.

		Group I (Moxonidine)		Group II (Amlodipine)	
	Weeks	Mean ± SD	P-value	Mean ± SD	P-value
SBP	0-week	167.36 ± 14.46	<0.001	162.96 ± 13.82	< 0.001
	8-weeks	159.72 ± 12.58		153.80 ± 12.98	
DBP	0-week	102.88 ± 7.57	<0.001	100.88 ± 7.57	<0.001
	8-weeks	97.20 ± 6.76		96.16 ± 7.59	

All values are presented as Mean ± SD.

SBP-Systolic Blood Pressure; DBP-Diastolic Blood Pressure.

All values are presented as Mean ± SD.

BMI-Body Mass Index; FBS-Fasting Blood Sugar; TC-Total cholesterol; LDL-Serum Low Density Lipoprotein; TGs-Serum Triglycerides; HDL-Serum High Density Lipoprotein

Table 3. Serum Metabolic Parameters At Baseline And 8-weeks Of Drug Therapy

		Group I (Moxonidine)		Group II (Amlodipine)	
	Weeks	Mean ± SD	P-value	Mean ± SD	P-Value
BMI (kg/m^2)	Baseline	32.98 ± 1.49	0.14	33.36 ± 1.32	0.25
	8 weeks	32.86 ± 1.34		33.44 ± 1.31	
FBS (mg/dL)	Baseline	133.40 ± 52.72	0.008	130.04 ± 49.53	0.14
	8 weeks	125.12 ± 36.37		132.76 ± 46.72	
TC (mg/dL)	Baseline	204.66 ± 35.63	0.04	206.05 ± 26.76	0.13
	8 weeks	201.68 ± 35.71		207.35 ± 27.15	
Tgs (mg/dL)	Baseline	205.40 ± 58.32	<0.001	164.64 ± 31.06	0.64
	8 weeks	193.44 ± 55.14		164.36 ± 30.33	
LDL (mg/dL)	Baseline	127.86 ± 31.92	0.72	135.72 ± 26.17	0.27
	8 weeks	128.07 ± 32.16		136.60 ± 26.60	
HDL (mg/dL)	Baseline	35.96 ± 4.83	0.02	37.40 ± 4.32	0.13
	8 weeks	36.72 ± 5.33		37.80 ± 4.69	

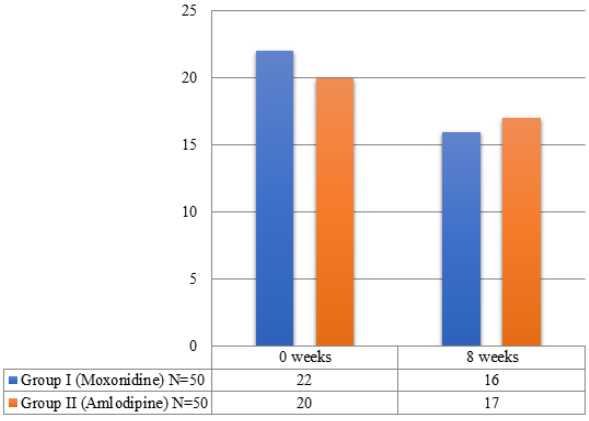

Figure 1. Effect Of Moxonidine And Amlodipine Treatment On Microalbuminuria At 8-weeks.

None of the patients in both the study groups were withdrawn from the study because of their side effects. The most common side effects observed in moxonidine group were dry mouth in 1 patient (2%) and dizziness in 2 patients (4%). In amlodipine group, the most common and only side effect observed was pedal edema in 3 patients (6%).

DISCUSSION

The prevalence of metabolic syndrome in the hypertensive population is high. Metabolic syndrome and the accompanying cardiometabolic risk result in a significant increment in cardiovascular morbidity and mortality in several population-based studies as well as in hypertensive patients.

In our study, effect of moxonidine on blood pressure in hypertensive patients was comparable to various studies. In moxonidine group, there was statistically highly significant reduction in SBP and DBP. In TOPIC study[7] there was mean reduction of 17 mm of Hg in SBP from baseline of 165.5 ± 15.1 (p<0.001) after 8 weeks of treatment. The mean reduction in DBP was 13 mm of Hg from 101.2 ± 4.1 (p<0.001), which was again highly significant. In amlodipine group, the mean reduction in SBP and DBP was comparable to a study conducted by J Webster et al[8]. In this study mean reduction was 14/11 mm of Hg with p<0.001. There was no significant difference observed in our study with regard to BMI. These findings are similar to other studies from literature,[9,10] in which no effect on BMI is seen with either moxonidine or amlodipine treatment.

In moxonidine group, the mean reduction in total cholesterol was 0.80 mg/dl from baseline value of 204.66 ± 35.63 with p<0.05 which was statistically significant. However the LDL levels which were 127.86 ± 31.92 at baseline and 128.07 ± 32.16 at 8 weeks after treatment with p=0.72, a non-significant value. Our study is in line with a study[9] done on hypertensive patients, which also showed a significant decrease in total cholesterol with no significant change in LDL levels. Serum triglycerides, HDL levels and FBS were significantly improved in our study after 8-weeks of treatment with moxonidine, and is in

concordance with already available literature.[9,11-13] In amlodipine, the baseline total cholesterol level was 206.05 ± 26.76 and 207.35 ± 27.15 at 8 weeks after treatment with p=0.134. The change in triglyceride levels, LDL, HDL levels and FBS were also not significant in amlodipine group. These findings of our study are in line with several other studies.[14-16] At baseline in moxonidine group, microalbuminuria was present in 22 patients and in 16 patients at the end of 8 weeks. There was significant reduction in microalbuminuria as was also seen in other studies.[9,13] This reduction in microalbuminuria was not seen in amlodipine group.

We believe that the most important limitations of our study are its open-label design and the small number of participants, and there was no long-term follow-up. Impact on clinical endpoints and major adverse cardiovascular events were also not seen. These issues will require further study.

CONCLUSION

The present study shows that both the drugs, moxonidine and amlodipine are equally effective antihypertensives and safe in obese hypertensives. Moxondine has additional favourable effects on lipid profile (serum cholesterol, TGs and LDL), fasting blood glucose and microalbuminuria in the study group.

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DECLARATIONS

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REFERENCES

1. Eurosurveillance editorial team. WHO launches the World Health Statistics 2012. Euro Surveill. 2012;17(20).
2. Kearney PM, Wheton M, Reynolds K, Muntner P, Whelton PK He J. Global burden of hypertension. Lancet 2005;365(9455);217-23.
3. Rodgers A, Lawes C, MacMahon S. Reducing the global burden of blood pressure related cardiovascular disease. J Hypertens 2000; **18**(Suppl 1): S3–S6.
4. Ellekjaer H, Holmen J, Vatten L. Blood pressure, smoking and body mass in relation to mortality from stroke and coronary heart disease in the elderly. A 10-year follow-up in Norway. Blood Press 2001;10(3):156-63.
5. Kannel WB. Prevalence and implications of uncontrolled systolic hypertension. Drugs Aging 2003;20(4):277-86.
6. Haenni A, Lithell H. Moxonidine improves insulin sensitivity in insulin-resistant hypertensives. J Hypertens 1999;17(Suppl. 3):29–35.
7. Van Zwieten PA. Centrally acting antihypertensives: a renaissance of interest. Mechanisms and haemodynamics. J Hypertens 1997;15(Suppl 1):S3–S8.
8. J. Webster, 0. J. Robb. T. A. Jeffers, A. K. Scott J. C. Petrie & H. M. Towler. Once daily amlodipine in the treatment of mild to moderate hypertension. Br. J. clin. Pharinac 1987;24:713-9.
9. H. Ebinç, Z. N. Ozkurt, F. A.Ebinç, D. Ucardag, O. Caglayan and M. Yilmaz. "Effects of sympatholytic therapy with moxonidine on serum adiponectin levels in hypertensive women". Journal of International Medical Research 2008;36(1): 80–7.
10. CananErsoy, SaziImamoglu, FerahBudak, ErcanTuncel, ErdinçErtürk & Barbaros Oral. Effect of amlodipine on insulin resistance & tumor necrosis factor- alphalevels in hypertensive obese type 2 diabetic patients. Indian J Med Res 2004Nov;120(5):481-8.
11. Irina Chazova and Markus P. Schlaich. Improved Hypertension Control with the Imidazoline Agonist Moxonidine in a Multinational Metabolic Syndrome Population: Principal Results of the MERSY Study. International Journal of Hypertension, 2013. doi:10.1155/ 2013/541689.
12. Derosa G, A. F. G. Cicero, A. D'Angelo et al., "Metabolic and antihypertensive effects of moxonidine and moxonidine plus irbesartan in patients with type 2 diabetes mellitus and mild hypertension: a sequential, randomized, double-blind clinical trial," Clinical Therapeutics 2007;29(4):602–10.
13. Krzysztof Strojek, Wladyslaw Grzeszczak, JutaGorska, Monika I. Leschingerand Eberhard Ritz. Lowering of Microalbuminuria in Diabetic Patients by a Sympathicoplegic Agent: Novel Approach to Prevent Progression of Diabetic Nephropathy? JASN 2010;12(3):602-5.
14. Chait A. Effects of antihypertensive agents on serum lipids and lipoproteins. Am J Med 1989;86(Suppl 1B):5-7.
15. Ashraf H. Ahmed, Rami M. A. Al-Hayali. Effect of amlodipine on serum lipid profile in hypertensive patients. Ann. Coll. Med. Mosul 2009;35(1):8-12.
16. Jalal S, Sofi FA, Abass SM, Alai MS, Bhat MA, Rather HA, Lone NA, Siddiqi MA. Effect of amlodipine and lisinopril on microalbuminuria in patients with essential hypertension: A prospective study. Indian J Nephrol 2010 Jan;20(1): 15-20.