Original Article

Herbal Medicines

New Perspectives in the Management of Hypertension: Role of Herbal Medicines

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ABSTRACT

Objective: To compare the efficacy of coded herbal medicine (Hyprol) and losartan in hypertensive type II diabetic patients.

Study Design: Case control study

Place and Duration of Study: This study was carried out at the Out-patient Department of JPMC, Karachi and Herbal Clinics of Karachi from January 2014 to June 2014.

Materials and Methods: This study is a case control prospective study to compare the effects of Losartan with herbal medicine (Hyprol) in type 2 diabetic hypertensive patients. 200 patients were enrolled and divided in two groups 'A' (Control group) & 'B' (Test group) treated with Losartan and Hyprol respectively.

Results: With ARB (Losartan) baseline to final change for SBP as well as DBP was significantly reduced i.e. 22.45 %($p<0.001$) and 16.84% ($p<0.001$) respectively and FBS was reduced by 21.85% ($p<0.001$) while Hyprol shows comparable results i.e. difference in SBP, DBP and FBS was 14 %($p<0.001$), 15.31 %($p<0.001$), 34.57% ($p<0.001$) respectively.

Conclusion: ARBs are the first line drug of choice for hypertension since long time. Use of herbal medicine is an alternative mean of therapy to treat these patients and limit its cardiovascular and renal complications.

Key Words: Hypertension, Type 2 diabetes mellitus, ARB, Losartan

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INTRODUCTION

Hypertension is a global health problem including Pakistan[1]. Rise in systemic blood pressure occurs with increasing age and so does the incidence of cardiovascular disease[2]. Though it is common and known as "Silent Killer" because it remains asymptomatic but readily detectable and usually easy to treat[3]. For cerebrovascular and cardiovascular diseases the most important risk factor is hypertension. Prevention of the onset of disease can be done by controlling blood pressure within appropriate levels[4].

Globally diabetes is one of the major health problems. In an estimate it is noted that worldwide 246 million people are affected from this disease. In the next 30 years it is expected that this prevalence of diabetes is going to be doubled[5]. According to World Health Organization (WHO) 170 million patients are affected with type 2 diabetes mellitus which will be enhanced twice by the year 2030 and it is a global epidemic[6].

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The prognosis of a combination of diabetes and hypertension is particularly very poor. This can be explained by several research trials in the general population with type 2 diabetes that have shown that controlling blood pressure under 130/80 mmHg changes the morbidity and mortality[7]. Risk of cardiovascular diseases is proportionally greater in patients with elevated systolic hypertension which indicates a greater potential for controlling cardiovascular deaths associated with elevated blood pressure in diabetic patients[8].

Extensively used antihypertensive agents that act via inhibition of angiotensin II type 1 (AT1) receptors are Angiotensin Receptor Blockers (ARBs). Organ protection like vasculoprotection, cardioprotection and renoprotection are additive effects of ARBs[9]. Blockade of renin-angiotensin system (RAS) by improving insulin sensitivity reduce the risk of developing type 2 diabetes[10]. Similarly losartan and Valsartan are classified as competitive antagonist at AT1 receptor while Irbesartan and Candesartan act as full antagonists. The administration of large doses of less potent ARBs can also be done to improve their antihypertensive property[11]. Losartan delays the progression of diabetic

nephropathy and also treat hypertension. In patients with hypertension, type 2 diabetes, glomerulonephritis and nephritic syndrome losartan prevents the progress of renal disease[12].

Plants are used as a source of medicine from the ancient times in all cultures. Traditional medicines are utilized in health care both in developed and developing countries[13]. Cichorium intybus also known as cichory, is very famous for its biological activities[14]. Rauwolfia serpentina belongs to botanical class of Apocynaceae family[15]. It is observed that alkaloids present in the root of Rauwolfia serpentina have antihypertensive effects[16]. Tribulus terrestris is a very well known herbal medicine since ancient time and also in modern world[17]. It is also use to treat hypertension, as a diuretic, in urinary tract infections and for lithotripsy[18]. Valeriana officinalis decrease systolic blood pressure and feelings of stress[19]. Withania somnifera L. Dunal is a plant of Solanaceae family, it is used in the disorders of stress like arteriosclerosis, aging, arthritis, diabetes mellitus, hypertension and malignancies can be prevented and managed by Withania somnifera[20].

MATERIALS AND METHODS

The study comprises of six month duration. Patients were selected from outpatient department at JPMC and Amna Ibrahim Unani Clinic, Karachi. 200 patients of hypertension with type 2 diabetes were enrolled in the study. All patients had mild to moderate hypertension with type II diabetes which was not treated previously. Before starting the study an informed written consent was taken. Patients were divided in two groups each consisting of 100 patients**. Group A** was treated with allopathic medicine Losartan 50 mg once daily and **Group B** was treated with Hyprol 500mg once daily (a combination of five herbal plants named Cichorium intybus (Kasni 100mg), Rauwolfia serpentine (Asrol) 200mg, Tribulus terrestris (Kharkhask) 50mg, Valeriana officinalis(Balchar) 50mg and Withania somnifera (Asgand) 100mg) for a period of 12 weeks and kept as control and test groups respectively. 5 mg Glibenclamide was added to control group for the regulation of blood glucose levels. Drug dosages were adjusted appropriately during the study period. Newly diagnosed untreated patients of hypertension with type 2 DM from either sex between 25 to 65 years of age were included. Patients with any other comorbidity were excluded from the study. Laboratory investigations were performed as baseline to evaluate patients according to inclusion criteria. Systolic and diastolic blood pressure measurements were taken at fortnightly visits in sitting position according to the recommendation s of JNC 7 while fasting blood glucose levels, serum urea and serum creatinine were measured as baseline and 6 weekly intervals.

RESULTS

All 200 subjects completed the study successfully. Data was analyzed on SPSS version 14 and student 't' test was applied. Mean systolic blood pressure among groups A and B were found 147 ± 13.55 and 150 ± 11.38 respectively at day 0 while at day 90 it was found 114 ± 8.61 and 129 ± 6.82 respectively. The difference between groups A v/s B was found statistically significant with P <.001. Group A performed 8.45 % better than group B at 90th day of treatment. The average difference from baseline to final i.e. from day 0 to day 90 showed significant changes in group A and B (P < .001). The percentage change in groups A and B from base line to final i.e. day 0 to day 90 have shown reduction of 22.45 % and 14 % respectively. (Table-1 & Figure- 1).

Mean diastolic blood pressure among groups A and B were found 95 ± 7.40 and 98 ± 7.55 respectively at day 0 while at day 90 it was found 79 ± 6.57 and 83 ± 9.05 respectively. The difference between groups A v B was found statistically insignificant with P <0.42. Group A performed slightly better with 1.53 % more reduction than group B at day 90th of treatment. The average difference from baseline to final i.e. from day 0 to day 90 showed significant changes in group A and B (P < .001). The percentage change in groups A and B from base line to final i.e. day 0 to day 90 have shown reduction of 16.84 % and 15.31 % respectively. (Table-2 & Figure- 2).

Table No.1: Changes in the mean Systolic Blood Pressure at Day- 45 and Day – 90 of treatment in groups A and B in Hypertensive Type II Diabetic patients.

	Day 0	Day 45	Day 90	P – value			% Change
				D 0−45	D 45−90	D 0−90	
Group A	147	122	114	t = 19.54	t = 8.18	t = 24.11	↓ 22.45
	±13.55	±10.31	±8.61	p < 0.001	p < 0.001	p < 0.001	
Group B	150	133	129	t = 21.39	t = 9.66	t = 24.42	↓ 14
	±11.38	±7.56	±6.82	p < 0.001	p < 0.001	p < 0.001	
All observations are measured in mmHg							
Each group consist of 100 observations							
A VS B				t = -8.99		t = -12.92	
				p < 0.001		p < 0.001	

Group A = Diabetic diet + Tab. Glibenclamide + Tab. Losartan Group B = Diabetic diet + Tab. Hyprol

Table No. 2: Changes in the mean Diastolic Blood Pressure at Day- 45 and Day – 90 of treatment in groups A and B in Hypertensive Type II Diabetic patients

	Day 0	Day 45	Day 90	P – value			% Change
				D 0–45	D 45–90	D 0–90	
Group A	95	82	79	t = 15.7	t = 3.87	t = 18.27	↓ 16.84
	±7.40	±7.83	±6.57	p < 0.001	p < 0.001	p < 0.001	
Group B	98	87	83	t = 17.92	t = 6	t = 20.1	↓ 15.31
	±7.55	±8.16	±9.05	p < 0.001	p < 0.001	p < 0.001	
All observations are measured in mmHg							
Each group consist of 100 observations							
A VS B				t = 0.90		t = 0.88	
				p < 0.45		p < 0.42	

Group A = Diabetic diet + Tab. Glibenclamide + Tab. Losartan Group B = Diabetic diet + Tab. Hyprol

Table No.3: Changes in the mean Fasting Blood Sugar (FBS) level at Day- 45 and Day – 90 of treatment in groups A and B in Hypertensive Type II Diabetic patients

	Day 0	Day 45	Day 90	P – value			% Change
				D 0–45	D 45–90	D 0–90	
Group A	154.3	130.5	120.58	t = 12.3	t = 7.93	t = 14.35	↓ 21.85
	±32.23	±21.92	±17.49	p < 0.001	p < 0.001	p < 0.001	
Group B	162	124	106	t = 15.32	t = 10.02	t = 21.65	↓ 34.57
	±27.23	±19.71	±9.89	p < 0.001	p < 0.001	p < 0.001	
All observations are measured in mg/dl							
Each group consist of 100 observations							
A VS B				t = 2.38		t = 7.27	
				p<0.02		p < 0.001	

Group A = Diabetic diet + Tab. Glibenclamide + Tab. Losartan Group B = Diabetic diet + Tab. Hyprol

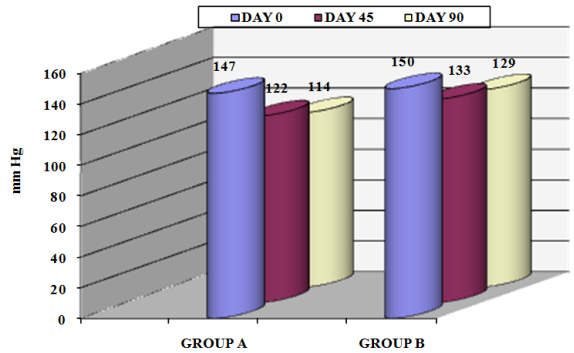

Figure No.1: Changes in the mean Systolic Blood Pressure at Day- 45 and Day – 90 of treatment in groups A and B in Hypertensive Type II Diabetic patients

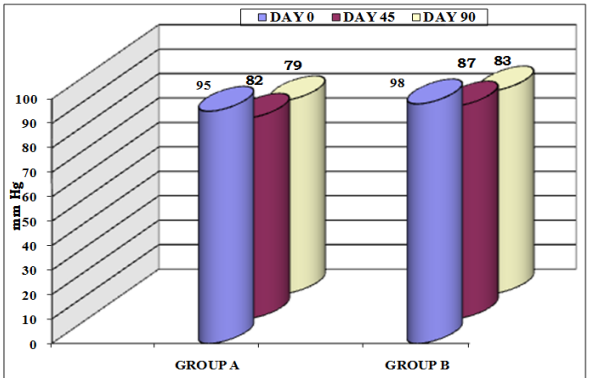

Figure No.2: Changes in the mean Diastolic Blood Pressure at Day- 45 and Day – 90 of treatment in groups A and B in Hypertensive Type II Diabetic patients

Mean fasting blood sugar among groups A and B were found to be 154.3 ± 32.23 and 142 ± 27.23 respectively at day 0 while at day 90 it was found 120.58 ± 17.49 and 106 ± 9.89 respectively. The difference between groups A v B was found statistically significant with P <.001. Group B performed 12.72 % better than group A at 90th day of treatment. The average difference from baseline to final i.e. from day 0 to day 90 showed significant changes in group A and B (P < .001). The percentage change in groups A and B from base line to final i.e. day 0 to day 90 have shown reduction of 21.85 % and 34.57 % respectively. (Table-3 & Figure- 3)

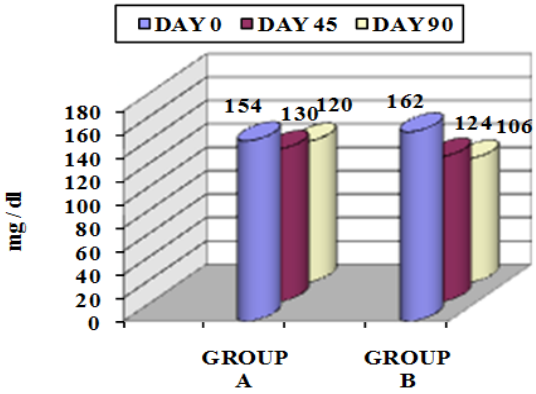

Figure No.3: Changes in the mean Fasting Blood Sugar (FBS) level at Day- 45 and Day – 90 of treatment in groups A and B in Hypertensive Type II Diabetic patients

DISCUSSION

High blood pressure is responsible for one death in every eight people. It is estimated by world health organization that hypertension is the third leading cause of death all over the world. Worldwide one billion people are suffering from hypertension.

The results of our present study are in consistent with Ito et al. who reported a reduction of 20 mmHg in systolic blood pressure and 10 mmHg reductions in diastolic blood pressure after 3 month treatment with Losartan[21]. The results of our study also correlated with the results of Miyauchi et al. who observed a reduction in mean systolic blood pressure by 10 mmHg and mean diastolic blood pressure by 8 mmHg with Losartan treatment for 12 weeks[22]. Similarly Iino et al. reported a decrease of 11.3% in systolic blood pressure and 10.8% decrease in diastolic blood pressure after 6 week treatment with Losartan[23]. Holdass et al. also found a decrease in systolic blood pressure from 162 mmHg to 148 mmHg and diastolic blood pressure from 105 mmHg to 96 mmHg with the significant p value of <0.001 in Losartan group after 2 months treatment[24].

The decrease of systolic and diastolic blood pressure with group B patients have also been reported and found in literature with research studies of Baren et al., Salma et al., Von poser et al., and Vakil RJ[25] .

As Hyprol is a combination formula of different herbal compounds so its cumulative effect have not been reported as a whole magnitude of response but as a single compound the effect of this coded herbal drugs has been reported and document by various researchers in their clinical research findings. The antihypertensive effects of Tribulus terrestris due to inhibition of angiotensin converting enzyme was reported by Sharifi AM et al[26]. Similarly Klausgraber F, Arnold OH et al., and Bhatia BB reported the hypotensive effects of Rauwolfia serpentina in their research trials[27].

Losartan, an angiotensin receptor blocker is known for its effects on glycemia control and improvement in blood glucose levels. Both the groups have significant effects on blood glucose & levels of HbA1c. In case of group A, 21% decrease in blood glucose level was found. While group B shows highly significant reduction in blood glucose level i.e. 34.57%.

Our results of group B patients treated with Hyprol on glycemia control are correlated with study conducted by Udayakumar et al., who found 35% reduction in blood glucose level and 45% fall in HbA1c with p value of <0.001[28]. Similarly Gauttam et al., in another study on Withania somnifera found 54% fall in blood glucose level[29]. Another study conducted by Nowouzi et al., on Cichory seeds, one of the components of Hyprol showed decrease in blood glucose level from baseline 408 mg/dl to 286 mg/dl[30]. Study conducted on Rauwolfia serpentina by Qureshi et al., also document reduction in blood glucose levels that are coincides with the results of group B in present study[31].

CONCLUSION

We observed that losartan produces highly significant effect over proteinuria, systolic and diastolic blood pressure and 24 hr creatinine clearance; in contrast this herbal combination gives promising results with regard to these parameters. The reason of this impact might be because of a cumulative effect of five herbal components in a single drug formulation.

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