Original Article

Treating Prehypertension

To Observe the Role of Angiotension Receptor Blocker Losartan in Treating Prehypertension

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ABSTRACT

Objective: The primary objective of the present study was to determine whether in patients with prehypertension six months of treatment with an angiotensin II, type 1 receptor antagonist (at a dose of 8mg once a day) reduces the incidence of hypertension in borderline patients

Study Design: Randomized, open-labeled, prospective study.

Place and Duration of Study: This study was conducted in the department of pharmacology and therapeutics, Basic Medical Sciences Institute (BMSI), Jinnah Post Graduate Medical Centre (JPMC), Karachi, from July 2007 to January 2008.

Materials and Methods: This study involved eighty untreated participants between 30 to 60 years of age of either sex with blood pressure on study entry in high-normal range i.e. systolic blood pressure of 130 to 139 mmHg and diastolic blood pressure of 85 to 89 mmHg, according to the classification developed by Joint National Committee on prevention, Detection, Evaluation, and Treatment of high blood pressure (JNC-VI). All participants were randomized and enrolled in study after baseline investigations and informed written consent.

Results: All values have been expressed in standard error of mean (± SEM). Forty patients were treated with DR1 and DR2 from day 0 to day 90^{th} of study period respectively. InDR1 group the mean systolic B.P was decreased from 138 mmHg to 125.8 mmHg from day 0 to day $90^{th.}$ In DR2 group an increase was observed in systolic B.P from 128 mmHg to 136 mmHg from day 0 to day 90^{th}. An average percentage decrease of 8.21 % in case of DR1 while, 5.52 % was increased in DR2 group. In same way a decrease of 11.82 % in DR1 group, while, an increase of 11.5 % was observed in case of DR2 group in mean diastolic blood pressure respectively from day 0 to day 90^{th} of study duration.

Conclusion: Treatment of prehhypertension with an angiotension receptor antagonist May decreases incident hypertension. Additional studies will be needed to ascertain whether this or other strategies involving early pharmacological treatment of prehypertension would positively affect clinical outcomes.

Key Words: Prehhypertension, Candesartan Cilexetil, Systolic blood pressure, Diastolic blood pressure.

INTRODUCTION

Regardless of terminology, Prehypertension is considered as a precursor of hypertension[1] and is associated with excess morbidity and deaths from cardiovascular cause[2], The name of the range of blood pressure between what is clearly normal and what is definitely hypertensive changed from transient hypertension in the 1940s[3] to borderline hypertension in the 1970s[4] high- normal blood pressure in the 1990s[5] and most recently prehhypertension in 2003[6]. Furthermore, an association of prehypertension with other cardiovascular risk factors has been established· We justified our study of pharmacological intervention with the use of an angiotensin-receptor blocker in prehypertension is based on following three grounds. One, in prehypertension, blood pressure remains a strong predictor of cardiovascular events after a statistical adjustment for other risk factors[7] suggesting that lowering blood pressure might be beneficial. Hypertension is a self-accelerating condition. The transition from prehypertension to established hypertension reflects in part ongoing changes such as arterial hypertrophy[8] and endothelial dysfunction[9].

Increased vasoconstriction and diminished vasodilatation, consistent with these structural and functional findings have been described in prehypertension [10]. Two, Growth factors mediated by stimulation of the sympathetic nervous system[11] and excess activity of the renin-angiotensin system [12] tend to promote vascular hypertrophy by direct as well as hemodynamic effects. Third, present guidelines recommend that prehypertension be managed with changes in the participants lifestyle, weight loss [13], salt restriction, exercise, and dietary modifications have been shown to reduce blood pressure in clinics specializing in lifestyle modifications.[14] Despite

intensive community efforts to promote healthful lifestyles, however, the prevalence of prehypertension in the United States is increasing [15]

MATERIALS AND METHODS

This study was conducted in the department of pharmacology and therapeutics, Basic Medical Sciences Institute (BMSI), in collaboration with the department of medicine, Jinnah Post-graduate Medical Centre, Karachi, from July 2007 to January 2008. This six months, randomized study involved eighty untreated participants between 30 to 60 years of age of either sex with blood pressure on study entry in high-normal range i.e. systolic blood pressure of 130 to 139 mmHg and diastolic blood pressure of 85 to 89 mmHg, according to the classification developed by Joint National Committee on prevention, Detection, Evaluation, and Treatment of high blood pressure (JNC-VI). All participants were randomized and enrolled in study after baseline investigations and informed written consent.

The study period was consisted of 24 weeks with weekly follow-up visits of participants; but the observations of the parameters were recorded on day 0, day45 and day 90 of the study period. The selected participants were divided into two groups. DR1 (losartan) and DR2 (Placebo). The DR1 group received Tab. losartan 50 mg once a day for 90 days, while DR2 group received Placebo once a day for 90 days. Following parameters were observed in the present study.

- Systolic blood pressure
- Diastolic blood pressure

RESULTS

The results have been expressed as mean ± SEM (standard error of mean). Forty participants were treated with DR1 and DR2 from day 0 to day 90th of study duration respectively. In DR1 group the mean systolic blood pressure was decreased from 138 mmHg on day 0 to 125.8 mmHg on day 90th. This reduction was found statistically highly significant ($p < 0.001$). The average percentage reduction in systolic B.P was 8.21 % from day 0 to day 90th of the treatment as shown in table 1A and figure 1A. In DR2 group 40 study participants were treated form day 0 till day 90th of study duration. The mean systolic blood pressure was increased from 128 mmHg on day 0 to 136 mmHg on day 90th of the treatment. This increase was also observed statistically significant. The average percentage increase in systolic blood pressure was observed 5.52 % from day 0 to day 90th of treatment as depicted in table 1.

In DR1 group, the mean diastolic blood pressure on day 0 was 87 mmHg which decreased to 75.8 mmHg on day 90th. This decrease in diastolic blood pressure was found statistically significant with a p- value ($p<0.001$), while in case of DR2 group the mean diastolic blood pressure was increased from 74 mmHg on day 0 to to 85 mmHg on day 90th of study period. This increase in mean diastolic blood pressure was found statistically significant. The mean diastolic changes have been depicted in Table 2.

Table No.1: Changes in mean systolic B.P from Day 0 – Day 90th, of the treatment with DR1, DR2 groups

Groups	Day -0 B.P (mm Hg)	Day-90 B.P (mm Hg)	% change from day 0 – day 90th
DR1	138 ± 0.07 (40)	125.8 ± 0.6 (38)	↓8.21 %
DR2	128 ± 0.41 (40)	136 ± 0.2 (36)	↑5.52 %

Key:

- DR1 (losartan)
- DR 2 (Placebo)
- Values are in (mean ± SEM)
- All observations are in mmHg
- ↓shows decrease in percentage in B.P
- ↑ shows increase percentage in B.P

Table No.2: Changes in mean diastolic B.P from Day 0 – Day 90th, of the treatment with DR1, DR2 Groups

Groups	Day -0 B.P (mm Hg)	Day -90 B.P (mm Hg)	% change from day 0 – day 90th
DR1	87 ± 0.2 (40)	75.5±8.33 (38)	↓11.82 %
DR2	74 ± 0.58 (40)	85 ± 0.24 (36)	↑11.5 %

Key

- DR1 (Losartan)
- DR 2 (Placebo)
- Values are in (mean ± SEM)
- All observations are in mmHg
- ↓shows decrease in B.P
- ↑ shows increase percentage in B.P

DISCUSSION

Untreated hypertension is a self-accelerating condition; evolving arteriolar hypertrophy and endothelial dysfunction facilitate the later increase of blood pressure and contribute to the transition from prehypertension to established hypertension. Abnormalities in cardiovascular structure and function and in neuroendocrine control occur in young adults with a predisposition to hypertension[16]. Therefore, we hypothesized that an intervention in humans with prehypertension might alter the natural history and prevent or delay the onset of established hypertension [17] The results of our study are in accordance with clinical trials of Julius et al 2006[18] and Whelton PK et al 2002.[19] The main objective of the present study was to

realize and recognize the importance of prehypertension and its intervention at its initial stages. The current international guidelines recommend lifestyle modifications for the management of prehypertension. The findings of our study can also be correlated with the findings of the Trial of Hypertension preventions.

CONCLUSION

Treatment of prehhypertension with an angiotension receptor antagonist May decreases incident hypertension. Additional studies will be needed to ascertain whether this or other strategies involving early pharmacological treatment of prehypertension would positively affect clinical outcomes.

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