Original Article

Placebo-Controlled Trial of Pharmaceutical Optimized Hydralazine 25mg (F-6) in Patients with Essential Hypertension

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ABSTRACT

Objective: The objective of this study evaluating biochemical effects and efficacy of optimized Hydralazine 25mg (F-6) as compared to placebo in adult hypertension patients

Study Design: Randomized placebo-controlled trial, Double-blind

Place and Duration of Study: This study was conducted at the Mohtarma Benazir Bhutto Shaheed Medical College, Biochemistry Department Mirpur, AJK from October 2014 to January 2015.

Materials and Methods: In this study we selected 80 patients, from different hospital of Mirpur AJK and 20 patients take as placebo. We measured blood pressure at baseline and after 8 week for both groups that one group received Hydralazine 25mg (F-6) and one group received placebo. Biochemical safety parameter was also measured for both groups. In these parameters we studied protein profile, enzymeselectrolytes, liver function, renal function and complete blood count. In basic metabolism we studied glucose metabolism and lipid metabolism in which triglycerides, LDL-cholesterol, HDL-cholesterol and total cholesterol was included. Microlab 300 was used for analysis of samples for both groups. Merck kits were used for analysis of sample.

Results: Baseline systolic blood pressure for Hydralazine 25mg (F-6) was 148.8± 10.2 and for placebo was 148.4± 10.3. After 8 weeks was for Hydralazine 25mg (F-6) was 140.1 ± 10.4and for placebo was 148.2 ± 10.2. . Baseline Diastolic blood pressure for Hydralazine 25mg (F-6) was 97.6± 6.3 and for placebo was 96.9± 6.5. After 8 weeks was for Hydralazine 25mg (F-6) was 86.5 ± 5.9 and for placebo was 96.2 ± 5.9. Blood glucose was observed as no significant variations such as Fasting Blood Glucose (mg/dl) 98.8 ± 10.2 at base line and 98.7 ± 10.3 after 8 weeks. Lipid profile was also observed no significant variation. Such as Total Cholesterol (mg/dl) 196.8 ± 42.8 as baseline and 195.5 ± 42.6 after 8 weeks.LDL - Cholesterol (mg\dl) 113.9 ± 32.5 at base line and 113.8 ± 32.6 after 8 weeks.HDL - Cholesterol (mg\dl) 54.6 ± 12.5 at baseline and 54.6 ± 12.5 after 8 weeks, Triglycerides (mg\dl) 138.3 ± 87.5 at baseline and 138.7 ± 88.1 after 8 weeks. The optimized product was observed best regarding glucose metabolism and also lipid metabolism because both biomolecule metabolisms remain unchanged and not affected with drug.

Conclusion: Hydralazine 25mg (F-6) showed best result to achieve and maintain blood pressure for eight weeks. Due to high antihypertensive efficacy it is best choice for blood pressure patients and it is safe for metabolic syndrome patients

Key Words: Hypertension, Hydralazine, Biochemical effects

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INTRODUCTION

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Morbidity and mortality are the risk factor of cardiovascular diseases and hypertension. With the help of adequate blood pressure we can manage easily Mostly prescribed Hydralazine for the treatment of hypertension which act as vasodilator. Absorption of this drug is very high after the oral administration and significant first-pass metabolism The guideline of blood pressure of 140/90mmHg treatment is 130/85 mmHg according World Health Organization (WHO) and it was actually 140/90 mmHg on previous guideline of WHO.[1-6] For renal diseases one risk factor is high blood pressure.[7] Angiotensin-converting enzyme (ACE) is also play important role in controlling of blood pressure. It has significant role macroalbuminuria with renal diseases and this result also observed in microalbuminuria patients.[8]

For the treatment of hypertension, mostly prescribed Hydralazine which act as vasodilator. Absorption of this drug is very high after the oral administration and significant first-pass metabolism[9]. According the acetylation of the drug, the Oral availability t range between 10 and 35 %, is reported. Hydralazine has high physiochemical stability, low dose (50–100 mg) and its short biological half-life (2–4 h). So these properties of the drug facilitate researcher to formulate the drug into once-a-day CR formulation[10–12]. This drug has very affective property as antihypertensive in severe hypertension in pregnancy. It is mostly prescribed in pregnancy.[11] Headache, nausea, and vomiting are side effects which are common and its deteriorating pre-eclampsia symptoms which are mimic.Olmesartan have superior tolerability and antihypertensive efficacy[13]. For effectiveness and tolerance in patientmedoxomil and amlodipine besylate sowed result with hypertension[14]. Amlodipinebesylate alone and with combination with benazepril hydrochloride with valsartan and with perindopril showed good result[15,16] The objective of this study, determining biochemical basic metabolism and efficacy of pharmaceutical optimized product Hydralazine 25mg (F-6) in patients with essential hypertension in also in placebo for comparison.

MATERIALS AND METHODS

This was multicenter, randomized, placebo-controlled, comparative study. Patient was randomized to receive optimized Hydralazine 25mg (F-6) once daily and Placebo once daily for 8 weeks. The study was conducted in Department of Biochemistry, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJK from October 20 14 to January 2015. Patients were selected from four different hospitals of MirpurAJK In this study we selected 80 patients, from different hospital of Mirpur AJK and 20 patient take as placebo. We measured blood pressure at baseline and after 8 week for both groups that one group received Hydralazine 25mg (F-6) and one group received placebo, Biochemical safety parameter was also measured for both groups. In these parameters we studied protein profile, enzymeselectrolytes, liver function, renal function and complete blood count. In basic metabolism we studied glucose metabolism and lipid metabolism in which triglycerides, LDL-cholesterol, HDL-cholesterol and total cholesterol was included. Microlab 300 was used for analysis of samples for both groups. Merck kits were used for analysis of sample.

RESULTS

Baseline systolic blood pressure for Hydralazine 25mg (F-6) was 148.8± 10.2 and for placebo was 148.4± 10.3. After 8 weeks was for Hydralazine 25mg (F-6) was 140.1 ± 10.4 and for placebo was 148.2 ± 10.2. . Baseline Diastolic blood pressure for Hydralazine 25mg (F-6) was 97.6± 6.3 and for placebo was 96.9± 6.5. After 8 weeks was for Hydralazine 25mg (F-6) was 86.5 ± 5.9 and for placebo was 96.2 ± 5.9. Blood glucose was observed as no significant variations Such as Fasting Blood Glucose(mg/dl) 98.8 ± 10.2 at base line and 98.7 ± 10.3 after 8 weeks. Lipid profile was also observed no significant variation. Such as Total Cholesterol (mg/dl) 196.8 ± 42.8 as baseline and 195.5 ± 42.6 after 8 weeks.LDL - Cholesterol (mg\dl) 113.9 ± 32.5 at base line and 113.8 ± 32.6 after 8 weeks.HDL - Cholesterol (mg\dl) 54.6 ± 12.5 at baseline and 54.6 ± 12.5 after 8 weeks, Triglycerides (mg\dl) 138.3 ± 87.5 at baseline and 138.7 ± 88.1 after 8 weeks. The optimized product was observed best regarding glucose metabolism and also lipid metabolism because both biomolecule metabolisms remain unchanged and not affected with drug.

Table No.1: Baseline characteristics

	Hydralazine 25mg (F-6) (n=60)	Placebo (n=20)
Age (years)	50.3± 8.2	50.5 ± 8.6
Male / Female (%)	41.2 / 58.8	35.5 / 64.5
Body weight (Kg)	70.2± 12.5	70.5± 12.4
BMI (kg/m2)	27.1± 2.9	27.2± 2.8
SBP sitting (mmHg)	148.9± 10.2	148.4± 10.3
DBP sitting (mmHg)	97.6± 6.3	96.9 ± 6.5

Table No.2: Ambulatory blood pressure monitoring. Mean values of blood pressure

	Hydralazine 25mg (F-6) (n=60) Systolic BP - 24 hours (mmHg)	Placebo (n=20)	*P-value*
Baseline	148.8± 10.2	148.4± 10.3	NS
Week 8	140.1 ± 10.4	148.2 ± 10.2	0.0036
	Diastolic BP - 24 hours (mmHg)		
Baseline	97.6± 6.3	96.9 ± 6.5	NS
Week 8	86.5 ± 5.9	96.2 ± 5.9	0.0002

NS: Non significant, *p*: probability

DISCUSSION

For stroke one is risk factor is high blood pressure.[17] Dementia and cognitive impairment are present in high blood pressure patient and it is present with metabolic syndrome.[18,19] In table No1, baseline characteristics are

present. The study was conduct in Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJK from October 20 14 to January 2015

Table 3: Baseline Biochemical characteristics

	Hydralazine 25mg (F-6) (n=60)	Placebo (n=20)
	Fasting Blood Glucose (mg/dl)	
Baseline	98.8 ± 10.2	98.4 ± 9.4
Week 8	98.7 ± 10.3	98.5 ± 9.3
	Total Cholesterol (mg/dl)	
Baseline	196.8 ± 42.8	195.7 ± 34.5
Week 8	195.5 ± 42.6	195.3 ± 34.7
	LDL (mg\dl)	
Baseline	113.9 ± 32.5	119.5± 26.5
Week 8	113.8 ± 32.6	119.7 + 27.3
	HDL (mg\dl)	
Baseline	54.6 ± 12.5	48.5 ± 12.2
Week 8	54.3 ± 12.7	48.9 ± 12.5
	Triglycerides (mg\dl)	
Baseline	138.3 ± 87.5	146.2 ± 87.2
Week 8	138.5 ± 88.1	144.7 ± 87.5

In this study we selected 80 patients, from different hospital of Mirpur AJK and 20 patient take as placebo. We measured blood pressure at baseline and after 8 week for both groups that one group received Hydralazine 25mg (F-6) and one group received placebo. Biochemical safety parameter was also measured for both groups. In these parameters we studied protein profile, enzymes electrolytes, liver function, renal function and complete blood count. In basic metabolism we studied glucose metabolism and lipid metabolism in which triglycerides, LDL-cholesterol, HDL-cholesterol and total cholesterol was included. Microlab 300 was used for analysis of samples for both groups. Merck kits were used for analysis of sample. The antihypertensive efficacy result was present in table No.2. The optimized product showed significant efficacy for systolic and diastolic blood pressure. Baseline systolic blood pressure for Hydralazine 25mg (F-6) was 148.8± 10.2 and for placebo was 148.4± 10.3. After 8 weeks was for Hydralazine 25mg (F-6) was 140.1 ± 10.4 and for placebo was 148.2 ± 10.2. Baseline Diastolic blood pressure for Hydralazine 25mg (F-6) was 97.6± 6.3 and for placebo was 96.9± 6.5. After 8 weeks was for Hydralazine 25mg (F-6) was 86.5 ± 5.9 and for placebo was 96.2 ± 5.9. Blood glucose was observed as no significant variations Such as Fasting Blood Glucose (mg/dl) 98.8 ± 10.2 at base line and 98.7 ± 10.3 after 8 weeks. Lipid profile was also observed no significant variation. Such as Total Cholesterol (mg/dl) 196.8 ± 42.8 as baseline and 195.5 ± 42.6 after 8 weeks.LDL - Cholesterol (mg\dl) 113.9 ± 32.5 at base line and 113.8 ± 32.6 after 8 weeks.HDL - Cholesterol (mg\dl) 54.6 ± 12.5 at baseline and 54.6 ± 12.5 after 8 weeks, Triglycerides (mg\dl) 138.3 ± 87.5 at baseline and 138.7 ± 88.1 after 8 weeks . The optimized product was observed best regarding glucose metabolism and also lipid metabolism because both biomolecule metabolism remain unchanged and not affected with drug. However, some drugs used in the treatment of hypertension, such as diuretics and beta-blockers, are known to be able to promote harmful alterations in lipid metabolism, especially in glucose metabolism. 70.2% of the patients treated with Hydralazine 25mg (F-6) to achieve and maintain for eight week ·It means it has high antihypertensive efficacy it is best choice for blood pressure patients and is it is safe for metabolic syndrome patients

CONCLUSION

Hydralazine 25mg (F-6) showed best result to achieve and maintain blood pressure for eight weeks. Due to high antihypertensive efficacy it is best choice for blood pressure patients and it is safe for metabolic syndrome patients.

Author's Contribution:

Concept & Design of Study:	Sohail Iqbal
Drafting:	Khurram Shahzad Khan
Data Analysis:	Farooq Munfaet Ali Khan, Asnad
Revisiting Critically:	Sohail Iqbal, Khurram Shahzad Khan
Final Approval of version:	Sohail Iqbal

Conflict of Interest: The study has no conflict of interest to declare by any author.

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