Original Article

Placebo- Controlled Trial of Pharmaceutical Optimized Captopril 60mg (F-9) in Patients with Essential Hypertension for Efficacy & Biochemical Evaluation

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ABSTRACT

Objective: The aim of study , to evaluate the efficacy of optimized Captopril 60 mg (F-9) with compare to placebo control for eight weeks and also analyze basic metabolism parameter such as Total Cholesterol, LDL-Cholesterol, HDL- Cholesterol, Triglycerides and Fasting blood glucose for test and control patients

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

Place and Duration of Study: This study was conducted at the Department of Biochemistry, University of Karachi from September 2011 to January 2012.

Materials and Methods: Patients were selected from different area of orange town and surrounding area , such as pirabad, mangopir, Pathan colony, impear colony, mastanchali , Metrovell and site area. Total eighty (80)patients were analyzed for Total Cholesterol (mg/dl**) ,** HDL-Cholesterol mg/dl**)**, LDL-Cholesterol mg/dl**)** , Triglycerides (mg\dl) and for fasting glucose level . The analysis was performed by Micro Lab 300 and kits were used of Merck. Other biochemical parameters(Liver function test, Urea, Complete blood counting, uric acid , electrolytes and protein profile) were used for safety purpose. All the parameter were studied at initial phase for test and control and after completion of trial such as eight weeks (8 weeks), parameters were studied again for test and control. Primary blood pressure such as Systolic BP - 24 hours (mmHg) and Diastolic BP - 24 hours (mmHg) was analyzed by manual method patients. After eight weeks (8weeks) trial, blood pressure was determined by same manual method for test and placebo control patients.

Results: Initial result systolic blood for test patient was 149.3 ± 11.2 mmHg and for placebo control was 149.2± 10.5 mmHg. After eight week trial of optimizedCaptopril 60mg (F-9), systolic blood was reduced (140.1 ± 11.4 mmHg) as compared to placebo control such as (148.9 ± 11.3 mmHg). Like systolic blood pressure, initial diastolic blood pressure for test patient was (97.7 ± 7.2 mmHg) and for placebo was (95.3± 7.7mmHg) but after eight week trial of optimizedCaptopril 60mg (F-9), diastolic blood pressure was reduced in test patients (86.6 ± 5.4 mmHg) as compared to placebo control such as (93.9 ± 7.9 mmHg).

Conclusion: The optimized Captopril 60mg (F-9)it is an excellent option for the treatment of hypertension withhigh antihypertensive efficacy, good tolerability and no biochemical effects. . It is due to low dose drug and also no effect of excipient of formulation of F-9.

Key Words: Hypertension, Captopril, Biochemical effects

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INTRODUCTION

The treatment of hypertension is an accurate blood pressureand high blood pressure is the risk of morbidity and mortalitycardiovascular so it isessential to treat it properly. The additional benefits regarding both protection of organs and cardiovascular mortality to control blood pressurelower than 130/85 mmHg according Guidelines of World Health Organization for the treatment of hypertension while the previous limit was 140/90 mmHg.[1-6]

Blood pressure is also associated with the progression of renal disease.[7] for the limiting renal-disease progression antihypertensive agents; inhibitors of angiotensin-converting enzyme (ACE) are regarded as particularly effective. The patients with macro-albuminuriain renal diseases ACE inhibitors significantly effective[7]. The beneficial effect also found in microalbuminuria patients.[8,9] It is reasonable to investigate whether use of ACE inhibitorsin patients with normoalbuminuria may also be beneficial.ACE

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inhibitors can slow the relentless decline of renal function in patients However, previous trials of ACE inhibitors innormoalbuminuric patients are few, [10]and have eitherlacked poweror have not been designed as randomized and controlled.[10, 11]For congestive heart failure andtreatment of hypertension Captopril, (1-[(2S)-3-mercapto-2-methyl propionyl]-lproline),an angiotensin-converting enzyme inhibitoris used [12].

This drug is water soluble and 1.7 h iseliminationhalf-life after an oral dose. [13] pH 1.2 is stable pH and degradation reaction of drug occurred with increasing pH[14]. The controlled release dosage form of the drug is beneficial [15,16] The hydrodynamically balanced system in which to develop floating systems to control drug releaseVarious attempts have been made.[17, 18] For the managing children with heart failure Captopril is established pharmacological treatment With acquired heart disease in adult drug efficacy and safety is foundeddata from studies, these drugs used. [1 9, 20] Clinicians used without any doubt regarding efficacy and utility of captopril for the treatment of children with heart failure, also regarding toxicity and optimal dosing schedules.[1 9,20] Formulation of the dosage form is also important factor regarding toxicity and optimal dosing schedules.[21] Studies showed that angiotensin receptor blockers like olmesartanmedoxomil have and antihypertensive efficacy andsuperior tolerability[22]. Another study showed that for the effectiveness and tolerance in patient with hypertension, olmesartan, medoxomil and amlodipine besylate is used[23]. Amlodipine besylate alone as indicated with benazepril hydrochloride with valsartan and with perindopril showed best result in reduction of blood pressure in combination form. [24, 25]

The aim of study, to evaluate the efficacy ofoptimizedCaptopril 60 mg (F-9) with compare to placebo control for eight weeks and also analyze basic metabolism parameter such as Total Cholesterol, LDL-Cholesterol, HDL- Cholesterol, Triglycerides and Fasting blood glucose for test and control patients.

MATERIALS AND METHODS

In this study, Patient was received randomizedCaptopril 60mg (F-9) for eight weeks and control received placebo for eight weeks so it was multicenter, comparative study.In September 20 11 to January 2012, this study was completed in the department of biochemistry, University of Karachi.Patients were selected from different area of orange town and surrounding area, such as Pirabad, Mangopir, Pathan colony,Impear colony, Mastanchali ,Metrovell and site area. Total eighty (80) patients were analyzed for Total Cholesterol (mg/dl**) ,**HDL-Cholesterol mg/dl**)**, LDL-Cholesterol mg/dl**)** , Triglycerides (mg\dl) and for fasting glucose level . The analysis was performed by Micro Labe 300 and kits were used of Merck. Other biochemical parameters (Liver function test, Urea, Complete blood counting, uric acid, electrolytes and protein profile) were used for safety purpose. All the parameters were studied at initial phase for test and control and after completion of trial such as eight weeks (8 weeks), parameters were studied again for test and control. Initial characteristics of patients were determined such as age, body weight, BMI for both test and control patients. Like, the biochemical parameters of the patients, primary blood pressure such as Systolic BP - 24 hours (mmHg) and Diastolic BP - 24 hours (mmHg) was analyzed by manual method for both test and control patients . After eight weeks (8weeks) trial, blood pressure was determined by same manual method for test and placebo control patients.

RESULTS

Initial result systolic blood for test patient was 149.9 ± 11.2 mmHg and for placebo control was 149.2± 10.5 mmHg. After eight week trial of optimizedCaptopril 60mg (F-9),systolic blood was reduced (140.1 ± 11.4 mmHg) as compared to placebo control such as (148.9 ± 11.3 mmHg). Like systolic blood pressure, initialdiastolic blood pressure for test patient was (97.7 ± 7.2 mmHg) and for placebo was (95.3± 7.7mmHg) but after eight week trial of optimizedCaptopril 60mg (F-9), diastolic blood pressure wasreduced in test patients (86.6 ± 5.4 mmHg) as compared to placebo control such as (93.9 ± 7.9 mmHg). All the biochemical parameters were not changed for test patient after eight week trial such as (Total Cholesterol 198.2 ± 42.3 (mg/dl**) ,** HDL-Cholesterol 53.8 ± 13.2mg/dl**)**, LDL-Cholesterol 113.6 ± 32.9 mg/dl**)** , Triglycerides 137.8 ± 88.6 (mg\dl) and for fasting glucose 97.4 ± 11.3mg/dl level) as compare to placebo such as (Total Cholesterol 192.3 ± 33.5 (mg/dl**) ,** HDL-Cholesterol 46.6 ± 11.3 mg/dl**)**, LDL-Cholesterol 118.4 + 25.6 mg/dl**),** Triglycerides 145.7 ± 88.6 (mg\dl) and for fasting glucose 96.8 ± 8.8 (mg\dl) level. The optimized product Captopril 60mg (F-9)is showed no biochemical effects regarding lipid metabolism and glucose metabolism. It is due to low dose drug and also no effect of excipient of formulation of F-9.

Table No.1: Baseline characteristics

	Captopril 60mg (F-9) (n=60)	Placebo (n=20)
Age (years)	50.2 ± 9.5	51.1± 9.6
Male / Female (%)	45.4 / 54.6	37.0 / 63.0
Body weight (Kg)	69.9 ± 13.5	70.2 ± 12.2
BMI (kg/m2)	27.4± 3.6	27.8 ± 3.4
SBP sitting (mmHg)	149.9 ± 11.2	149.2±10.5
DBP sitting (mmHg)	97.7 ± 7.2	95.3± 7.7

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

	Captopril 60mg (F-9) (n=60)	Placebo (n=20)	P-value
Systolic BP - 24 hours (mmHg)			
Baseline	149.9 ± 11.2	149.2±10.5	NS
Week 8	140.1 ± 11.4	148.9±11.3	0.0037
Diastolic BP - 24 hours (mmHg)			
Baseline	97.7 ± 7.2	95.3± 7.7	NS
Week 8	86.6 ± 5.4	93.9± 7.9	0.0001

NS: Non significant, p: probability

Table No.3: Baseline Biochemical characteristics

	Captopril 60mg (F-9)(n=60)	Placebo (n=20)
Fasting Blood Glucose(mg/dl)		
Baseline	96.3 ± 11.2	97.3 ± 9.3
Week 8	97.4 ± 11.3	96.8 ± 8.8
Total Cholesterol (mg/dl)		
Baseline	196.8 ± 42.4	193.8 ± 34.3
Week 8	198.2 ± 42.3	192.3 ± 33.5
LDL - Cholesterol (mg\dl)		
Baseline	113.5 ± 32.8	117.8± 23.7
Week 8	113.6 ± 32.9	118.4 + 25.6
HDL - Cholesterol (mg\dl)		
Baseline	52.9 ± 12.8	46.8 ± 11.4
Week 8	53.8 ± 13.2	46.6 ± 11.3
Triglycerides (mg\dl)		
Baseline	137.2 ± 89.3	144.3 ± 88.7
Week 8	137.8 ± 88.6	145.7 ± 88.6

DISCUSSION

For stroke, hypertension is a major risk factor. Brain tissue loss as a consequence of stroke has been associated with cognitive impairment,... relation to other stroke-specific factors, these strokes may be isolated or strategically located ones (e.g. in the thalamus, angular gyrus, frontal white matter).[26] Also, because hypertension is no single factor but exist with other metabolic risks factors, such as (inflammation of brain , abnormal insulin signaling in the brain) and existing other metabolic syndrome and underlie (cognitive impairment or dementia) in persons with hypertension.[27,28] Patients were selected from different area of orange town and surrounding area, such as Pirabad, Mangopir, Pathan colony, Impear colony, Mastanchali , Metrovell and site area. Total eighty (80) patients were analyzed for Total Cholesterol (mg/dl**) ,**HDL-Cholesterol mg/dl**)**, LDL-Cholesterol mg/dl**)** , Triglycerides (mg\dl) and for fasting glucose level . The analysis was performed by Micro Labe 300 and kits were used of Merck. Other biochemical parameters (Liver function test, Urea, Complete blood counting, uric acid, electrolytes and protein profile) were used for safety purpose. All the parameters were studied at initial phase for test and control and after completion of trial such as eight weeks (8 weeks), parameters were studied again for test and control. Initial characteristics of patients were determined such as age, body weight, BMI for both test and control patients. Like, the biochemical parameters of the patients, primary blood pressure such as Systolic BP - 24 hours (mmHg) and Diastolic BP - 24 hours (mmHg) was analyzed by manual method for both test and control patients . After eight weeks (8weeks) trial, blood pressure was determined by same manual method for test and placebo control patients.

The baseline characteristics are shown in Table no1. We can observe that the groups were not different in relation to (age, body mass index, weight, heart rate, systolic and diastolic pressure values). Initial result systolic blood for test patient was 149.9 ± 11.2 mmHg and for placebo control was 149.2± 10.5 mmHg. After eight week trial of optimizedCaptopril 60mg (F-9), systolic blood was reduced (140.1 ± 11.4 mmHg) as compared to placebo control such as (148.9 ± 11.3 mmHg). Like systolic blood pressure, initial diastolic blood pressure for test patient was (97.7 ± 7.2 mmHg) and for placebo was (95.3± 7.7mmHg) but after eight week trial of optimizedCaptopril 60mg (F-9), diastolic blood pressure was reduced in test patients (86.6 ± 5.4 mmHg) as compared to placebo control such as (93.9 ± 7.9 mmHg). All the Biochemical parameters were not changed for test patient after eight week trial such as (Total Cholesterol 198.2 ± 42.3 (mg/dl**) ,** HDL-Cholesterol 53.8 ± 13.2mg/dl**)**, LDL-Cholesterol113.6 ± 32.9 mg/dl**)** , Triglycerides137.8 ± 88.6 (mg\dl) and for fasting glucose 97.4 ± 11.3mg/dl level) as compere to placebo such as (Total Cholesterol 192.3 ± 33.5 (mg/dl**) ,** HDL-Cholesterol 46.6 ± 11.3 mg/dl**)**, LDL-Cholesterol 118.4 + 25.6 mg/dl**),** Triglycerides 145.7 ± 88.6 (mg\dl) and for fasting glucose96.8 ± 8.8 (mg\dl) level. Table No.2 result showed that the optimized product Captopril 60mg (F-9) has best antihypertensive efficacy for long time .For the achieving the goals (pressure levels equal to or lower than 90 mmHg), the treatment of hypertension withoptimized product of Captopril 10mg (F-9) , we got result more than68.9% of the patients treated with optimized product . Result showed thatoptimized product of Captopril 10mg (F-9) didnot affect sympathetic activity and not cause any significant variations of heart rate.Our results showed that the optimized product of Captopril 10mg (F-9)at low doses has a very good biochemical profile with no adverse effects.

The good biochemical profile of the optimizedCaptopril 10mg (F-9) was found in the study because we use very low dose of drug and the excipients in formulation do not affect the biochemical profile. Diuretics and beta-blockers, promote significantly change lipid profile, glucose metabolism. But in ourstudy,the optimized product Captopril 10mg (F-9) did not alter parameters

of either glucose metabolism or plasma lipids, thus having a neutral biochemical profile even when used for 8 weeks. Table.No.3

The optimized product Captopril 10mg (F-9)is safe because result showed and best for the treatment of hypertension in patients with (metabolic syndrome, diabetes mellitus and dyslipidemias).

CONCLUSION

The optimizedCaptopril 60mg (F-9)it is an excellent option for the treatment of hypertension with high antihypertensive efficacy, good tolerability and no biochemical effects. . It is due to low dose drug and also no effect of excipient of formulation of F-9.

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

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