

COMBINED EFFECT OF CAPTOPRIL AND THIAZIDE DIURETIC ON SERUM LIPID PROFILE IN HYPERTENSIVE WOMEN

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Background: Hypertension has long been recognized as the major risk factor for the development of coronary disease. It was found that the combination of thiazide diuretic and ACE inhibitor has favorable antihypertensive and metabolic effect i.e the combination reduces the levels of lipid. **Methods:** 40 women aged between 35-60 years having systolic blood pressure equal to or greater than 160mmHg were included in the study. Captopril in a dose of 25-75 mg plus thiazide 25-50mg orally per day was given in divided doses. Before starting therapy and then after 4 and 10 week of therapy, 5ml of fasting blood was drawn to analyze lipid profile like serum triglyceride, cholesterol and lipoprotein (HDL and LDL-Cholesterol). **Results:** Study observed a marked decrease of blood pressure after taking captopril with diuretics. Level of triglyceride and of HDL and LDL-cholesterol were also significantly changed ($P<0.01$) as compared to their controls. **Conclusion:** It was observed that captopril in combination of thiazide diuretics not only decrease blood pressure but also a beneficial effect on lipid profile. Hence further research is needed on large number of patients of both sexes.

INTRODUCTION

Hypertension is the most powerful vascular disease in all of the world and contributor of death. In primary hypertension a mild hyper-responsiveness of hypothalamic, sympho-hormonal centers to psychosocial stimuli forms a major pathogenetic element, although high salt intake in some subjects may contribute via volume expansion. Hypertension is often associated with another "civilization" disorder, the metabolic syndrome, defined as abdominal obesity, insulin resistance and dyslipidaemia¹.

Hypertension has long been recognized as the major risk factor for the development of coronary disease and other vascular disease. The benefits of blood pressure lowering have been documented in terms of reducing the risk of cerebrovascular accidents, renal failure and hypertensive cardiomyopathy².

Antihypertensive drugs fall into 4 major groups, diuretics, sympatholytic, vasodilator and angiotensin converting enzyme inhibitors (ACE). A group of workers³ reported that an overactive brain renin-angiotensin system is one of the factors contributing to the pathogenesis of hypertension.

A commonly used angiotensin converting enzyme inhibitor is captopril. It is orally active and competitive inhibitor of angiotensin converting enzyme. It also blocks degradation of bradykinin, and bradykinin stimulates prostacyclin synthesis⁴. Besides, thiazide is an effective diuretic in hypertension. It directly acts on the kidney to increase the excretion of sodium chloride, potassium accompanying increase volume of water. It was found that the combination of thiazide and ACE inhibitor has favorable metabolic effect i.e the combination reduces the level of lipid profile⁶.

Atherosclerosis is a multi-factorial illness involving numerous factors initiating or aggravating the arterial lesion, out of which hypertension,

hypolipoproteinemia, and diabetes mellitus play an essential role. The altered lipoproteins are elevated plasma total cholesterol, low density lipoprotein (LDL) and triglyceride with a decreased level of high density lipoprotein (HDL).

Therefore, we set out to determine the effects of captopril (ACE inhibitors) in combination with thiazide diuretic on lipid profile of hypertensive females.

MATERIALS AND METHODS

40 women of ages between 35-60 years having systolic blood pressure equal to or greater than 160mmHg and diastolic blood pressure between 95-115 mmHg⁸ were included in this study. The patients excluded from this study were those who had history of cerebrovascular accidents, heart failure, secondary or malignant hypertension, diabetes mellitus.

Captopril in a dose of 25-75 mg plus thiazide 25-50 mg orally/day was given in divided doses. Before starting therapy and then after 4th and 10 week of therapy a 5ml of fasting blood was drawn to analyze lipid profile. Serum triglyceride, cholesterol, HDL and LDL-cholesterol were estimated by standard kit (Merck) methods.

RESULTS

Variation in the level of serum lipid profile is tabulated in table I and 2.

Table 1 shows a decrease in the level of triglyceride and cholesterol after taking captopril and thiazide. It was found that a mean %age change in the level of serum triglyceride and cholesterol at 4th and 10th week as compared to these level at 0 week but a Significant difference ($P<0.01$) only observed in case of serum cholesterol at 10th week.

Table 2 shows a marked increase in the level of HDL-cholesterol was observed after 4th and 10th week of taking drug as compared to this level with 0 week. This shows a highly significant difference (P<0.01). On

Table I: Combined effect of Captopril and Thiazide on Serum Triglyceride and Cholesterol before and after 4th and 10th week of its administration in hypertensive subjects (Values expressed as mean ± S.K. M.)

Time of administration	Triglyceride (mg/dl)	Mean % Change	Cholesterol (mg/dl)	Mean % change
At 0 week	191.25±7.13	X	204.78±6.54	
After 4 week	184.14±6.48	3.71	195.58±5.82	4.99
After 10 week	173.97±6.28	9.03	183.885.73	10.20**

**P<0.01 = Highly significant difference

Table-2: Combined effect of Captopril and Thiazide on serum HDL and LDL Cholesterol before and after 4th and 10th week of its administration in hypertensive subjects (Values expressed as mean ± S.E.M)

Time of administration	HDL-CH (mg/dl)	Mean % Change	LDL-CHOL (mg/dl)	Mean % change
At 0 week	40.61±1.91	-	68.89±4.05	-
After 4 week	45.57±0.91	12.21**	65.77±3.52	4.52
After 10 week	57.91±2.36	42.60**	58.6±3.08	14.93*

*P<0.05= Significant difference **p<0.01 = Highly significant difference

DISCUSSION

Hypertension is accompanied by increased morbidity and mortality and constitutes a substantial part of medical care. Anti-hypertensive intervention reduces the cardiovascular morbidity and mortality. An ideal anti-hypertensive agent would control blood pressure without interfering with lipid metabolism. The aim of the present study was to assess whether in addition to angiotensin-converting enzyme inhibitors, thiazide diuretic the first anti-hypertensive drug has any effect on lipid profile.

Present study shows marked decrease of blood pressure (i.e from 157.5/101.25 to 137.5/87/75) after taking captopril with diuretics. Study is in accordance to a study¹⁰ that established the safety of aggressive blood pressure lowering to diastolic targets of less than 80 mmHg. Moreover, they observed that hypotensive mechanisms of ACE inhibitors might be mediated by an increase in prostacyclin production.

Our study found that the drugs show prominent effect on lipid profile. Level of triglyceride and cholesterol was decreased after 4th and 10th week of medication. Our study is in accordance with a study that observed minor changes in the level of serum cholesterol and

triglyceride. Level of lipoprotein (LDL and HDL-cholesterol) was significantly changed in our study after medication. Our study is in contrast to a study¹¹ that Verapamil/captopril had a number of significant effects on serum lipid profile (increased total cholesterol, increased HDL-cholesterol, and reduced LDL-cholesterol). A group of workers¹³ stated that no difference was observed on the changes of lipid parameters between week 0 and week 8 visits.

Present study shows a close association of hypertension with lipid profile. It was observed that captopril in combination of thiazide diuretic not only decreases blood pressure but also has beneficial effect on lipid profile. A number of studies¹⁴⁻¹⁵ show the same results. Hence further research is needed on large number of patients of both sexes.

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