

Lipid Profile and Antihypertensive Drugs

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Abstract

Background: Hypertension and dyslipidemia are cardiovascular risk factors that commonly coexist .

Objective : To evaluate the effects of β - blocker (Atenolol) , ACE inhibitor (Captopril) calcium Channel blocker (Nefidipin) and diuretics on serum lipid profiles .

Method: Thirty untreated hypertensive and 147 hypertensive patient treated with these antihypertensive drugs, attending different public health clinics in Basrah province were enrolled in this study .

Serum lipid profile were determined enzymatically using kits from BioMerieux, France .

Result : The study has revealed that β -blocker do not significantly affect total cholesterol (TC) and LDL-

cholesterol , but increase significantly triglyceride (TG) and VLDL – cholesterol and decrease HDL – cholesterol.

Diuretics causes a significant elevation of TG with generally no significant changes in TC , LDL – cholesterol , VLDL – cholesterol and HDL-cholesterol. ACE inhibitor and calcium channel blockers appears to have no significant effect on plasma lipids .

Conclusion :It may important to measure blood lipid levels to identify pre-existing hyperlipidemia before starting the antihypertensive therapy and to select antihypertensive agent that will not influence the lipid profile or interfere with the therapy of hyperlipidemia

Key words: Hypertension, lipid and lipid profiles, antihypertensive,drugs

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Introduction

The objective of treating patients with hypertension is not simply to reduce blood pressure, but rather to prevent the associated morbidity and mortality⁽¹⁾ . Hypertension is well established a risk factor for coronary heart disease (CHD) , however the treatment of hypertension has not unequivocally shown a preventive effect on the incidence of CHD , as it has for cerebrovascular disease^(2,3,4) .The failure to show a reduction in CHD morbidity with antihypertensive treatment has raised the possibility that metabolic side effects of the drugs used could negate the benefits of blood pressure reduction^(5,6,7) .

Hypertension and certain alteration in serum lipoproteins such as a decrease high density lipoprotein cholesterol (HDL-C) , an increase in low density lipoprotein cholesterol (LDL-C), and perhaps also elevated triglycerides (TG) are complementary coronary risk factors^(8,9) Several antihypertensive agent have been found to influence serum lipid profile^(1,8,9,10,11,12,13) Indeed , a few studies claimed that the effects of antihypertensive agents on serum lipid might differ in different patient population⁽¹⁴⁾

The present study was designed to evaluate the effect of the commonly used antihypertensive drugs on blood lipids in this locality.

Methods

One hundred forty seven patients with essential hypertension consented to participate in this study. Fifty patients were treated with β -blocker

(atenolol) , 43 patients with (nefidipin) and 25 patient with diuretics. Patients on combined of treatment, diabetes mellitus, hyperlipidaemia, asthma, hepatic or renal impairment, or received the antihypertensive drugs for less than one year were excluded from this study.

Control: Thirty untreated hypertensive individuals were selected with on the bases of at least two recording of diastolic blood pressure of 90 mm Hg and above.

All patients and controls were attendance of different public health clinics in Basrah province.

Venous blood was collected into clean tubes after an average fast of 14 hours. Specimens were allowed to clot at room temperature, serum then separated and stored at – 18 °C until subsequent analysis, which was performed within 1-4 days of collecting the blood samples.

Serum concentration of total cholesterol(TC),triglyceride (TG) and high density lip otein cholesterol (HDL-C) , (after precipitation with ¹ ium phosphotungstat–MgCl₂) were determined enzymatically using kits from BioMerieux , France. All procedure was followed according to instructions of manufacture. Quality control sera (lytrol) were included in each assay batch for all above analytes . Data were expressed as mean \pm SD and comparison between the mean was made using the student's t-test. P value < 0.05 was considered as significant.

reduced significantly serum HDL-C (P< 0.05) and increased significantly both serum TG and VLDL-C

($P < 0.005$ and 0.05 respectively). On the other hand β - blocker causes no significant increase in both TC and LDL-C ($p > 0.05$).

The lipid data for subjects on diuretic treatment that serum TG was significantly elevated as compared with controls ($P < 0.01$). On the other hand diuretic cause no significant increase in serum TC, LDL-C and VLDL-C

and no significant decrease in serum HDL-C ($P > 0.05$). The lipid profiles obtained for subjects taking ACE inhibitor and calcium channel blocker were not significantly altered as compared with controls ($P > 0.05$).

Result

In (Table-1) the characteristics (number , age , sex , weight , systolic and diastolic blood pressure) for all subjects participated in this prospective study. There were no significant differences between the different groups.

(Table-2) shows the mean levels of total serum cholesterol (TC) , triglyceride (TG) , high density lipoprotein cholesterol (HDL-C) , low density lipoprotein cholesterol (LDL-C) ,and very low density lipoprotein cholesterol (VLDL-C). Comparison of the data obtained for different groups as compared with controls revealed that β -blocker

(Table- 1)
Characteristics of Controls and Hypertensive Patients Treated with Different Antihypertensive Drugs

Characteristics	Control	β – blocker	ACE inhibitor	Calcium channel blocker	Diuretic
No.	30	50	43	29	25
Age (yr)	40 \pm 9	50 \pm 13	46 \pm 12	45 \pm 11	49 \pm 13
Sex (M / F)	19 / 11	29 / 21	25 / 18	18 / 11	16 / 9
Weight (kg)	71.8 \pm 16.4	74 \pm 12.9	72.6 \pm 19.3	76 \pm 15.2	70 \pm 10.3
Systolic blood (mm Hg)	165.6 \pm 11.8	158.1 \pm 12.8	150.4 \pm 15.4	160 \pm 7.3	155 \pm 10.5
Diastolic	105.9 \pm 6.1	95.2 \pm 7.3	90.4 \pm 8.7	101.3 \pm 13.3	99.7 \pm 14.3

Data are presented as mean \pm SD

(Table- 2)
Mean Fasting TC , TG , HDL-C * , LDL-C and VLDL-C According to Drugs Used

	Control No. 30	β – blocker no. 50	ACE inhibitor No. 43	Calcium antagonist No. 29	Diuretic No.25
TC (mg / dl)	211.63 \pm 53.91	220.43 \pm 43.83	209.89 \pm 50.32	216.88 \pm 49.85	230.67 \pm 48.57
TG (mg / dl)	145.78 \pm 41.35	185.58 \pm 67.31***	139.98 \pm 38.11	152.33 \pm 50.19	177.47 \pm 58.63**
HDL-C (mg / dl)	47.73 \pm 12.09	41.34 \pm 16.27*	48.33 \pm 10.57	46.88 \pm 11.98	45.92 \pm 11.99
LDL-C (mg / dl)	133.75 \pm 33.58	141.78 \pm 26.94	132.09 \pm 33.13	139.12 \pm 27.84	149.26 \pm 27.55
VLDL-C (mg / dl)	29.16 \pm 8.47	35.33 \pm 12.63*	30.47 \pm 7.62	28.99 \pm 10.04	34.59 \pm 9.43

Data are presented as mean \pm SD

Mean \pm S * $P < 0.05$ ** $P < 0.01$ *** $P < 0.005$

Discussion

The present study was designed to evaluate the effect of β -blocker, ACE inhibitor, calcium channel blocker and diuretic on blood lipids. These drugs affect lipid metabolism on quite different way⁽³⁾.

In this study β -blocker reduce serum HDL-C and increase serum TG. Previous reports have a direct attention toward the probable unfavorable effects of β -blocker on lipid metabolism. Tanaka *et al*⁽¹⁵⁾ found a distinct reduction in HDL-C and an increase of VLDL-C and triglyceride but no significant increase on total serum TC. Wall-manning (16) showed a 42 % increase in total TG after a year treatment with metoprolol.

Others have reported varying effects of β -blocker on blood lipids. Weidmann *et al*⁽⁸⁾ stated that several β -blockers given as monotherapy induce significant increases in TG and a tendency for decreases in HDL-C. Breglund⁽¹⁷⁾ observed a rise in TG and fall in TC after propranolol treatment. Shaw *et al*⁽¹⁸⁾ comparing the effect of different β -blocker found a significant rise in TG but no effect on TC.

The formation of HDL-C probably results from the catabolism of triglyceride-rich lipoproteins^(19,20) Metcalfe *et al*⁽²¹⁾ concluded that the inverse

correlation between TG (increase) and HDL-C (decrease) and a fall in intralipid clearance during adrenergic blockade, suggest that all these changes might to mediated through inhibition of lipoprotein lipase activity. The changes in triglyceride concentration can not be related to changes in plasma insulin or glucose concentration⁽²²⁾ In addition the consistent decrease in free fatty acid concentrations during treatment with β -blockers argues against an increase rate of synthesis of TG⁽²¹⁾ Inhibition of lipoprotein lipase could be achieved through either a direct inhibitory action of adrenergic blocking agents themselves or secondary unopposed alpha adrenergic stimulation⁽²¹⁾.

In diuretics treated patient, the main finding in the present study is a significant increase in serum TG. Despite the increment in serum TC, LDL-C and VLDL-C, however these changes were of no

significance as compared to the data obtained from the labile hypertensive subjects. Several previous reports concluded that diuretics increases serum TG^(1,8,10,23) There was controversial finding about the effects of diuretics on serum TC and lipoprotein cholesterol fraction. Grimm⁽¹⁰⁾ and hunninghake⁽²⁴⁾ found that diuretics increase TC and LDL-C and slightly reduce HDL-C. krone *et al*⁽²³⁾ showed that diuretics cause a marked elevation of VLDL-C and minor increases of TC and LDL-C, but have little effects on HDL-C. Weidmann *et al*⁽⁸⁾ and Kasiske *et al*⁽¹⁴⁾ observed that diuretics can significantly increase TC, LDL-C and VLDL-C, while the HDL-C is often largely unchanged. The mechanism underlying the diuretics induced disturbances in lipid metabolism are unclear. They occurred independently of changes in blood pressure, and there was no associated haemoconcentration or alteration in basal and glucose stimulated insulin concentration and glucose tolerance⁽²⁵⁾.

From the overall data obtained for patients treated ACE inhibitor or calcium channel blocker it seems that neither ACE inhibitor nor calcium channel blocker altered lipid profiles as compared with controls. This result confirmed the previous observations, which stated that both ACE inhibitor, and calcium channel blocker seems to be largely devoid of undesirable effects on serum lipoproteins^(8, 10, 12, 23, 26)

In conclusion the influence of antihypertensive drugs on additional cardiovascular risk factors should considered when selecting medication to reduce blood pressure. Nevertheless, before antihypertensive drug treatment is initiated, blood lipid levels should be measured to identify preexisting hyperlipidaemia. Patient with elevated lipid levels, β -blocker and diuretics may make the management of lipid disorder more difficult and for such patient it may be desirable to select alternative antihypertensive agents that will not influence the lipid profile or interfere with the therapy for hyperlipidaemia. However long term study may be needed to evaluate whether lipoprotein abnormalities offset partly the beneficial effect of a lowered blood pressure in β -blocker and diuretic treated patients with hypertension and this study should be more attentive to differences among patient populations

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