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BIOCHEMICAL PROFILE IN HYPERTENSIVE AND ISCHEMIC HEART DISEASE PATIENTS

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The present study was designed to test the diagnostic importance of biochemical parameters and the changes observed during chemotherapy in hypertensive and ischemic heart disease patients. Sixty patients of hypertension and ischemic heart disease were selected randomly in three groups (20 in each group) irrespective of age and sex. Three combinations of drugs: Isosorbide dinitrate + diltiazem HCl, isosorbide dinitrate + atenolol and isosorbide dinitrate + atenolol + diltiazem HCl were administered orally to Group I, II and III respectively. Samples of blood were collected from each patient in the three groups, after 7-10 days interval for one month. Lipid profile, renal function tests, enzymes and serum electrolytes were analyzed and compared with the healthy control subjects of control group. Serum concentrations of triglycerides, LDL-cholesterol, creatinine, urea and sodium increased, while HDL cholesterol level decreased significantly when compared to normal healthy individuals. Isosorbide dinitrate and Atenolol combination was observed to be more effective therapeutically with minimum side effects.

Keywords : *Hypertension; Ischemic heart disease; Biochemical profile; Chemotherapy*

Introduction

Hypertension is a sustained diastolic blood pressure greater than 90 mmHg accompanied by an elevated systolic blood pressure (>150 mmHg). Hypertension results from increased peripheral vascular smooth muscle tone, which leads to increased arteriolar resistance and reduced capacitance of the venules. Hypertension may occur secondary to other disease processes. More than 90% of patients have essential hypertension- a disorder of unknown origin affecting the blood pressure regulating mechanism. Ischemia refers to a lack of oxygen due to inadequate perfusion. Ischemic heart disease is a condition of diverse etiologies all having in common a disturbance of cardic function due to an imbalance between oxygen supply and demand. The most common cause of ischemia is atherosclerotic disease of the epicardial coronary arteries.

The aim of the present study was to test the diagnostic importance of biochemical parameters in the hypertensive and ischemic heart disease patients. Mild hypertention can be controlled with a single drug. More severe hypertention may require treatment with several drugs that are selected to minimize adverse effects of a combined regimen. Where ischemic heart disease is complicated with hypertention, as is true in our study cases, organic nitrates and calcium channel blockers are indicated in different combinations.

Another aspect of our study was to compare the effect and to evaluate the efficacy of various combinations of drugs (vasodilators, beta-blockers and calcium antagonists) on the lipid profile, renal function tests, cardiac enzymes and serum electrolytes in the hypertensive and ischemic heart disease patients.

Materials and Methods

Chemicals

Diagnostic kits were used for the analysis of different parameters:

a) Triglycerides, cholesterol, HDL-cholesterol, LDL-cholesterol, creatinine, urea and uric acid (Randox Lab. Ireland)
b) Aspartate aminotransferase (AST) (Boehringer Mannheim GmbH, France)
c) Creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) (E-Merck, Germany)

Drugs used (Trade name)-name of company

Isosorbide dinitrate (Isordil)-Wyeth Labs, Pakistan
Atenolol (Blokium)-Highnoon Labs, Pakistan

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Diltiazem hydrochloride (Herbesser)-Highnoon Labs, Pakistan

Instruments and apparatus used

1. Double beam Spectrophotometer (Model U-2000 Hitachi, Japan)
2. Flame Photometer (Corning 400 Halstead, Essex, England)
3. Centrifuge machine (Type H-18, Kokusan Ensinki, Japan)

Patients selection criteria

Sixty hypertensive patients associated with the ischemic heart disease were selected after thorough screening from the Outdoor Patients Department of Istitute of Cardiology, Lahore. Among the sixty patients 46 were male and 14 female and their ages ranged from 30 to 65 years. Patients with an old myocardial infarction, cardiomyopathy, valvular heart disease, diabetes mellitus, asthma, tuberculosis and other organic heart diseases were excluded from the investigation.

Experimental procedure

Four groups comprising eighty human subjects were selected for this comparative study. A Control Group of twenty healthy individuals was not given any medication. The sixty patients effected with hypertensive and ischemic heart disease were divided equally into three groups. They were given orally three different drug regimens. All the medications previously being used were stopped and replaced with the new regimens of one month duration.

Control Group : Comprised 20 healthy control subjects receiving no medication.

Treated Group I : Comprised 20 patients receiving isosorbide dinitrate (60mg/day) with diltiazem HCl (180 mg/day).

Treated Group II : Comprised 20 patients receiving isosorbide dinitrate (60mg/day) with Atenolol (100mg/day).

Treated Group III : Comprised 20 patients receiving isosorbide dinitrate (60mg/day) with atenolol (100mg/day) and diltiazem HCl (180mg/day).

Blood sampling

Fasting blood samples were taken from twenty healthy volunteers without administration of any drug which served as a control. After 7-10 days of administration of the drugs: The first fasting blood sample was drawn from the three groups of hypertensive and ischemic heart disease patients, the 2nd sample after 7-10 days of the first sample and similarly the last sample was taken. Samples were analyzed for serum triglycerides, cholesterol, HDL-cholesterol, LDL-cholesterol, creatinine, urea, uric acid, CPK, AST, LDH, sodium and potassium.

Immediately after sampling, the serum was separated by centrifugation at 3000 rpm for 15 minutes and serum samples were stored in a refrigerator at -4°C until the determination was done for the biochemical parameters.

Test methodology

1. Triglyceride(Trinder, 1969) 2. Cholesterol (Roeschlau et al., 1974) 3. HDL-cholesterol (Lopes Virella, 1977) 4.LDL-cholesterol (Wieland and Seidel, 1983) 5.Creatinine (Bartels and Boehmer, 1971) 6. Urea (Weatherburn, 1967) 7. Uric acid (Fossati et al., 1980) 8.Creatine-phosphokinase (CPK)(Witt and Trendelenburg, 1982) 9. Aspartate aminotransferase (AST)(Bergmeyer, 1978) 10. Lactate dehydrogenase (LDH)(Kaplan et al., 1988) 11. Sodium and 12. Potassium (By Flame Photometer)

Results and Discussion

The mean of the three readings in each of the Groups was analyzed statistically and presented as Tables 1-4. The values were

Table 1. Biochemical changes in lipid profile in control and treated groups of hypertensive and ischemic heart disease patients after oral administration of different drug regimens (M±SD)

Parameters	Normal values	Control Group	Treated Group-I	Treated Group-II	Treated Group-III
		N=20	N=20	N=20	N=20
Triglycerides (mg/dl)	80-150	94.05 ±36.58	187.5** ±83.31	144.05** ±55.81	193.95** ±55.81
Cholesterol (mg/dl)	150-250	147.8 ±12.21	182.9** ±39.76	154.95* ±35.78	177.8** ±32.29
HDL-cholesterol (mg/dl)	35-55	47.3 ±3.85	42.1** ±5.14	39.5** ±2.10	41.95** ±4.79
LDL-cholesterol (mg/dl)	Up to 150	77.55 ±18.25	101.45** ±30.95	98.05* ±10.29	102.2** ±33.14

N=Number of subjects *P<0.05 **P<0.01

expressed as mean±standard devation (M±SD). The Control Group value was compared with the respective normal value. The value of the Treated Group I was compared with its respective control value; that of the Treated Group II with the respective value of the Treated Group I; and that of the Treated Group III with the respective value of the Treated Group II (Daly et al., 1991).

Table 2. Biochemical changes in renal function tests in control and treated groups of hypertensive and ischemic heart disease patients after oral administration of different drug regimens (M±SD)

Parameters	Normal values	Control Group	Treated Group-I	Treated Group-II	Treated Group-III
		N=20	N=20	N=20	N=20
Creatinine (mg/dl)	0.6-1.1	0.82 ±0.09	1.30** ±0.63	0.90* ±0.18	1.085* ±0.58
Urea (mg/dl)	10-50	33.4 ±5.55	51.85** ±18.38	39.65* ±14.13	45.1* ±20.97
Uric acid (mg/dl)	3.4-7.0	6.075 ±5.55	6.99* ±1.48	6.74* ±1.92	7.59* ±2.10

N= Number of subjects *P<0.05 **P<0.01

Table 3.Biochemical changes in cardiac enzymes in control and treated groups of hypertensive and ischemic heart disease patients after oral administration of different drug regimens (M±SD).

Parameters	Normal Values	Control Group	Treated Group-I	Treated Group-II	Treated Group-III
		N=20	N=20	N=20	N=20
Creatine phosphokinase (U/L)	24-195	152.65 ±56.57	97.85** ±35.5	76.65** ±14.27	83:00** ±32.87
Aspartate aminotransferase (U/L)	Up to 37	32.1 ±11.5	29.25* ±6.17	29.1* ±7.74	27.9* ±8.09
Lactate dehydrogenase (U/L)	80-240	132.20 ±21.42	82.00** ±33.85	60.85** ±18.92	80.70** ±27.05

N= Number of subjects *P<0.05 **P<0.01

Table 4. Biochemical changes in serum electrolytes in control and treated groups of hypertensive and ischemic heart disease patients after oral administration of different drug regimens (M±SD)

Parameters	Normal values	Control Group	Treated Group-I	Treated Group-II	Treated Group-III
		N=20	N=20	N=20	N=20
Sodium [Na+] (mEq/L)	135-154	136.65 ±2.59	138.8** ±1.88	137.25** ±1.39	138.65** ±1.88
Potassium [K+] (mEq/L)	3.5-5.4	3.84 ±0.13	3.92* ±0.18	3.95* ±0.22	3.84* ±0.27

N= Number of subjects *P<0.05 **P<0.01

Triglyceride levels in the serum of hypertensive and ischemic heart disease patients in the Treated Groups I, II and III were found to be significantly higher (P<0.01) than that in the healthy control subjects (Table 1). Elevated triglyceride level is a risk factor associated with the following pathologic conditions; hypothyroidism, nephrotic syndrome, diabetes mellitus, acute alcoholism, obstructive liver disease and acute pancreatitis (Zilva et al., 1988). Serum cholesterol in the Treated Group I and III was significantly higher (P<0.01).There is a particularly high risk of ischemic heart disease if serum cholesterol exceeds 235 mg/100ml (Verschuren et al., 1995). The serum level of HDL-cholesterol was found significantly lower (P<0.01) in the Treated Group I, II and III when compared with that of the control healthy subjects. A lowered concentration of HDL-cholesterol increases the danger of coronary artery disease (Wannamethee et al., 1995). LDL-cholesterol level in the serum of patients in the Treated Group I and III was elevated significantly (P<0.01) when compared with the control group value (Table 1) which may be responsible for ischemic heart disease in obese patients (Aro, 1995)

Creatinine and urea levels increased significantly (P<0.01) in the Treated Group I and (P<0.05) in the Group III while no significant change was observed in the Group II. This may be due to an increased concentration of serum creatinine when formation or excretion of urine is impaired, irrespective of whether the causes are prerenal, renal or postrenal as is observed in the congestive heart failure and shock. Serum urea concentration may rise due to some stressful conditions or to an increased level of cortisol-like steroids. The concentration of serum uric acid was not significantly altered in all of the three Treated Groups (Table 2) similar to the findings of Sasaki et al. (1992).

AST was not significantly decreased while the CPK and LDH levels were significantly reduced (P<0.01) in the Treated Groups I, II and III, as compared with the Control Group value (Table 3), similar to the findings of Rich et al. (1992).

Serum potassium showed no significant change in any one of the three Treated Groups, while the serum sodium level increased significantly (P<0.01) in all of the three Groups of the hypertensive and ischemic heart disease patients (Table 4). The increased sodium level may be due to an inappropriate secretion of aldosterone or other corticosteroids in primary hyperaldosterosism or in Cushing's syndrome (Kaplan et al., 1988).

In a comparison between Treated Group I and II, the serum levels in the Treated Group II were significantly lower (P<0.05) for triglycerides, cholesterol, HDL & LDL-cholesterol, CPK, LDH and urea while (P<0.01) for creatinine and sodium in Treated Group-II than found in Treated Group I. The concentration of serum AST, potassium and uric acid showed no significant change.

When the treated Group II was compared with the Treated Group III there was a significant decrease (P<0.05) in the serum concentrations of the total HDL & LDL-cholesterol, LDH and sodium in the Treated Group II. A significant decrease (P<0.01) was observed in the serum triglycerides in the Group II. There was no significant decrease in CPK, AST, creatinine, urea, uric acid and potassium in the Treated Group II in comparison with the Treated Group III.

Conclusion

The serum concentration of triglycerides, LDL-cholesterol, creatinine, urea and sodium in the hypertensive and ischemic heart disease patients increased significantly when compared with that in the normal healthy individuals. While there was a significant decrease in the HDL-cholesterol level, the levels of serum AST, uric acid and potassium were not altered significantly. Treatment of the hypertensive and ischemic heart disease patients with isosorbide dinitrate + atenolol is preferable to the treatment with the other combinations of drugs used and moreover can be safely prescribed without any serious side effects.

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