A Comparative Study of the Antihypertensive Agents on Serum Liver Enzymes ALT, AST and ALP of Hypertensive and cardiac Patients

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Abstract: Present study is done to compare serum Liver enzymes including Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) and Alkaline Phosphatase (ALP) in hypertensive and cardiac patients. 24 patients were divided into 4 groups according to their treatment with 4 different types of antihypertensive drugs. Group I treated with Beta-blockers (1+1). Group II treated with ACE-Inhibitor once a day. Group III treated with Nitrates once a day. Group IV is taking Diuretics once a day. Data showed non-significant difference in serum ALT concentration in all groups. A significant rise ($p< 0.05$) in serum AST and ALP levels among hypertensive and cardiac patients is observed, ranging from 24.63-47.33U/L and 110-2484 U/L respectively when compared with normal controls. Thus, not only the risk of cardiac diseases in future might be predicted by altered levels of enzymes ALT, AST and ALP in serum but their concentrations should be monitored during the treatment of cardiac diseases to minimize the risk of cardiac arrest.

Keywords: Angiotensin-II, Catecholamines, Diuretics, Nitrates, Cardiac dysfunction, Liver injury.

INTRODUCTION

In addition to lifestyle changes for persistent high blood pressure (BP), medications are recommended to lower BP and the category of medication prescribed depends on the stage of high BP and other medical conditions.

The principle agents used in single drug treatment of cardiac and hypertension include, Beta-Blockers, Acetylcholine Esterase(ACE) inhibitors, Nitrates and Diuretics [1, 2].

Beta-Blocking Drugs

Beta-blockers block the action of endogenous catecholamine, epinephrine and nor epinephrine. The beneficial effects of Beta-blocking agents are related to their hemodynamic effects including decreased heart rate, blood pressure and contractility, which decrease myocardial oxygen requirement at rest and during exercise [1].

ACE Inhibitors

ACE inhibitors may inhibit synthesis of Angiotensin II and lowers the blood pressure principally by decreasing peripheral vascular resistance. Cardiac output and heart rate are not significantly changed [2].

Nitrates

Nitrates appear to combine the activity of nitric oxide release with potassium channel-opening action, thus providing an additional mechanism for causing vasodilation [2].

Diuretics

Diuretics increase urine flow and also act as ion transport inhibitors that decrease reabsorption of sodium ions (Na+) at different sites in the nephron. In hypertension diuretics cause a decreased blood volume, leading to a reduction in blood pressure [1].

Liver Enzymes

Alanine Aminotransferase (ALT)

ALT, is an enzyme which appears in liver cells, with lesser amounts in the kidneys, heart, and skeletal muscles, and is a relatively specific indicator of acute liver cell damage. Human ALT levels in serum are used in clinical diagnosis of liver and heart diseases [3].

Marginal elevations of ALT occasionally occur in acute myocardial infarction, reflecting secondary hepatic congestion or the release of small amounts of ALT from cardiac tissues. Many medications produce hepatic injury by competitively interfering with cellular metabolism [4, 5].

Aspartate Aminotransferase (AST)

Serum AST levels in healthy subjects are low, but the levels are significantly elevated in a number of clinical conditions such as acute and chronic hepatitis,

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Table 1: Hypertensive and Cardiac Patients Groups Receiving Different Treatments with their Respective Daily Doses

Patients Group	Drugs		
	Category	Example	Daily Dose
I	Beta-blocker	Tenormin	(1 +0 + 1)
II	ACE-Inhibitor	Zestoretic, Coversyl	(1 +0 + 0)
III	Nitrate	Elantanlong	(1 +0 + 0)
IV	Diuretic	Lasix, Lasoride	(1 +0 + 0)

obstructive jaundice, carcinoma of liver, myocardial infarction and muscular dystrophy [3-5].

Moderately high to slightly high levels of AST may be caused by heart attack or heart failure.

Alkaline Phosphatase (ALP)

ALP are group of enzymes found primarily in the liver and bone. There are also small amounts produced by cells lining the intestines, the placenta, and the kidney. In addition to several clinical conditions, increased serum ALP may be due to congestive heart failure [3-5].

Present work is done to compare these serum enzymes levels in hypertensive and cardiac patients, receiving four different types of drug treatments as well as with normal control group.

MATERIALS AND METHODS

Blood samples of 24 hypertensive and cardiac patients were collected each day from Civil Hospital Karachi. Patients were divided into 4 equal groups according to their treatment with specific drug (Table **1**).

Blood was drawn from the cubital vein of the patient by 5cc disposable syringe and transferred into the centrifuge tubes. All tubes were kept undisturbed at room temperature for 30 minutes followed by centrifugation for 5 minutes at 25000 rpm. The supernatant was transferred in eppendrof tubes and stored at 4°C [6].

Bio-Chemical Estimation

Serum samples were used for determination of liver enzymes i.e. ALT, AST and ALP by the method of Reitman [7], using biochemical kits. The absorbances of samples were read on spectrophotometer and collected data was analyzed statistically by two-way ANOVA.

RESULTS

ALT

Table **2** shows normal serum ALT level ranges between 8 - 10 U/ L. In group - I, 5 hypertensive and cardiac patients who were taking Beta- blockers, the estimated serum ALT levels ranged from 4 - 18 U/ L and only 1 patient shows slightly higher serum ALT level i.e. 18 U/ L.

In group - II, patients treated with ACE inhibitors, the estimated serum ALT levels ranged from 4 - 12 U/L.

Table 2: Effect of Antihypertensive Drugs on Serum Enzyme ALT Concentration (U/L) in Hypertensive and Cardiac Patients

Samples	Normal	Patients Groups			
		I	II	III	IV
1	8	12	8	8	4
2	8	8	8	8	8
3	8	4	4	8	8
4	8	18	12	4	4
5	10	8	8	8	17
6	8	4	8	12	4

I = Beta-blocker, II = ACE-inhibitor, III = Nitrate, IV = Diuretic.

Table 3: Effect of Antihypertensive Drugs on Serum Enzyme AST Concentration (U/L) in Hypertensive and Cardiac Patients

Samples	Normal	Patients Groups			
		I	II	III	IV
1	10	44.44	45.8	45.89	38.64
2	8	24.63	46.33	41.06	38.643
3	12	45.4	27.64	27.64	43.47
4	11.8	38	21.73	21.73	42.99
5	18	47.33	33.81	33.91	46.37
6	16.78	44.44	43.47	43.47	45.4

I = Beta-blocker, II = ACE-inhibitor, III = Nitrate, IV = Diuretic.

The group - III, patients were treated with Nitrates; their estimated serum ALT levels ranged from 4 - 12 U/L.

The group - IV patients treated with diuretics. 5 patients showed serum ALT levels between 4 - 8 U/L and 1 patient had slightly higher level i.e. 17 U/L.

All 4 groups showed non-significant (p=0.9333) difference in serum ALT levels when compared with controls.

AST

Table **3** shows serum AST levels in normal adults, ranged in between 8 - 16.78 U/L.

In group - I estimated serum AST levels ranged in between 24.63 - 47.33 U/L. 4 patients showed higher AST levels ranged from 44.33 - 47.33 U/ L.

In group - II, patients were treated with ACE-inhibitors; their estimated serum AST levels ranged between 21.73 - 46.33 U/L and 3 patients showed higher serum AST levels in between 43.47 - 46.33 U/L.

In group - III patients were treated with Nitrates, their serum AST levels ranged between 30.42 - 47.33 U/L and 5 patients showed higher serum AST levels ranged from 41.06 -47.33 U/L.

In group - IV patients were on diuretics, their estimated serum AST levels were 38.64 -46.37 U/L.

All the 4 groups showed a significant difference in serum AST levels ($P < 0.05$) in comparison to control group.

ALP

Table **4** showed serum ALP concentration in normal adults ranged between 98 - 270 U/L.

Group - I patients treated with Beta-blocker, their estimated ALP concentration ranged between 188 - 883.2 U/L. Most of the patients showed higher serum ALP concentration. 2 out of 6 patients showed ALP levels ranged in between 188 - 414 U/L, another 2 patients showed serum ALP concentrations in between 717.6 - 883.2 U/L while remaining 2 patients showed very high levels of serum ALP i.e.1214 U/L and 1242 U/L.

Table 4: Effect of Antihypertensive Drugs on Serum Enzyme ALP Concentration (U/L) in Hypertensive and Cardiac Patients

Samples	Normal	Patients Groups			
		I	II	III	IV
1	98	1214	634.8	358.8	1656
2	102	414	1932	607.2	800.4
3	150	883.2	110	129.2	1104
4	270	188	833.2	662.4	2484
5	200	1242	386.4	276	662.4
6	115	717.6	220.8	966	1242

I = Beta-blocker, II = ACE-inhibitor, III = Nitrate, IV = Diuretic.

In group - II patients taking ACE-inhibitor, had serum ALP levels ranged between 110 -1932 U/L, 2 patients showed serum ALP levels 110 U/L and 220.8 U/L, while 3 patients showed serum ALP levels in between 386.4 - 833.2 U/L and remaining 1 patient had very high serum ALP level i.e.1932 U/L.

Group - III patients treated with Nitrates, had serum ALP levels ranged from 129.2 - 966 U/L. 2 patients showed normal serum ALP levels i.e.129.2 U/L and 276 U/L while rest of the 4 patients showed high serum ALP concentrations ranged from 358.8 - 966 U/L.

The group - IV patients who were treated with diuretics, showed serum ALP concentrations ranged in between 662.4 - 2484 U/L. Most of the patients showed very high ALP levels.

The patients of groups I, III and IV showed a significant difference ($P<0.05$) in serum ALP level after the comparison with control group, however a non significant difference ($p=0.0808$) was observed in group II patients receiving ACE- inhibitor.

DISCUSSION

Present work is done to compare the serum levels of hepatic enzymes ALT, AST and ALP in hypertensive and cardiac patients, who were receiving different therapeutic drugs and also compared with normal healthy control group.

These enzymes are indicative of various aspects of metabolism, which have been used to determine and evaluate the physiological and biochemical metabolic defects in liver and muscles [8].

Both ALT and AST are excellent markers of liver damage caused by exposure to toxic substances and also by several therapeutic drugs [9]. However ALT is a better marker of liver problems. Injury to the heart, muscles or liver can raise serum AST level [10].

Table **2** shows a comparison of serum ALT levels in hypertensive and cardiac patients treated with different therapeutic antihypertensive drugs, falling in normal range, except only two patients receiving treatment of Beta- blockers and diuretic, showing slightly high serum ALT levels. According to Chernecky and Berger [11], there is indicative effect of the Beta-blockers on liver, and probably resulting in liver damage [12].

However another study by Ford *et al*. [13], in middle- to- older aged subjects without evidence of clinically significant liver damage showed an inverse relationship between ALT levels and risk of fatal and non fatal cardiovascular diseases.

The comparison of serum AST levels in hypertensive and cardiac patients who were taking different therapeutic agents, shows a significant difference in serum AST levels ($P<0.05$). Most of the patients showed increased levels of serum AST, this increase may be due to cardiac dysfunction. Determination of serum AST activity is particularly useful in myocardial infarction; its activity increases 3-8 hours after a heart attack and returns to normal in 3-6 days, the duration and extent of the serum AST increment is related with the size of the infarct [9].

The significant high levels of AST and bilirubin not only indicating liver dysfunction, poor hemodynamic status and ultimate cardiac failure in middle aged males [14] but elevated levels of both ALT and AST are strongly correlated with myocardial infarction, resulting in high incidence of mortality in patients [15, 16].

Table **4** shows a significant difference ($p< 0.05$) in serum ALP levels of hypertensive and cardiac patients compared with normal healthy controls and most of the patients who were taking different therapeutic antihypertensive agents showed high serum ALP levels.

The serum ALP levels in adults appear to be mainly derived from liver with small variable intestinal component [9]. Changes in ALP levels are often associated with cholestasis induced by drugs like diuretics as a consequence of hepatocellular toxicity [9, 17].

Finally it is concluded that beside the evidences of altered levels of liver enzymes in hypertensive and cardiac patients, still the studies are required to explore the underlying mechanisms. Also the levels of these enzymes should be monitored regularly during the treatment of hypertensive and cardiac patients.

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