EFFECT OF ANTIHYPERTENSIVE DRUGS ON CARDIAC ENZYMES IN HYPERTENSION WITH MYOCARDIAL INFARCTION IN NIDDM

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ABSTRACT

Enzymology is a diagnostic indicator for myocardial infarction and diabetes in hypertension patients. Therefore the selection of methods for measurement of cardiac enzyme, Aspartate transaminase (AST), Creatine kinase(CK),and isoenzyme of creatine kinase (MB form), determine the effectiveness of antihypertension drug would provide the physician with diagnostic and prognostic clinical evidence.

KEY WORDS

Aspartate transaminase (AST), Creatine kinase (CK), Isoenzyme of creatine kinase (MBform), Myocardial infarction (MI), Non insulin dependent diabetes mellitus (NIDDM).

INTRODUCTION

Hypertension plays a dominant role in cardiovascular disease and diabetes. The metabolic disorder of diabetes is worsened by supervening of hypertension with moderate to high blood pressure with cardiac disease in NIDDM influences markedly on AST, CK and CKMB (1). Rise in level of these enzymes and isoenzyme have been reported in hypertension with MI (2,3). Enzymes always have, been identified as a specific and sensitive markers of both clinical and subclinical myocardial injury (4). Therefore biological markers like CK, isoenzyme CKMB and AST to quantify MI have been widely used in clinical practice. In cardiac muscle they are tightly bound to the contractile apparatus and therefore plasma concentrations are extremely low. With acute myocardial injury there is release of CKMB into the serum. The CKMB isoenzyme is considered to have greater cardiospecificity and greater predictivity for diagnostic accuracy. Hence to establish the definitive diagnosis of myocardial infarction which is still a frequent clinical problem has led us to evaluate the effect of antihypertension drug Enalapril and Atenolol on cardiac enzymes. Treatment of hypertension patients with antihypertensive drug implicates clinical and circulating improvement (5,6). The present study was oriented with an aim to assess the status of

cardiac enzyme and isoenzyme after the onset of symptoms of MI and after three months of treatment with Enalapril or Atenolol. This would provide a diagnostic and prognostic index in hypertension with MI in NIDDM.

MATERIALS AND METHODS

The present study was conducted at Government Medical College Nagpur. The study was comprised of 30 hypertension patients in each group of both sex between 35 to 60 years of age who had MI and Diabetes Mellitus diagnosed by WHO criteria (7). All subjects of the study group were screened to exclude evidence of hyper or hypothyroidism, chronic renal failure and other ailments. The patients selected for study group were divided into group II and group III. Group II patients, treated with Enalapril, required a dose of 5 mg. per day whereas group III treated with Atenolol required 20 mg. per day. Normal controls of group I (30 in number) of same age and sex matched were also selected from hospital staff.

During treatment some of the patients were dropped out due to various reason.

The venous blood samples were drawn from all subjects of study groups II and III at an interval of 8 hours upto 48 hours after the onset of symptoms of MI and thus 6 samples were collected from each group. Followup was done after three month treatment. Blood samples of the control group I and study groups II and III were collected in plain bulb and serum was used for the estimation of AST, CK

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and iso-enzyme CKMB were carried out on Express plus autoanalyser (8,9).

RESULT

Findings presented in Table I showed that the levels of enzyme AST, CK and isoenzyme CKMB differ significantly from that of normal control ($P<0.001$). The increase of enzyme activities of CK, and isoenzyme CKMB in first 8 hours after onset of

symptoms of MI was highly significant ($P<0.001$). CKMB, the transient fraction of creatine kinase reached a peak at 24 hours seemed to return to normal within 48 hours even though the total serum CK activity remains maximum. The activity of CK, CKMB, AST assay in group II treated with enalapril was found to have potential advantages in lowering cardiac enzyme significantly ($P<0.01$) over the non specific changes in atenolol treated group III patients.

Table I - ENZYME PROFILE IN HT WITH MI IN NIDDM

Group	CK (U/l)	CKMB (U/l)	AST (U/l)
Normal control Group I (n=30)	86 ± 20.12	22 ± 7.81	11 ± 4.04
Before treatment Group II (n=30)			
8 hours	*310 ± 90.11	*82 ± 21.05	65 ± 15.85
16 hours	*550 ± 110.05	*130 ± 25.86	90 ± 24.36
24 hours	*605 ± 115.65	*155 ± 32.14	115 ± 25.01
32 hours	*310 ± 87.52	*72 ± 20.04	52 ± 15.09
40 hours	*286 ± 60.15	*55 ± 12.56	26 ± 8.05
48 hours	*205 ± 52.04	24 ± 8.15	12 ± 4.6
Group III (n=30)			
8 hours	*290 ± 82.18	*74 ± 20.01	*58 ± 14.42
16 hours	*520 ± 105.66	*120 ± 22.14	*85 ± 22.11
24 hours	*630 ± 120.52	*140 ± 34.22	*105 ± 29.05
32 hours	*360 ± 90.45	*60 ± 18.61	*55 ± 16.95
40 hours	*315 ± 85.63	42 ± 10.09	32 ± 9.09
48 hours	*275 ± 54.11	26 ± 8.62	18 ± 6.11
after 3 months of treatment			
Group II (n=28)	**142 ± 34.56	24 ± 7.01	9 ± 4.05
Group III (n=26)	225 ± 54.15	28 ± 9.14	12 ± 4.85

- Values are means ± SD of number of patients given in parenthesis
- Activity of CK, CKMB and AST expressed as u/l.
- *($P<0.001$) as compared to normal control using student 't' test
 **($P<0.01$) as compared to normal control using student 't' test

DISCUSSION

The systemic metabolic responses of hypertension patients with MI in NIDDM occurs due to poor control of diabetic state in human being attributed to changes in physiological concentration of several biochemical markers (10). It is just for this reason that the study of biochemical aberrations resulting from MI is vital. The results presented in Table I shows the relationship between enzyme activity and influence of antihypertensive drug Enalapril and Atenolol after three months of treatment. The findings suggest that peak serum enzyme and isoenzyme activities at 24 hours incorporate the assumption that CK, CKMB released within myocardium after the onset of symptoms. The entry of these enzymes in circulation depends upon the rate of passive diffusion of enzyme from infarct myocardium cells (11). The metabolic state of severely infarct myocardium is indicated by the increase of marker enzyme CK and isoenzyme CKMB. However the levels of enzyme profile in group II subjects who were given Enalapril found to have promising effect than Atenolol. The mechanism of biochemical marker abnormalities have been suggested as the cause for structural and functional alterations due to alteration in activity of Angiotensin Converting Enzyme (ACE) localised on endothelium cells (12).

Cardiac ACE activation enhances the conversion of Angiotensin I (ANG) to Angiotensin II and ANG II has been suggested to play a role in development of pathological hypertrophy of myocardial cells, causing alteration in bradykinin degradation and nitric oxide synthesis (13,14). Thus depletion of enzyme profile after the treatment with enalapril which is a Angiotensin Converting Enzyme inhibitor (ACEI), provides the beneficial effect in study group and may be related to changes in endothelial functions that involve co-ordinate changes in the relative balance between ANG II, bradykinin and nitric oxide (15). Nitric oxide reduces the size of myocardial infarctions in animals (16). Hence in the present study, endothelial cells may be the target of ACE inhibitors in enalapril treated group II which corroborate the above hypothesis (15, 16).

It is obvious from the present study that the potentiality of Enalapril on cardiac isoenzyme CKMB is involved in nearly all aspects of cellular metabolism and particularly in the repair process of the heart after MI. Therefore CKMB is considered to have greater predictive diagnostic accuracy than CK. However the question of non significant changes of CK in group III Atenolol treated patients can be solved only by further randomised trials.

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