EFFECTS OF TRAINING ON THE EXTENT OF EXPERIMENTAL MYOCARDIAL INFARCTION IN AGING RATS

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Summary : The effects of exercise on the severity of isoproterenol–induced myocardial infarction were studied in female albino rats of 20,40,60 and 80 weeks of age. The rats were trained to swim for a specific duration and for a particular period. The occurrence of infarcts were confirmed by histological methods. Elevations in the serum GOT and GPT were maximum in the sedentary-isoproterenols and minimum in the exercise-controls. These changes in the serum transaminases were associated with corresponding depletions in the cardiac GOT and GPT. However, age was seen to interfere with the responses exhibited by the young and old rats. Studies dealing with myocardial infarction are more informative when dealt with age.

Key words : age glutamate oxaloacetic transaminase glutamic pyruvic transaminase exercise myocardial infarction

INTRODUCTION

Studies concerning physical activity and myocardial infarction (MI) has been a field of intense research (9,10). Results demonstrating an inverse relation between exercise and MI are largely based on investigations dealing with the morbidity and mortality of individuals (9,10,15,16). Exercise is shown to reduce the mortality associated with large doses of isoproterenol (ISO), with the trained rate exhibiting a better cardiac performance to hypoxic conditions (5,7,17,20). In an earlier work, we have reported an increase in serum glutamate pyruvate transaminase (GPT) in the untrained rats (2). Large doses of ISO result in alterations in serum enzymes, catecholamines and ECG recordings in rats similar to those occurring in man (19,24). Though a number of workers have reported on the effects of exercise of different durations and intensities on serum enzymes and isozymes, very scanty information is available on the interaction of age, exercise and MI. The purpose of this study was to evaluate the effects of training on the biochemical responses to MI, specifically in relation to the transaminases. Our studies on the animal experiments, using rat as a model, have been attempted to know the effect of exercise on the heart i.e., if exercise can act as a negative risk factor in the incidence of MI, and if so, at what age can exercise prove to be most beneficial in the prevention of myocardial infarction.

MATERIAL AND METHODS

A albino rats (Wistar) of 20,40,60 and 80 weeks of age were used in our investigations. These rats were housed three to a cage, and were fed with the commercial diet (Hindustan Lever, Bombay) and water *ad libitum*. The animals of all ages were classified into four groups – Sedentary–isoproterenol (A), Exercise-isoproterenol (B), Exercise-control (C) and Sedentary-control (D). Rats of group-A remained sedentary throughout and received a single subcutaneous injection of DL-isoproterenol (ISO) hydro-chloride (Sigma Chemical Company, USA) at a dose of 30 *mg/100 g* B.W. These rats were sacrificed 4 hr later. Rats of group-B and -C were forced to exercise by letting them to swim in a glass tank (61 X 31 X 33 cm) filled three-fourths with water (28-30°C). Precautions were taken to put a few animals together so that they swim and not float. These rats were exercised for 30-35 min daily for a total period of 45 days. The exercise period/day was gradually increased as the rats got accustomed to swimming. Twenty four hours later rats of group-C were injected with 0.9% saline and sacrificed four hours later. Rats of group-B received a single injection of ISO at a dose mentioned as above. Rats of group-D remained sedentary and received neither ISO nor saline.

Serum was obtained by the method of Wacker *et al.* (23). Blood drawn from the heart was allowed to clot on ice blocks The sample was centrifuged at 4°C for 10 min. and at 3000 rpm. The separated serum was stored at 4°C until further use. Hemolysed samples were discarded. The normal and infarcted hearts were isolated washed in ice-cold 0.9% saline. A 5% (w/v) homogenate was prepared in 0.1M ice-cold phosphate buffer (pH 7.2). The homogenate was centrifuged at 6000 rpm for 30 minutes at 0°C. The extraction was repeated twice and the combined supernatants were used for the assays.

The activities of glutamic oxaloacetic transminase (GOT) and glutamic pyruvic transaminase (GPT) were estimated in the serum and heart by the spectrocolorimetric methods (3).

The data was statistically analysed and the significant levels between the mean of sedentary–controls and other experimental groups were calculated using student's t-test and the p-values are given.

Confirmations of myocardial infarction were by histological procedures. The normal and infarcted hearts were fixed in Bouin's fluid. Sections of the heart were obtained at 5-20 um thickness and stained with hematoxylin and eosin by the conventional technique. Infarcts were confirmed in the different regions of the heart.

RESULTS

The results presented here deal with three factors i.e. age, exercise and myocardial infarction. The absolute values for serum (S) and cardiac (C) GOT are given in Table I and the per cent change as compared to the sedentary–controls in Fig. 1 (a-d) and Fig. 2 (a-d). Activity of SGOT was lowest in the sedentary-controls and highest in the sedentary-

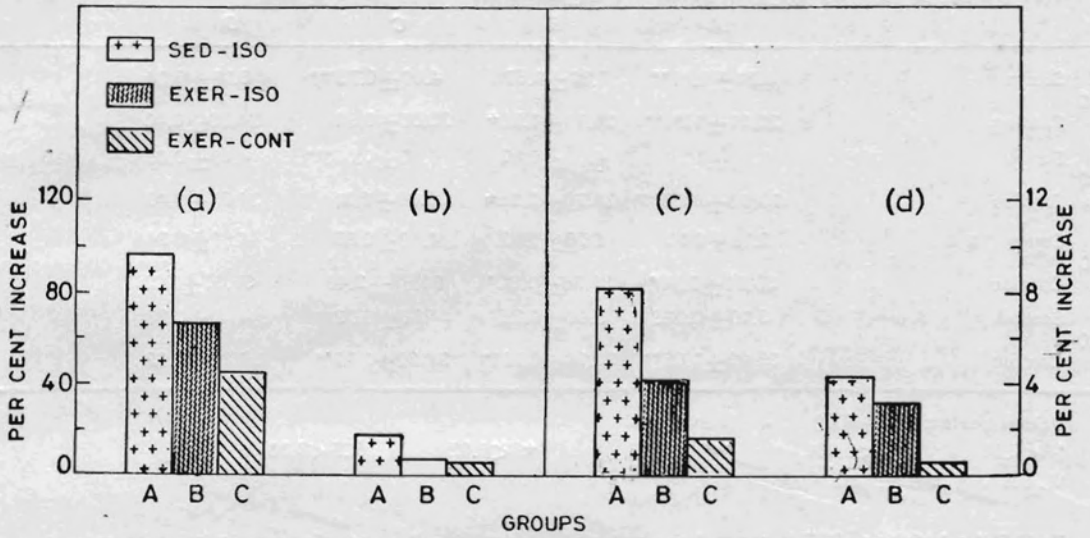

Fig. 1 : Per cent increase in SGOT as compared to sedentary-controls (a) 20 week, (b) 40 week, (c) 60 week and (d) 80 week.

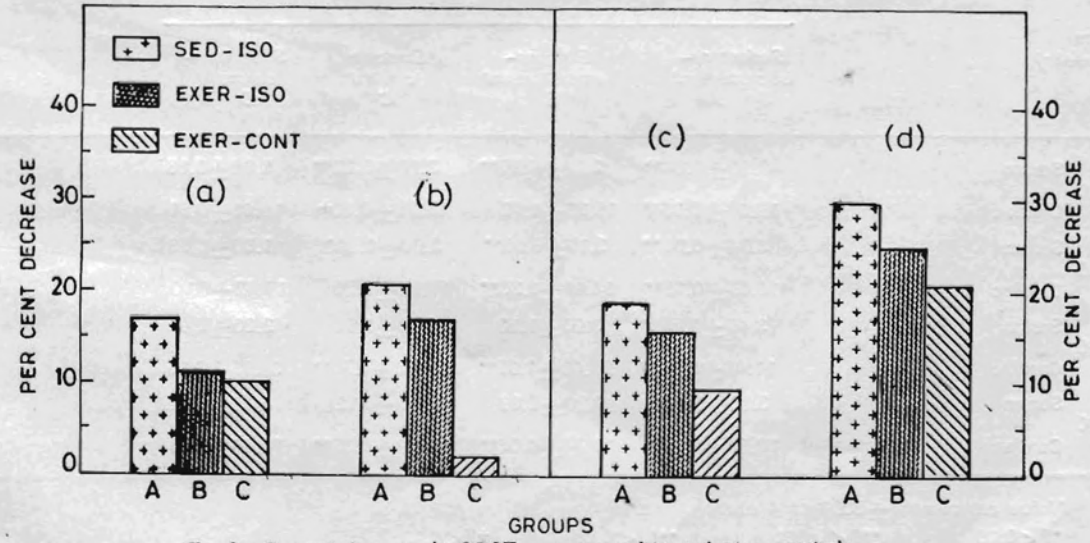

Fig. 2 : Percent decrease in CGOT as compared to sedentary-controls (a) 20 week, (b) 40 week, (c) 60 week and (d) 80 week.

TABLE I : Activity of GOT in serum (micromoles of pyruvate/hr/*ml*) and cardiac muscle (micromoles of pyruvate/hr/g tissue) as a function of age, exercise and myocardial infarction.

Age (weeks)		*Groups*			
		Sedentary–iso–proterenol A	*Exercise–iso–proterenol B*	*Exercise–control C*	*Sedentary–control D*
20	Serum	6.31±0.61**	5.30±1.57	4.60±0.76***	3.19±0.04
	Cardiac	20.21±1.05**	21.76±1.73+	22.00±0.80	24.50±0.40
40	Serum	5.59±1.20	4.65±0.82	4.62±0.08***	4.49±0.05
	Cardiac	27.00±6.03***	28.20±2.29+	33.00±2.36	34.00±2.40
60	Serum	5.19±0.60	5.00±0.82	4.88±0.37	4.80±0 24
	Cardiac	30.00±2.60*	31.36±1.90*	34.66±2.49	37.30±203
80	Serum	5.10±0.08£	5.00±0.25	4.90±0.22	4.89±0.28
	Cardiac	35.00±1.05**	36.16±0.50**	38.60±1.77**	50.25±2.02

Values are mean (±S.D) of 4 observations
*P<0.01 **P<0.001 ***P<0.05 +P<0.02 £P<0.10
Values not marked are insignificant.

TABLE II : Activity of GPT in serum (micromoles of pyruvate/hr/*ml*) and cardiac muscle (micromoles of pyruvate/hr/g tissue) as a function of age, exercise and myocardial infarction.

Age (weeks)		*Groups*			
		Sedentary–isoproterenol A	*Exercise–isoproterenol B*	*Exercise control C*	*Sedentary–control D*
20	Serum	3.80±0.04**	2.24±0.17**	2.10±0.20**	1.32±0.13
	Cardiac	12.36±0.28**	15.12±1.02	15.36±0.10+	16.46±0.51
40	Serum	3.74±0.06**	2.17±0.05**	2.00±0.50*	1.50±0.03
	Cardiac	10.97±0.13**	14.61±1.23**	16.75±2.20	17.42±0.10
60	Serum	3.40±0.55**	3.00±1.10	2.70±1.00	2.20±0.05
	Cardiac	11.40±0.66**	27.48±1.02**	28.52±1.75**	36.93±0.18
80	Serum	3.30±0.04	3.20±0.13	3.20±0.12	3.25±0.38
	Cardiac	10.38±3.24*	11.34±0.04**	12.29±1.38**	14.48±0.81

Value are mean (±S.D) of 4 observations.
*P<0.05 **P<0.001 ***P<0.05 +P<0.10
Values not marked are insignificant

isoproterenols. 20 week old of group-A exhibited significant elevation ($P<0.001$) in SGOT while 80 week old rat demonstrated a less significant rise ($P<0.10$). However, between the groups 40,60 and 80 week old exhibited in significant increases in the SGOT titers. These changes in the SGOT were in parallel with the alterations in CGOT in the infarcted

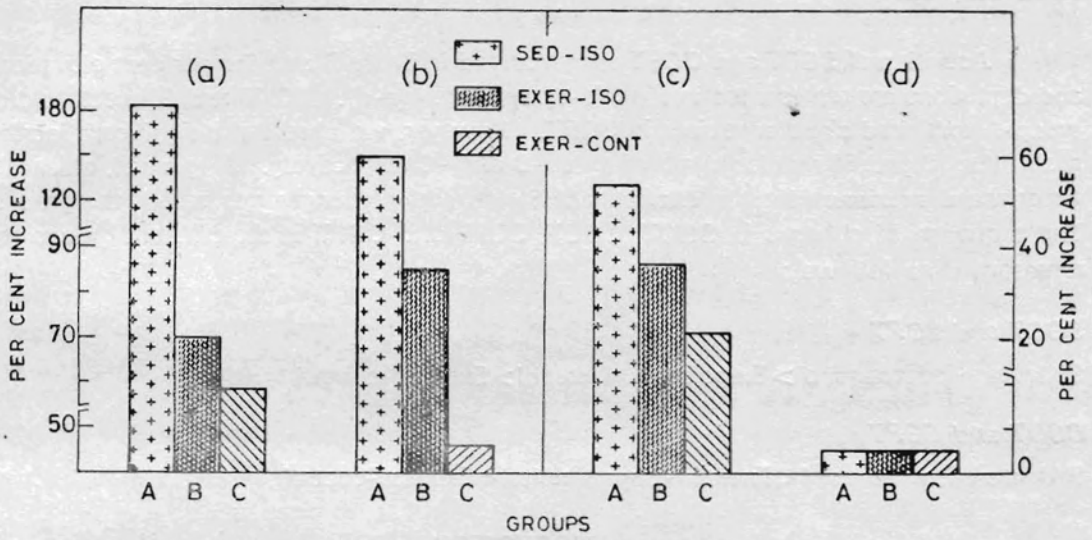

Fig. 3 : Per cent increase in SGPT as compared to sddentary controls (a) 20 weeks, (b) 40 week, (c) 60 week and (d) 80 week.

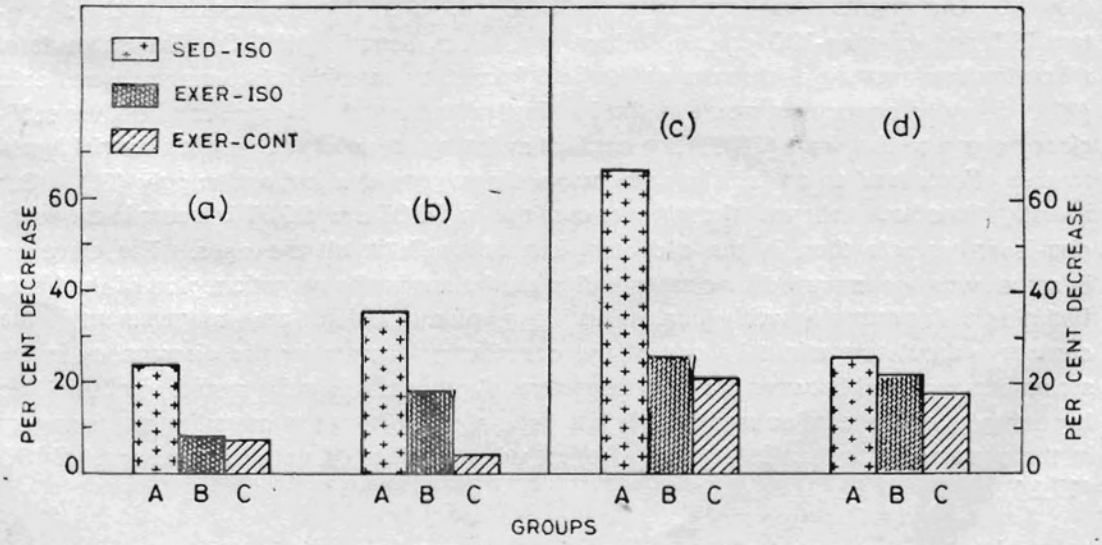

Fig. 4 : Per cent decrease in SGPT as compared to sedentary-controls (a) 20 week, (b) 40 week, (c) 60 week and (d) 80 week.

region of the heart. Significant depletions ($P<0.001$) of 17.51% and 30.26% were observed in the CGOT of 20 and 80 week old rat of group-A. Rats of all ages of group-C except 80 week old suffered insignificant loss in enzyme activity. In group-B 20 and 40 week old experienced less significant losses ($P<0.02$) than the 60 ($P<0.01$) and 80 ($P<0.001$) week old rats.

Activities of SGPT and CGPT are presented in Table II and the per cent elevations and depletions are represented in Fig 3(a-d) and Fig. 4(a-d). 20,40 and 60 week old of group-A exhibited significant rises in SGPT. However, we observed insignificant increases in the 60 and 80 week old rat of group-B and -C respectively. In general, older rats experienced maximum loss in enzyme activity than the younger rats in all the groups. The sequence of changes in SGOT, CGOT, SGPT and CGPT in the different groups are represented as follows :

SGOT and SGPT

Sedentary-isoproterenol > Exercise-isoroterenol > Exercise-control

CGOT and CGPT

Sedentary-isoproterenol < Exercise-isoproterentol < Exercise-control

DISCUSSION

Exercise is known to favorably alter the risk factors responsible for coronary heart disease. Our results demonstrate that the SGOT and SGPT levels increase in the sedentary-ISO and exercise-ISO groups, following the administration of ISO. Excess levels of these transaminases in the serum are derived from the necrotic or fatty parenchymal cells (22). Lesions occur as a result of the inability of the circulatory system to deliver sufficient oxygen to the heart (28). The cardiostimulatory action of ISO and it's arterial hypotensive effects lead to an imbalance between the oxygen demand and supply (25). Our investigations have shown that the per cent rise in SGOT and SGPT is lesser in the exercise-isoproterenols than in the sedentary-isoproterenols in all the ages. The elevation in serum was accompanied by corresponding depletions in the necrotic region of the heart. Pathologic hypertrophy with increase in fiber volume without any improvement in the coronary vasculature might be one of the contributing factors for the discrepancy in the serum enzyme level between the two isoproterenol groups. Exercise results in physiologic hypertrophy of the cardiac muscle. It has been reported that the mortality rate is higher in the untrained rats than in the trained ones, when challenged with high dosages of ISO (17,24).

We have observed slight increase in the serum enzymes in the exercise-isoproterenols of all ages. However, the elevations in SGOT and SGPT were definitely less

compared to that occurring in the sedentary-isoproterenols. The necrogenic and hypertrophying effects of ISO in the exercise-isoproterenols is partly due to the drug and partly due to the exercise (11,12,14,22).

Unlike the serum, tissue transminases were lost to a greater extent in the older than in the younger rats. One possible reason for the differential loss of enzymes as a function of age, could be that the enzymes are degraded rapidly in the cardiac muscle of older rats before their efflux into the serum and hence contributing very little to the active form of the enzyme in the serum (1). The release of these enzymes into the serum is correlated with the hyperpermeability of the muscle cell membrane under hypoxic conditions (20). The hearts of trained rats can maintain a much better and enhanced performance during ischemia and is partly due to the alterations in he biochemistry of contracrion and relaxation of the cardiac muscle (4.7). The maximum depletions in the sedentary–isoproterenols could be attributed to the decline in the ATP and CP in the heart (8) and enhanced Ca^{++} inflow. However, the accumulation of Ca^{++} in the mitochondria is very much reduced by exercise (6).

The extent of myocardial damage caused by isoproterenol not only depends on age, but also varies with physical activity. Considering the differential adaptive capabilities of the aging heart, exercise programs could be more beneficial if started in childhood due to the superior and greater response of younger hearts to hypoxia.

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