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THE IMPACT OF ISCHEMIA REPERFUSION UPON THE PHYSIOLOGICAL PARAMETERS OF RABBIT HEART WITH EXPERIMENTAL HYPERTHYROIDISM

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Abstract

The aim of this study was to evaluate physiological parameters of cardiac contractility in rabbit heart with hyperthiroid condition experimentally induced with T3. Our study has been done on 10 male rabbits treated with T3 (i.p. injections 4.5 mg/kg body weight) fo 4 weeks. Rabbit hearts have been mounted in a Langendorf retrograde perfusion system and after 30 minutes ischemia followed by 60 minutes reperfusion with Krebs Hanseleit bicarbonate-buffered saline at 37°C, pH 7.6 supplemented with 10 mM glucose, left ventricular developed pressure (LVDP), heart rate (H.R.) and coronary flow (C.F.) have been measured. Our data have pointed out that as far as LVDP parameter is concerned, in T3 treated rabbits, cardiac recovery is achieved at higher values above those from controls. Cardiac frequency is not different in T3 treated rabbits in comparison with controls. There is a decrease in coronary flow in hyperthyroid rabbit heart in comparison with controls, in both cases there is a decrease of this parameter during reperfusion with lower values in controls and a tendency of reaching a plateau value.

Keywords: *ischemia-reperfusion, left ventricular developed pressure, heart rate, coronary flow, cardiac frequency, hyperthiroid rabbit heart*

INTRODUCTION

Cardiovascular pathologies are frequent observed in hyper and hypothyroidism conditions. Cardiac performances could be directly correlated with serum levels of thyroid hormones. Cardiac contractility, heart rate, ejection fraction and coronary flow are known to have increased values in hyperthyroid condition, while vascular peripheral resistance is concomitantly reduced. These modifications are accompanied by cardiac hypertrophy, leading finally to cardiac insufficiency. On the other hand, thyroid hormone deficit is associated with a decrease in cardiac contractility and cardiac dilatation; both modifications may be reverted by reducing the thyroid hormone balance.

Despite the fact that relation between thyroid pathology and cardiovascular hemodynamics is well known, biochemical basis of triiodotironin (T3) action in heart has been intensively investigated in the last 20 years. Modifications induced by T3 in cardiac function may result from the direct or indirect effects. (Cabai et al., 1994).

It has been observed that T3 may act as vasodilatator or innotrop.

It has been open the way to new strategies of treatment in cardiac insufficiency.

An understanding of thyroid hormone action upon heart and peripherial vascularisation is essential for implementation this hormone as therapeutic agent. It is suggested the possibility that T3 to increase the cardiac load and decrease vascular systemic resistance offering in such a way a new therapeutic option for cardiovascular pathology treatment (Brar et al., 2000).

Taking into account the research done on the effects of T3 at the cardiovascular level, our paper is aimed to complete the studies regarding modifications following experimental hyperthyroidism at the level of mechanic and biochemical parameters of rabbit heart.

MATERIALS AND METHODS

The biological material (10 rabbits), kept in standard biobase conditions have been treated for 4 weeks with T3 intraperitoneal injections (4.5 mg/kg body weight).
After the last day of treatment, the animals have been anesthetised with Na Pentobarbital to which has been added heparin, and after opening the thoracic cage the aorta has been excised and the heart quickly mounted in Langendorff retrograde reperfusion system and perfused with Krebs Hanseleit buffer at 37^{o}C, in order to evaluate physiological parameters (Ambrosio et al., 1999)

Determinations of physiological parameters of perfused heart

Langendorff system is designed to fix the heart by means of a canula inserted in aortic cross at the valve level on the isolate heart in a perfusion system with a liquid with a composition identical with that of plasma. The recipient with this liquid is suspended a certain level in order to assure a pressure of 85 mmHg, and the liquid circulates through coronary system and leave the heart through right atrium (Carmeliet, 1999).
In left ventricle is introduced a latex balloon which is connected with a pressure transducer. The balloon is inflated inside the ventricle and this records perfectly the contraction movements of ventrice wall. In such a way the pressure may be recorded on a pressure monitor as pressure developed by left ventricle (**LVDP**). The monitor permits the recording of cardiac frequency (**HR**). By collecting the perfusion liquid which leave the heart in a given time (1 min) in a beaker it can be determined the coronary flow (**CF**). These parameters have been determined from the hyperthyroid hearts versus controls (Kloner, 1989).

RESULTS AND DISCUSSIONS

After the heart has been mounted in Langendorff, system the heart has been perfused for 30 minutes with perfusion liquid during this time the heart arrives in a normal regimen of functioning (**stabilization period**). Then the heart is ischemised for 30 minutes by interruption of perfusion, and then reperfused for 60 minutes (reperfusion period). It have been recorded physiological parameters at the end of stabilization period and during reperfusion in order to see the capacity of heart recovery after a medium interval of ischemia. Our data pointed out that:
- The pressure developed by left ventricle (**LVDP**)

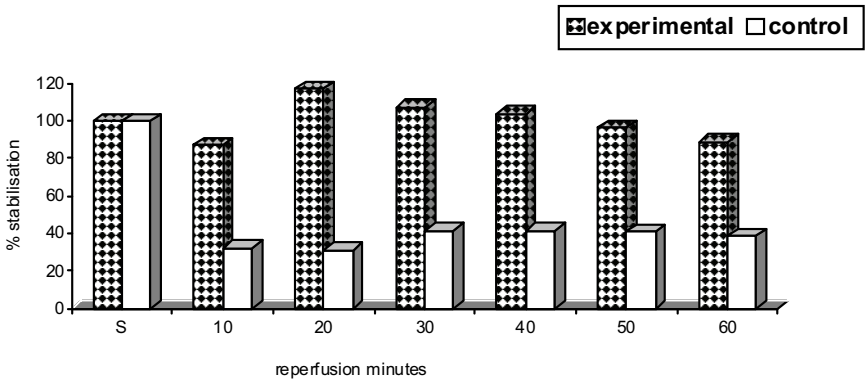

Figure 1. Evolution of pressure developed by the left ventricle in 60 minutes reperfusion in rats treated with T3 and in Controls

The values are given as % from the recorded value at the end of stabilising period. It can be observed that in the case of treatment with thyroid hormones, cardiac recovery, even does not exceed much the initial values (stabilization period), is realized at values much above the control heart. In both cases there is atendency of reaching a plateau value in function of left ventricle. The obtained differences between the two cases point out a high level of significance.

- Cardiac frequency (**HR**)

Cardiac frequency, measured by means of cardiac monitor, does not manifest a different allure in case of treated animals with T3, versus controls. Even, after a medium ischemia, the values do not reach those from stabilization, the obtained differences between the two cases are totally insignificant.

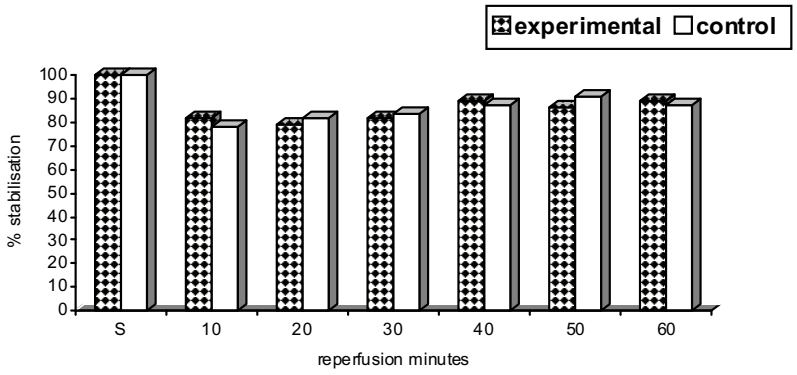

Figure 2. Heart rate (H.R.) in treated rats and in controls

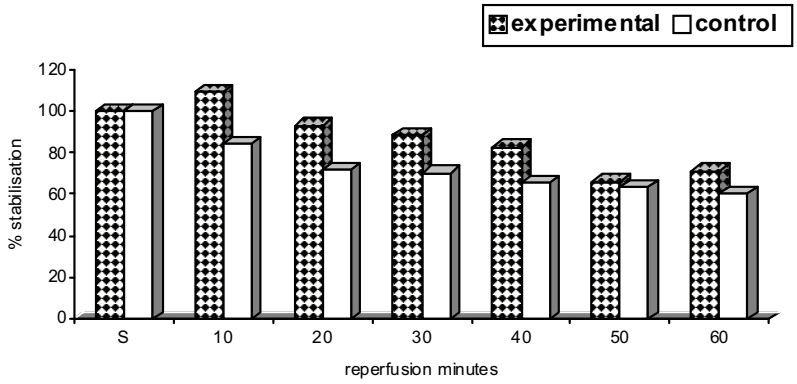

Figure 3. Coronary flow (C.F.) measured in treated rats and in controls

The evolution in time of coronary flow in T3 treated rabbits, comparatively with controls show that in both cases, a decrease in this parameter during reperfusion, with lower values in controls and with atendency to reach a plateau value.

Because heart is a major target organ for hormone action, many studies have examined modifications which appear in case of hyperthyroid condition. It has been established that (T3) influences amino acids, sugar and calcium transport through cell membranes. T3 stimulate the synthesis of myosin enzyme which present an increase ATP-ase activity, which results in an increased contraction speed of rabbit heart. Despite the fact that in heart there is an increased consumption of ATP, less from the chemical energy of ATP is used for contraction and much energy is directed for heat generation, which leads to a low efficiency of contraction in hyperthyroid heart (Braunwald et al., 1992).

On the other hand, one of the characteristics of arterial hypertension is deregulation of arterial hemodynamics. Every definition of arterial hypertension must take into account that fluctuations which appear during cardiac cycle, fluctuations in systolic pressure and diastolic

which accompany the heart dysfunction and result in pathological values of arterial hypertension. These fluctuations are determined by the ventricle ejection, by elasticity of arterial walls and by temporization of reflected waves in arteries (Opic, 1989).

CONCLUSIONS

The experimental model of arterial hypertension induced by means of T3 presents the following characteristics:
Cardiac frequency is measured by means of cardiac monitor and this does not manifest a different allure in case of treated animals versus controls. Even after a medium ischemia, the values do not reach those from stabilization period, differences obtained between the two groups are insignificant. Evolution in time of coronary flow in hyperthyroid hearts versus controls shows that in both cases there is a decrease of this parameter during reperfusion, with lower values in controls and with a tendency to reach a plateau.

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