CARDIAC METABOLISM

ON MYOCARDIAL ENERGY METABOLISM DURING EXERCISE IN PATIENTS WITH CIRCULATORY DISEASES

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There have been many reports on coronary circulation and myocardial metabolism during exercise in human beings, but about the energy metabolism of the diseased heart during exercise, many things remain still unknown. We studied the problem with coronary catheterization and bicycle ergometer, paying special attention to the severity of exercise and the classification of the diseases, so as to study the characteristics of coronary insufficiency.

To elucidate the production, reservation and utilization of cardiac energy, the myocardial metabolism of inorganic phosphorus and creatine were measured along with coronary circulation, myocardial metabolism of oxygen, glucose, lactate, pyruvate, nonesterified fatty acid and keton bodies and cardiac mechanical performance.

METHODS

The exercise was performed with Godalta's bicycle ergometer in supine position for 15 minutes at a rate of 50 watts. Coronary blood flow was measured by the nitrous oxide method, myocardial oxygen and other metabolites were measured by the methods which are shown in the slide and cardiac output was measured by direct Fick's method.

Forty one patients were examined. They were classified in 5 groups as shown by the slide; NCA group of neurocirculatory asthenia, HT group of hypertension without coronary insufficiency, HTC group of hypertension with coronary insufficiency CHD group of normotensive coronary diseases and HD group of other diseases.

RESULTS & DISCUSSION

1. Energy expenditure and ECG changes

The energy expenditure for exercise was nearly the same in each group; 4.4 Cal. per minute and 64 Cal. for 15 minutes. This is about half the energy expenditure per minute in the Master's double two step test, but about two and a half times the total energy.

The electrocardiographic changes during bicycle ergometry were quite similar to those of the two step test in all cases except for two patients. In 18 patients there was no ischemic change, in 19 patients there were changes, before and/or after exercise, and in 4 patients the ischemic ECG changes were reduced after exercise.

2. General oxygen consumption and heart function

General oxygen consumption increased to about four times that of pretest value, about equally in all groups. Between general oxygen consumption and cardiac output there was positive correlation at rest and during exercise. The increase in cardiac output and decrease in systemtic vascular resistance during exercise were similar in all groups. But changes in blood pressure and cardiac mechanical performance varied. Blood pressure, left ventricular work and myocardial tension were the highest, both at rest and during exercise, in HT group. In CHD group, mechanical work was the lowest at rest but the increase by exercise was the largest among the groups, showing the hypodynamia and potential cardiac ability in the resting state.

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3. Coronary circulation and myocardial oxygen metabolism

Myocardial oxygen consumption had high positive correlation with coronary blood flow before and during exercise, regardless of coronary or heart diseases, but it did not correlate so linealy with cardiac work, especially not in coronary and heart diseases.

Coronary blood flow and myocardial oxygen consumption did not differ significantly among the groups at rest, but during exercise they increased significantly in cases without coronary disorder, namely in NCA, HT and HD groups. They did not increase significantly in cases of coronary disease, HTC and CHD groups. Moreover, the coronary blood flow during exercise in CHD was the lowest of all groups, and it was significantly lower than that of HT group. The ratio of myocardial oxygen consumption to left ventricular work or myocardial tension was maintained only in NCA, and in other groups it decreased significantly.

These findings clearly demonstrate that coronary insufficiency during exercise is a state of lack of myocardial oxygen for augmented cardiac work, due to insufficient coronary response. Therefore the relation between myocardial oxygen consumption and cardiac work should not be considered only from the point of cardiac efficiency for oxygen, but also from the viewpoint of the sufficiency of myocardial oxygen for cardiac work.

4. Myocardial metabolism of carbohydrates

In general, myocardial usage of substrate is regulated by coronary blood flow as a common factor, secondly it is influenced by the arterial concentration of each substrate, i.e., the whole body metabolism, and finally it is controlled by the metabolic function of the myocardium which is estimated by the myocardial extraction ratio.

In all groups, the arterial concentration of lactate and pyruvate increased significantly during exercise compared with the natural change before exercise, as the result of anerobic metabolism of skeletal muscles. The myocardial usage of carbohydrates increased significantly in NCA and HT, chiefly due to increase in coronary blood flow and arterial concentration, but in HTC and CHD the myocardial usage of carbohydrates did not sufficiently increase due to poor response of coronary blood flow. Moreover in CHD, there were many patients in which the myocardial extraction ratio of carbohydrate inverted to negative indicating anerobic metabolism and showing that the uptake of carbohydrates was remarkably disturbed. This was also true of some patients in HD group.

In a resting state, there was no significant difference in myocardial carbohydrate metabolism among the group. This was confirmed from our observation of about 150 patients with various diseases, and the significant lower value of cardiac output and left ventricular work in coronary heart diseases compared with control was also proven. From these results it is clear that in coronary heart diseases the myocardial carbohydrates metabolism is maintained normal due to the hypodynamia at rest, but the coronary insufficiency and latent myocardial metabolic disability are revealed by exercise.

5. Myocardial metabolism of fat

Ten or 15 minutes after starting exercise, the arterial concentration of NEFA generally decreased and the myocardial extraction tended to decrease, but the myocardial usage was maintained in many groups except for hypertension groups. Between myocardial extraction and the arterial level of NEFA there was a significant positive correlation but it disappeared during exercise. The oxygen extraction ratio of NEFA tended to correlate negatively better with that of pyruvate than that of lactate, showing the competition of carbohydrates and fat at the entrance of the TCA cycle.

Ketones bodies were expelled from the heart muscle chiefly in cases of coronary insufficiency, and also in HT group. But in HT group, there was no sign of heart ischemia but a decrease in the uptake of NEFA together with good increase in myocardial uptake of lactate due to strong increase in the arterial concentration. The expulsion of ketone bodies in HT cases therefore could not be considered the result of heart ischemia but an overflow of fat endproducts in competition with abundant uptake of lactate. In these cases, it is supposed that acetyl Co-A was transformed to free ketone bodies by Co-A transferase and they were driven out of the heart muscles. One molecular ATP is produced in this chemical reaction.

6. Myocardial metabolism of phosphocreatine

Creatine was extracted by the myocardium in correlation with its arterial concentration at rest. The extraction of inorganic phosphorus did not correlate with its arterial concentration but correlated with the extraction of glucose. These significant positive correlations at rest disappeared during exercise.

The extraction of creatine and of inorganic phosphorus did not correlate with each other at rest but they did correlate during exercise, and in NCA and HT the myocardial extraction of both metabolites was maintained during exercise. In CHD and HD, however, their extraction was reduced or they were expelled from the heart muscle.

These findings indicate the mobilization of reserve energy in myocardial phospho-creatine in cases with coronary insufficiency and heart diseases; this was not seen in cases without these diseases.

7. ECG change and myocardial energy metabolism

There was no significant difference among the three ECG change groups in the myocardial energy metabolism at rest. During exercise, in the normal ECG group, coronary vascular resistance decreased remarkably and myocardial oxygen consumption for cardiac work was maintained. In the ischemic ECG group, there was no significant decrease in coronary vascular resistance and the ratio of myocardial oxygen consumption to left ventricular work or myocardial tension decreased significantly. The myocardial extraction ratio and utilization of lactate and pyruvate was significantly lower than that in the normal ECG group. In the group of improved ischemic ECG, the coronary circulatory response and myocardial metabolism was as good as in normal ECG group.

From these findings, the ischemic ECG changes during exercise indicate the relative myocardial oxygen want for cardiac work and the disorder of metabolism due to poor response of coronary circulation or to myocardial injury.

8. Energy balance of myocardial substrates, oxygen and heart work

To compare the maximum energy from the substrates and oxygen extracted by heart muscles with the energy available for external heart work, the quantity in calories was calculated. The energy balance of myocardial substrates, oxygen and heart was, as the slide shows, almost the same in all groups at rest. The energy calculated from the total substrates was the largest if it is supposed to be entirely burned, and the energy calculated for external work was the smallest. This suggests that the substrates extracted are not entirely oxygenated and all of the oxygen is not utilized for heart work at rest.

During exercise, only in NCA was the energy balance seen at rest maintained; in other diseases the balance was broken down. In CHD especially the relation was completely inverted; the energy for external work was the highest and the energy from substrates was the lowest. The insufficiency of myocardial oxygen for left ventricular work was compensated by the mobilization of reserve energy in phosphocreatine and anerobic metabolism, as mentioned above. The lack of extraction of substrates was probably made up by the NEFA converted from triglyceride in the heart muscles or by oxidizing glycogenolysis.

9. Clinical features of myocardial energy during exercise

To summarize the features of myocardial energy in various circulatory diseases during exercise, the mean value and the standard deviation of left ventricular work, coronary blood flow, myocardial extraction ratio of lactate and change of myocardial creatine uptake during exercise were compared and the scales of the items were so determined that the mean value in the NCA group fall on the same line.

Compared with NCA, in CHD, the disturbance of coronary response and myocardial metabolism during exercise is observed along with the mobilization of reserve energy, and the presence of the coronary heart diseases can be recognized, as is suggested by ischemic ECG changes. In HD, as seen in patients with familiary primary cadiomyopathy or with beriberi heart, remarkable disorder of myocardial metabolism was observed with ischemic ECG changes; nevertheless the coronary blood flow responded normally.

CONCLUSION

In this experiment, we were able to demonstrate that the disability of coronary response and latent myocardial metabolic disorders in coronary diseases are revealed by exercise. As a substitute for oxidizing energy, the reserve energy in myocardial phosphocreattine is mobilized along with cabohydrate anerobic metabolism, but this disturbance is compensated for by hypodynamia in the resting state. The ECG changes in coronary insufficiency during exercise corresponded to the myocardial relative ischemia and metabolic disfunction, these ECG changes were also seen in primary myocardial diseases with myocardial metabolic damages, but along with the good response of coronary circulation.