Effect of Fat and Carbohydrate Supply on Myocardial Substrate Utilization during Prolonged Exercise

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While skeletal muscle utilizes the possibility of storing substrates during rest and covers a major fraction of its substrate demand from these stores during exercise, the heart muscle, which works continually throughout life, must rely mainly upon a continuous substrate provision from the bloodstream. Thus, it has been shown that in healthy humans under a variety of conditions, myocardial substrate extraction, from a quantitative point of view, equals simultaneous myocardial substrate oxidation (Lassers et al., 1972). However, some experiments with prolonged exercise in rats have resulted in the suggestion that this may lead to myocardial glycogen depletion (Blount & Meyer, 1959), and in humans signs of utilization of intramyocardial triglycerides have been found when exercise exceeds 1½ to 2 h (Kaijser et al., 1972).

Most studies of myocardial substrate metabolism in humans have been performed in the postabsorptive state while competitive exercise is most often performed with optimal nutrition. Since it has been shown that one of the major factors determining myocardial extraction of a substrate is its blood concentration (Wahlqvist et al., 1972) it was considered of interest to study to what extent increased availability of both carbohydrates and fat in blood affected myocardial substrate metabolism during prolonged exercise. To maintain constant substrate supply, studies were done during an artificial steady-fed state produced by constant rate infusion of glucose and a fat emulsion.

Methods and Procedures

Myocardial substrate utilization was estimated by simultaneous blood sampling from percutaneously introduced catheters in an artery (a) and the

coronary sinus (cs) with analyses of oxygen, glucose, lactate, pyruvate, free fatty acid (FFA) and triglyceride (TG) concentrations. To facilitate estimation of myocardial FFA extraction ^3H labelled palmitate was infused i.v. and fractional extraction of labelled fatty acid determined. Five healthy young male volunteers performed cycle exercise in the supine position for 2 h at 40% of Vo_2max during constant rate i.v. infusion of glucose (0.32 g/min) and a fat emulsion, a modified form of Intralipid^R (0.17 g/min) in which TG appears in chylomicron-size particles, and which contained only 0.8 mmol/l glycerol. Results were compared with those of 15 men performing the same work after an over-night fast (some of these data have been presented previously [Kaijser et al., 1972]).

Details regarding analytical methods have been presented elsewhere (Carlson et al., 1973; Kaijser et al., 1972). In the following the term *extraction* of a substrate will be used to denote its removal from the blood stream in μmol/l blood, i.e., in case it is based on chemical analysis of a and cs blood it equals the a-cs difference. When calculated from the isotope data it is the fractional extraction of labelled fatty acid multiplied by the arterial concentration. *Uptake* denotes the removal in μmol/unit time (i.e., extraction multiplied by blood flow).

Results

At Rest

The infusion doubled the blood glucose concentration and increased the TG concentration four-fold, but did not significantly alter the FFA concentration. This led up to markedly increased myocardial TG extraction: if fully oxidized, the removal of TG would have covered 40 to 45% of myocardial oxidative metabolism. Also myocardial glucose extraction was significantly increased, while FFA extraction was significantly decreased (Figure 1).

A significant release of glycerol from the heart, (which was not found in the overnight fasted subjects) suggested that triglycerides indeed underwent lipolysis on passage across the heart, which is a prerequisite for their myocardial uptake.

During Exercise

Shortly after the onset of exercise, blood glucose concentration was reduced to the normal resting preinfusion level, in spite of the continuous infusion. In the fasting subjects blood glucose tended to decrease and after 2 h of exercise they had slightly lower blood glucose concentration than i.v. fed subjects. TG concentration remained unaltered throughout the 2 h of

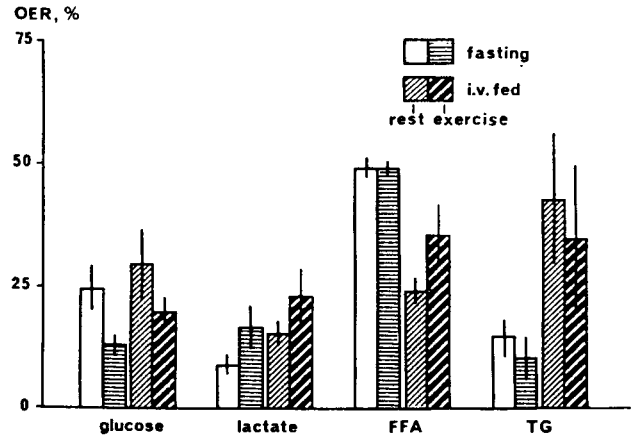

Figure 1—Myocardial extraction of glucose, lactate, free fatty acids (FFA) and triglycerides (TG) in fasting and i.v. fed subjects at rest and after 2 h exercise. Mean ± SE.

exercise. Measurements during the last 10 min of the exercise period showed a myocardial TG extraction, which was greater than during exercise in the postabsorptive state, although in relation to the oxygen extraction smaller (about half) than at rest with i.v. feeding. Arterial FFA concentrations increased towards the end of exercise similarly as in the fasting subjects. Myocardial extraction of FFA remained lower than in the fasting subjects, while extraction of glucose was insignificantly higher. Myocardial glycerol release (μmol/l blood) decreased to half the resting value, like the TG extraction.

Discussion

In the present study myocardial metabolism was measured in a condition where glucose and a chylomicron-like fat emulsion was infused i.v. to create a steady-fed state. Comparing exercise with resting conditions it may be noted that arterial concentrations of glucose rapidly decreased to preinfusion levels, suggesting that the infused glucose was taken care of, most probably by exercising skeletal muscle, since the a-cs difference of glucose was decreased by 40% at the same time as the coronary blood flow had a 2 to 3 fold increase (own unpublished data), indicating moderately increased myocardial glucose uptake which together with the small heart muscle mass makes myocardial removal insufficient to account for more than a small fraction of the infused glucose. Blood TG concentration, on

the other hand, remained unaltered throughout work, suggesting that skeletal muscle did not increase its TG removal during exercise.

This is in accordance with previous findings of significant removal of TG in skeletal muscle of a magnitude corresponding at rest, to about 20% of the oxidative substrate utilization, with no increase in uptake during exercise of moderate duration (Kaijser & Rössner, 1974). There are, on the other hand, indications that with exercise of very long duration (5 to 10 hours) the prerequisite for increased TG removal in the form of increased activity of lipoprotein lipase is at hand (Lithell et al., 1979).

In the heart muscle the decrease in blood glucose concentration led to a decrease in glucose extraction of similar magnitude, i.e., the fractional extraction remained unaltered. Myocardial TG extraction, on the other hand, decreased to ¾ the resting value in spite of unaltered blood concentration. The decrease was numerically slightly less than the calculated simultaneous increase in coronary blood flow, but the number of observations is too small to permit a conclusion as to whether myocardial TG uptake increased or remained unaltered during exercise. The significant myocardial glycerol release during exercise, with a negative a-cs difference which had decreased to the same extent as the positive a-cs TG difference, indicated that TG removed by the heart underwent lipolysis, which is a prerequisite for the TG uptake and utilization by the heart muscle, during exercise as at rest.

In comparing fed and fasting subjects it may be noted that myocardial FFA extraction was smaller in the fed subjects, during exercise as well as at rest. This is most probably a reflection of competition between FFA and fatty acids released from TG during passage in the heart vasculature. That the smaller a-cs difference of FFA in the fed state represents a true decrease in myocardial extraction of FFA, and not only reflects lipolysis of plasma TG without myocardial uptake of the released fatty acids is apparent from the finding of smaller myocardial FFA extractions in the fed state as calculated from radio-isotope data.

However, there was a difference between chemically and radio-isotopically estimated myocardial extraction of FFA at rest which tended to disappear during exercise suggesting more complete myocardial uptake of fatty acids released from TG during exercise compared to at rest (Kaijser et al., in press).

While at rest myocardial glucose extraction was greater in fed than in fasting subjects, this difference became insignificant during exercise, in accordance with the disappearance of the difference in arterial glucose concentration, i.e., the fractional extraction of glucose was the same in the fed as in the fasting state.

With regard to the total myocardial fraction of blood-borne substrates it may be noted that while in the fasting state the appearance after 2 h of work

of significant myocardial glycerol release indicated that the heart had started to utilize intra-myocardially stored TG, no indication of net utilization of intra-myocardial substrates was found in the fed state. On the contrary, extractions of glucose, lactate, FFA and TG together exceeded 100% of substrate oxidation suggesting that after 2 h of work the heart muscle still took up more substrate than it utilized.

Conclusions

Prolonged exercise in the fasting state may lead to partial depletion of myocardial substrate stores. This may be prevented by the supply of substrate, either i.v. or orally. Not only glucose or FFA, but also triglycerides may then serve as additional substrate. With regard to the ability to utilize additional amounts of triglycerides, the capacity of the heart muscle seems to exceed that of skeletal muscle.

Acknowledgments

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