IV. 6 Experimental Studies on Myocardial Metabolism with β-Methyl-(1\textsuperscript{11}C) Heptadecanoic Acid

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INTRODUCTION

We have been studying the myocardial uptake of F-18-labeled 2-deoxy-D-glucose (F-18 FDG) under the fed and fasted states and clarified that the myocardial uptake of F-18 FDG was extraordinarily suppressed in early stage of fasting. Free fatty acids are another major energy sources for myocardium. Fatty acids have been estimated to provide 65 % of the total energy requirement for heart muscle. Therefore, in the present study we investigated myocardial metabolism with β-methyl-(1\textsuperscript{11}C)heptadecanoic acid [(C-11)-BMHDA], a labeled fatty-acid analog that is partially metabolized and trapped in the myocardium.

MATERIALS AND METHODS

The synthesis of β-methyl-(1\textsuperscript{11}C) heptadecanoic acid was carried out according to the method developed by Livni et al. Young male Donryu rats (weighing 120 to 130 g) were used after free access to food and water only for 2.5 days prior to experiments. Appropriate doses of (C-11)-BMHDA were injected intravenously through a lateral tail vein. The rats were killed by cervical dislocation at 1, 5, 10 or 20 min after (C-11)-BMHDA injection. Blood, heart and liver were removed, bottled, weighed and counted by an automated NaI well counter. Each group had 6 to 8 rats. Three additional experimental groups of young male Donryu rats were fasted for 0.5, 1.5 and 2.5 days each. Each group including the control group which was fed ad libitum, had 6 to 8 rats each weighing 100 to 140 g. The rats were killed 10 min after the injection of (C-11)-BMHDA. Blood, heart and liver were removed, bottled, weighed and counted by automated NaI well counter. The radioactivity data were corrected for physical decay and expressed as the percent of the injected dose per gram tissue (% DOSE/g tissue). Simultaneously, blood glucose and free fatty acid measured.

RESULTS AND DISCUSSION

The uptake curve of (C-11)-BMHDA were shown in Fig. 1. The uptake by the heart of normal feeding rats decreased slightly from 3.8 to 3.3 % DOSE/g tissue. On the other hand, the myocardial uptake of fasted rats decreased markedly from
4.5 to 1.3 % DOSE/g tissue. In contrast, the liver uptake was entirely different from that of the heart. The uptake by the liver of normal feeding rats increased up to 5 min from 2.3 to 4.1 % DOSE/g tissue, then decreased linearly from 4.1 to 3.1 % DOSE/g tissue. Whereas the liver uptake of fasted fats increased rapidly up to 5 min from 2.0 to 6.2 % DOSE/g tissue, and remained essentially unchanged up to 20 min after injection. The time course of radioactivity in blood showed rapid clearance of (C-11)-BMHDA. Changes in uptake levels of (C-11)-BMHDA in relation to fasting time were shown in Fig. 2. Myocardial uptake decreased linearly with increased fasting time, whereas the liver uptake increased markedly from 3.5 to 5.3 % DOSE/g tissue after 12 hours of fasting and reached plateau. Blood activity increased slightly with increased fasting time. Blood glucose and free fatty acid levels in relation to fasting time were shown in Fig. 3. Blood glucose levels decreased gradually with increased fasting time from 170 to 105 mg/dl while free fatty acid levels increased after 12 hours of fasting and remained unchanged after 1.5 and 2.5 days of fasting. The correlations between myocardial uptake and blood glucose levels were presented in Fig. 4. There was a strong negative correlation between myocardial uptake and blood glucose.

Recently, the biodistribution of 8-methyl-(l-11C)heptadecanoic acid, a fatty-acid analog designed to inhibit the beta-oxidation process, was studied and its extraction and retention in the myocardium, as a function of time, were assessed by Livni et al. Their result suggest that (C-11)-BMHDA is trapped in the myocardium as a result of the beta-oxidative degradation process. But our present results do not agree with their data. The myocardial uptake of (C-11)-BMHDA decreased especially in fasted rats. These results suggest that (C-11)-BMHDA is not trapped in the myocardium. Further investigation may be needed to clarify the effect of fasting on myocardial metabolism of (C-11)-BMHDA.

References

Fig. 1. Uptake curves of the heart and the liver in the fed and fasted rats following injection of (C-11)-BMHDA.

Fig. 2. Changes in uptake levels of (C-11)-BMHDA in relation to fasting time.
Fig. 3. Blood glucose and free fatty acid levels in relation to fasting time.

Fig. 4. Correlation between myocardial uptake and blood glucose levels.