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Cardioprotective Effects of Increased Myocardial Glycogen Stores and β-Blockers in Cardiac Surgery

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During open heart surgery the heart is exposed to hypoxia. In order to minimize the effects of this several protective measures are taken. Probably the most effective precaution is lowering of the heart temperature below 28°C. There are also reasons to believe that the cardioplegic solution used is of importance in this context. In the work by Jynge et al (3) it was clearly shown that the protective effect judged as CK-MB leakage was substantially better when St Thomas' solution was used as compared to the leakage when Bretschneiders or Kirsch solutions were used on isolated rat hearts at 37°C. This difference was substantially diminisched when the temperature was lowered to 28°C. Even better protection is probably obtained if the temperature is decreased further and in the present work a temperature of about 20°C has been used. However, in a recent work by Hansson et al (2) no clear differences in protective effect could be observed in open heart surgery in humans when Bretschneiders, Ringer-K^+ and St Thomas' solution were compared.

It has been shown that elevated content of glycogen in the heart increases the cardiac tolerance to an oxic stress (4). Lolley et al. (5) published data indicating less atrial and ventricular arythmias and lesser vasopressor dependence in patients on elective coronary by-pass surgery if the patients had good glycogen stores prior to operation as compared to

patients with low stores.

We have in the present series studied the effect of increased cardiac glycogen stores on the release of creatine kinase (CK) and creatine kinase subunit B (CK-B) activity in patients subjected to valvular surgery. The control group consisted of 16 patients and the treated group of 11 patients. The diagnoses are given in Table 1. The treated patients recieved 1000 ml of 10% glucose solution, 20 units of fast acting insulin and 60 mmoles of potassium during 12h prior to surgery. During 15-20 minutes before aortic crossclamping, 0.6 g of glucose per kg body mass was administered as a 30% glucose solution in a central venous line. The patients were operated in cold cardioplegia according to St Thomas' method (1). A right auricular biopsy was taken for glycogen determination.

Table 1 Diagnosis of the patients in the glucose-insulin-potassium study.

	Controls	Treated
Aortic stenosis	1	2
Aortic insufficiency	2	5
Combined aortic valv. disease	5	0
Mitral stenosis	1	1
Mitral insufficiency	3	1
Combined mitral valv. disease	3	1
Aortic + mitral valv. disease	1	1
	16	11

Blood for enzyme activity determinations was drawn before aortic crossclamping, immediately after declamping and then after 30 minutes, 1,3,8,12 and 19 h. The subunit B activity of CK was determined by a immunoinhibition method (Merck, W. Germany). The obtained activities were corrected for changes in hematocrit.

Separation of CK isoenzymes was achieved by agarose gel electrophoresis.
Left ventricular ejection fraction and Mean V_{CF} were estimated with noninvasive technique.
The glycogen content was significantly higher in the treated group as compared to the control group (Fig 1) and as seen in figure 2 there is a fairly good correlation between right auricular glycogen content and mean S-CK B cumulative area.

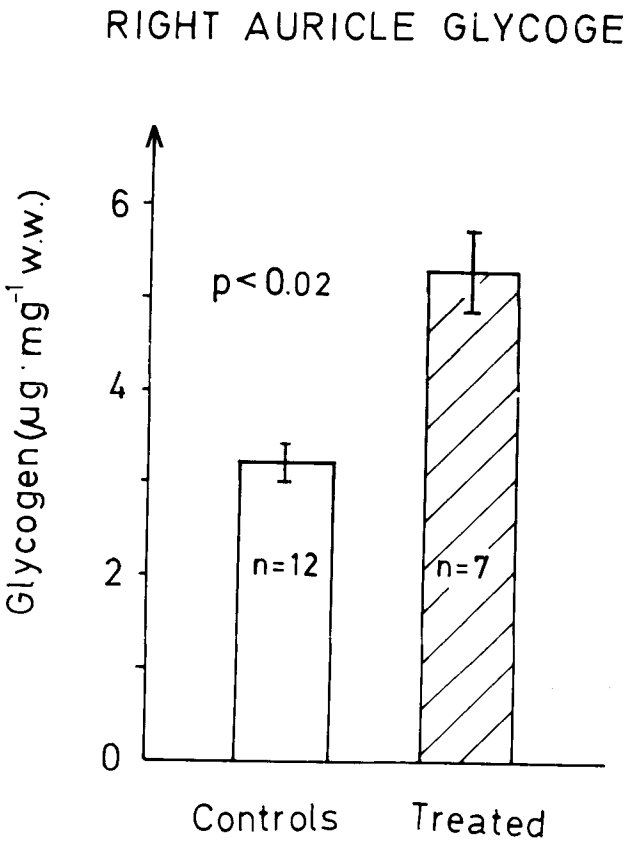


Fig. 1. Glycogen content in the right auricle in controls and treated patients.

The mean area under the S-CK B was significantly smaller in the treated group as compared to the control group (Fig 3).

The sera from 10 patients subjected to aortic valve surgery (both control and treated patients) were analyzed with gel electrophoresis. A faint CK BB band could be detected in only one case in contrast to the finding in sera from patients subjected to mitral valve surgery where CK BB bands were seen in 8 out of 9 patients examined.

No significant differences were seen between the two groups regarding left ventricular ejection fraction or Mean V_{CF}.

These results indicate that increased cardiac glycogen stores protect the heart from anoxic damage during open heart surgery.

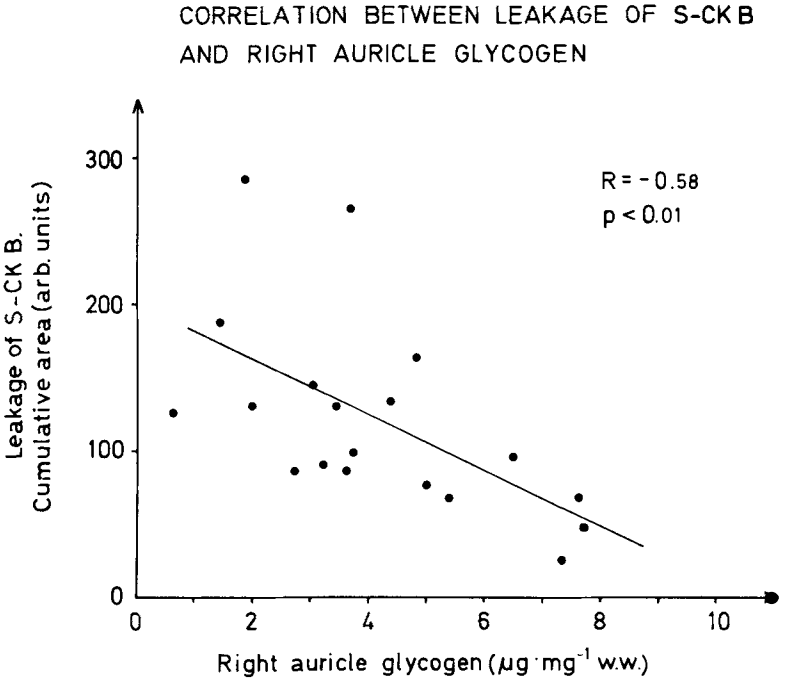
The fact that practically only patients subjected to mitral valve surgery showed CK BB bands could be explained by the reported finding of Gimpel et al. (1) that in papillary muscle as much as 20% of the total CK activity is CK BB.

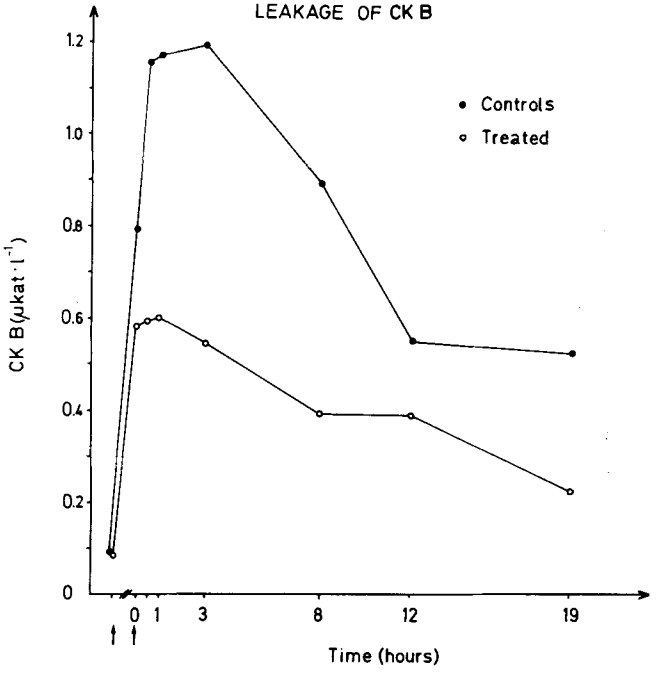
Induction of anaesthesia, surgical incisions on particulary cardio-pulmonary by-pass produces elevated circulating catecholamine concentrations. This results in an increased metabolic demand in the experimentally arrested heart. Slogoff et al (6) have shown that continuation of propranolol treatment had beneficial effects in patients subjected to coronary by-pass open surgery on ischemic signs such as ST segment deviation and ventricular arrythmics as compared to a control group who had never recieved propranolol.

Fig.2 Correlation between right auricular glycogen and CK-B leakage.

Fig.3 Leakage of CK-B in controls and treated patients.

(Opposite side)


CORRELATION BETWEEN LEAKAGE OF S-CK B
AND RIGHT AURICLE GLYCOGEN
Leakage of S-CK B.
Cumulative area (arb. units)
300
200
100
0
R = - 0.58
p < 0.01
0
2
4
6
8
10
Right auricle glycogen (µg · mg⁻¹ w.w.)


LEAKAGE OF CK B
Controls
Treated
CK B (µkat · l⁻¹)
1.2
1.0
0.8
0.6
0.4
0.2
0
0 1 3 8 12 19
Time (hours)

In the present study we compared the CK B leakage in two groups of patients undergoing aortocoronary by-pass surgery. In one group consisting of 15 men, metoprolol treatment was continued until the evening before operation and the patients recieved a dose of 100 mg metoprolol per os two h before surgery. In the other group consisting of 12 men and 2 women, medication was withdrawn 72 h before surgery. The patients were operated in cold cardoplegia as described above. The mean aortic cross-clamping time and number of peripheral anastomoses did not vary significantly between the two groups.

Blood was drawn for CK and CK B activity determinations at the same time intervals and determined as above. A right auricular biopsy for glycogen content determination was taken at the time of venous cannulation.

The glycogen content was numerically higher in the group with continued metoprolol medication as compared to the group with discontinued medication. This might indicate that the metabolic demand was lower in the first group.

The beneficial effect of continued β-blockade was indicated by the fact that the cumulative area under the CK B curve was significantly smaller in the group where medication was continued as compared to the other group. Peak CK B activity was reached simultaneously in both groups and no significant difference in disappearance rate could be observed between the two groups. According to these results metoprolol does not seem to change appearence- disappearence kinetics of CK B in connection with open heart surgery.

Whether the lower CK B leakage in the metoprolol continued is caused by a protective effect of this drug or whether there is an adverse effect of drug withdrawed can not be established in our study.

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