

VII. Summary

Investigations about the cardioprotective effect of pyruvate in isolated hemoperfused pig-hearts under ischemic conditions

In isolated pig-heart it is possible to induce acute myocardial ischemia under well-controlled experimental conditions to study their functional and biochemical consequences. The pig-heart is similar to the human heart with respect to anatomy, size and physiology. Because of these similarities, the model has a special suitability in the experimental cardiovascular research.

The aim of the present study was to demonstrate the cardioprotective effect of the glycolytic intermediate product pyruvate during normothermic perfusion and under ischemic conditions. The cessation of bloodflow was produced by occlusion of a coronary artery branch. Measurements were made of global (LVP) and regional (IMP, myocardial wall thickness) functional parameters. Additionally there were made measurements of coronary perfusion-pressure (CPP), heart rate (HR), coronary bloodflow and regional heartwork (pressure-length-loops).

The application of supraphysiological concentrations of pyruvate under non ischemic conditions of the isolated heart, presented no significant influence of pyruvate on global and regional functional parameters.

Because of short time (15 min) interruption of bloodflow by occlusion of the Ramus interventricularis paraconalis (RIVA) an ischemia was induced. Standard values derived under a first occlusion was essential for the assessment of changes that occurred in consequence of a second occlusion. Before a second period of ischemia there was supraphysiological concentrations of pyruvate (5 mMol/l) applied. These conditions showed a significant smaller increase of global function (LVP). The measurements of regional myocardial function demonstrate, under influence of pyruvate, significant improvements of intramyocardial pressure (IMP) and myocardial wall thickness (Wth) in the ischemic region.

These results indicate that pyruvate's positive inotropic effect is especially striking in hearts reversibly injured, the so called "stunned" myocardium. Against traditional positive inotropic

agents, there is no chronotropic effect in the hearts. The demonstration of pyruvates cardioprotective effect in the present study exerts a potential value in the treatment of ischemic injured myocardium.

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The results of the isolated pig-heart are mostly comparable to conditions of in-vivo-experiments. In a recent publication, after these experiments were finished, about the application of pyruvate in treating heart failure in humans, there could be obtained an improvement in cardiac contractility. Therefore, it has been shown that the isolated pig-heart model is suitable to replace experiments of animals. Especially the employment of hearts from slaughterhouse animals, it could reduce laboratory animals in experimental studies.