Experimental cardioprotection in myocardial ischemia and reperfusion assessed by sestamibi-MPI

Effects of glutamine, glutamate and erythropoietin

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ABSTRACT

The project was performed at Department of Nuclear Medicine, Cardiology and Clinical Institute, Skejby Hospital, and consists of four experimental substudies. The main issues were the use of sestamibi-SPECT as outcome parameter in the early reperfusion phase as well as potential adjunctive treatments to myocardial ischemia in a porcine experimental model. Study 1 compared the performance of sestamibi-MPI as early outcome parameter to a standard histochemical technique. Ex vivo tissue level sestamibi defect sizes closely parallelled the TTC-determined defect sizes. The in vivo SPECT defect sizes were overestimated compared to the histochemical defect sizes, but when infarct size was corrected for the ischemic area at risk, the correlation was very good, demonstrating that the SPECT overestimation is inherent in the SPECT process. Study 2 investigated glutamine and glutamate as adjunctive therapy in myocardial ischemia, since both are proposed to support resumption of oxidative metabolism after, as well as anaerobic ATP production during ischemia. Even though the intended concentrations of glutamine were obtained, the results were very clearly negative. Glutamine increased systemic vascular resistance. Infarct sizes actually turned out larger in the glutamine than in the control group. Further studies were therefore not performed.

Study 3 examined the potential cardioprotective effects of erythropoietin (EPO). EPO has previously been shown experimentally to possess tissueprotective effects by means of antiapoptotic properties in rodent studies. EPO was administered preischemically corresponding to intervals of early and delayed ischemic preconditioning (IP), since EPO has been proposed to be active by IP-like mechanisms. No beneficial effects was demonstrated in the short-term. Study 4 investigated the acute hemodynamic effects of EPO in a non-ischemic model and the response of co-administration of a sympathetic agonist (dopamine). In the short-term EPO increased pulmonary vascular resistance and tended to increase myocardial contractility with addition of dopamine.

In conclusion: Neither of the proposed cardioprotective interventions showed any beneficial effects. Glutamine increased systemic vascular resistance. Glutamate increased cardiac output. EPO increased sensitivity to dopamine as manifested by increased pulmonary vascular resistance with addition of dopamine. Sestamibi-SPECT in the early reperfusion phase correlated well with a histochemical method in determining infarct size corrected for the ischemic area at risk.