Porcine myocardial ischemia-reperfusion studies on cardioprotection, ventricular arrhythmia and electrophysiology

Akademisk avhandling

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av

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The thesis is based on the following papers:

I Odenstedt J, Månsson C, Grip L.
Failure to demonstrate myocardial protective effects of the ultra short-acting calcium antagonist clevidipine in a closed-chest reperfusion porcine model.
Journal of Cardiovascular Pharmacology 2004;44(4):407-415.

II Odenstedt J, Månsson C, Jansson SO, Grip L.
Endocardial electromechanical mapping in a porcine acute infarct and reperfusion model evaluating the extent of myocardial ischemia.
Journal of Invasive Cardiology 2003;15(9):497-501.

III Odenstedt J, Rubulis A, Grip L, Bergfeldt L.
Distorted T-vector loop and increased heart rate are associated with ventricular fibrillation in a porcine ischemia-reperfusion model.
Journal of Electrocardiology 2009;42(3):267-273.

IV Odenstedt J, Linderoth B, Bergfeldt L, Ekre O, Grip L, Mannheimer C, Andréll P
Effects of spinal cord stimulation on myocardial ischemia, infarct size, ventricular arrhythmia and non-invasive electrophysiology in a porcine ischemia-reperfusion model. *In manuscript.*

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ABSTRACT

Background: Coronary artery disease is the primary cause of death in adults in the industrialised world and ventricular fibrillation associated with myocardial ischemia is the main cause of sudden cardiac death. Restoration of blood flow and preservation of myocardial integrity throughout ischemia and reperfusion is essential to improve clinical outcome. Alteration in calcium handling and its consequences are central features of these events. Sympathico-vagal imbalance and electrophysiological alterations are important predisposing factors for malign ventricular arrhythmia and sudden cardiac death.
Aims: To investigate whether ultra-short acting calcium antagonism or spinal cord stimulation (SCS) could reduce myocardial ischemia and infarct size in a porcine closed-chest model. Furthermore, the feasibility of endocardial electromechanical mapping for defining myocardial viability during acute infarction was evaluated. Finally, non-invasive electrophysiological characteristics of ischemia-reperfusion and the occurrence of ventricular arrhythmias were investigated as well as the effects of SCS on these measures and events.
Methods: Myocardial infarction was induced by 45 minute coronary occlusion in closed-chest landrace pigs. An ultra-short acting calcium antagonist, clevidipine, was administered into the myocardium at risk. Myocardial viability was assessed by Evans Blue, tetrazolium and endocardial electromechanical mapping and the correlation between these methods was investigated. Three-dimensional vectorcardiography was continuously recorded, analysed offline with regard to depolarisation and repolarisation parameters, and later correlated to myocardial ischemia and ventricular arrhythmia. In a second series of experiments, the effects of SCS were investigated with regards to haemodynamics, infarct size, ventricular arrhythmia and electrophysiology.
Results: Clevidipine did not reduce infarct size. Electrical and mechanical activities were both impaired within the infarct zone, but the precision of electromechanical mapping to identify an infarct was poor, and due to intersegmental variability and arrhythmia. All T vector loop parameters changed in response to ischemia. Ventricular arrhythmia was more prevalent during proximal left anterior descending coronary artery occlusion, which was associated with more pronounced electrophysiological alterations. In the SCS group, ventricular arrhythmia occurred less frequently in association with signs of less ischemia and electrical alterations. SCS did not reduce infarct size.
Conclusions: Infarct size was neither reduced by ultra-short acting calcium antagonism nor by SCS, but the latter seemed to have cardioprotective properties as it reduced the occurrence of ventricular arrhythmia. Endocardial electromechanical mapping was not feasible for acute myocardial viability assessment.

Keywords: porcine; myocardial ischemia; ventricular arrhythmia; sudden cardiac death; electrophysiology; vectorcardiography; endocardial mapping; spinal cord stimulation

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