Glutamate for Metabolic Intervention in Coronary Surgery
with special reference to the GLUTAMICS-trial

av

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Akademisk avhandling

Avhandling för medicine doktorsexamen i Medicinsk vetenskap med inriktning Kirurgi, som enligt beslut av rektor kommer att förvaras offentligt fredagen den 11 november 2011 kl. 9.00, Wilandersalen, Universitetssjukhuset i Örebro

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Abstract


Myocardial ischemia is a major cause of postoperative heart failure and adverse outcome in coronary artery bypass graft surgery (CABG). Conventional treatment of postoperative heart failure with inotropic drugs may aggravate underlying ischemic injury. Glutamate has been claimed to increase myocardial tolerance to ischemia and promote metabolic and hemodynamic recovery after ischemia. The aim of this work was to investigate if intravenous glutamate infusion given in association with CABG for acute coronary syndrome can reduce mortality and prevent or mitigate myocardial injury and postoperative heart failure. We also wanted to assess neurological safety issues, as a concern with the use of glutamate is that it may act as an excitotoxin under certain conditions.

A metabolic strategy for perioperative care was assessed in an observational study on 104 consecutive patients with severe left ventricular dysfunction undergoing CABG. Based on encouraging clinical results, unsurpassed in the literature, the GLUTAMICS-trial was initiated. 861 patients undergoing CABG for acute coronary syndrome were randomly allocated to blinded intravenous infusion of L-glutamic acid solution or saline. The primary endpoint was a composite of postoperative mortality (≤30 days), perioperative myocardial infarction and left ventricular heart failure in association with weaning from cardiopulmonary bypass. Secondary endpoints included neurological safety issues, degree of myocardial injury, postoperative hemodynamic state, use of circulatory support and cardiac mortality. The event rate was lower than anticipated and the primary endpoint did not differ significantly between the groups. Regarding secondary endpoints there were significant differences compatible with a beneficial effect of glutamate on post-ischemic myocardial recovery. The putative effect of glutamate infusion was seen in more ischemic patients (CCS class IV) and in patients with evident or anticipated LV-failure on weaning from CPB. No evidence for increased incidence of clinical or subclinical neurological injury was found. In conclusion, intravenous glutamate infusion is safe in the dosages employed and could provide a novel and important way of promoting myocardial recovery after ischemic injury.

Keywords: myocardial ischemia, coronary artery bypass, cardiac surgery, acute coronary syndrome, glutamate, metabolic intervention, postoperative heart failure, myocardial recovery.

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