Glucose-insulin-potassium therapy in adult patients undergoing cardiac surgery: a meta-analysis

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CRD summary
This review found that use of glucose-insulin-potassium infusions was associated with reduced myocardial injury and improved haemodynamic performance in patients who underwent cardiac surgery. Reporting limitations, suboptimal included studies and uncertainty about the evidence synthesis mean that the authors’ conclusions might not be reliable.

Authors’ objectives
To assess the effectiveness of glucose-insulin-potassium infusions in adult patients who underwent cardiac surgery.

Searching
PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to December 2009; search terms were reported. Reference lists of relevant articles, conference proceedings, previous reviews and meta-analyses were checked for additional studies. Internet-based sources of clinical trial results in cardiovascular surgery were searched.

Study selection
Randomised controlled trials (RCTs) of adult patients who underwent cardiac surgery and that compared evaluated glucose-insulin-potassium infusions to placebo or standard treatment were eligible for inclusion. Trials needed to report at least one primary or secondary outcome. The primary outcomes were all-cause mortality two months post-surgery and perioperative myocardial infarction. Secondary outcomes were postoperative use of inotropic support, atrial fibrillation cardiac index and durations of intensive care stay/total hospital stay. Trials where patients underwent organ transplantations were excluded from the review.

Mean patient age ranged from 35 to 74 years. The proportion of male patients in the trials ranged from 12.8% to 100%. Patients with diabetes were included exclusively in some trials, excluded in others and some trials enrolled non-diabetic and diabetic patients. Most of the patients underwent coronary artery bypass graft (CABG). Insulin dose, timing and administration varied across the studies.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
Methodological quality was assessed using a modified two-point to 10-point Jadad scale of randomisation sequence, allocation concealment, investigator blinding, efficacy of randomisation and drop-outs.

It appeared that more than one reviewer carried out the quality assessment and disagreements were resolved by consensus.

Data extraction
Data were extracted to calculate relative risks (RR) for dichotomous data, mean differences for continuous data and 95% confidence intervals (CI) for each estimate.

Data were extracted by two independent reviewers. Any disagreements were resolved by consensus.

Methods of synthesis
Pooled relative risks, weighted mean differences (WMDs) and 95% CIs were calculated for each summary estimate using a random-effects model. Statistical heterogeneity was evaluated with $X^2$ and $I^2$. Significant heterogeneity was indicated by an $I^2$ score greater than 50%. Subgroup analyses were conducted on the basis of patient cohort (diabetic/non-diabetic patients) and aim of glucose-insulin-potassium therapy (glycaemic control with glucose goal <200mg/day or glucose-insulin-potassium therapy without aiming for glycaemic control). Sensitivity analyses and meta-
regression were used to explore potential sources of heterogeneity.

The authors assessed the likelihood of publication bias using the Egger's test.

**Results of the review**

Thirty-three RCTs (2,113 participants, range 14 to 391) were included in the review. Four studies used computer-generated random numbers. Four trials reported appropriate allocation concealment. Double-blinding was used in 11 trials. Eight studies clearly described drop-outs and withdrawals.

Treatment with glucose-insulin-potassium infusions was associated with statistically significant decreases in perioperative myocardial infarction (RR 0.63, 95% CI 0.42 to 0.95; 17 studies). Significant benefits of glucose-insulin-potassium treatment were observed with reductions in inotropic support (RR 0.66, 95% CI 0.45 to 0.96; seven studies), number of hours in the intensive care unit (WMD -7.96, 95% CI -13.36 to -2.55) and improvements in postoperative cardiac index (WMD 0.43, 95% CI 0.31 to 0.55). There were no statistically significant differences between glucose-insulin-potassium groups and control groups in all-cause mortality (13 studies), postoperative atrial fibrillation within two months post-surgery (11 studies) and length of hospital stay. The authors stated that statistically significant heterogeneity was present in postoperative cardiac index, inotropic support and length of intensive care unit and total hospital stay. The authors reported that there was no evidence of publication bias in the analyses.

Similar results were found in the sensitivity analyses, although there was a statistically significant reduction in total hospital stay for the glucose-insulin-potassium infusion group. In non-diabetic patients, glucose-insulin-potassium infusions were associated with reduced requirement for inotropic support (RR 0.58, 95% CI 0.36 to 0.93) and improved postoperative cardiac index (WMD 0.36, 95% CI 0.12 to 0.60). In the analysis of patients with diabetes (three studies), glucose-insulin-potassium was found to improve postoperative cardiac index (WMD 0.51, 95% CI 0.40 to 0.62), reduce incidence of atrial fibrillation (RR 0.40, 95% CI 0.22 to 0.71) and shorten length of intensive care unit stay (WMD -15.50, 95% CI -16.16 to -14.84). In trials conducted after 2000, patients who received glucose-insulin-potassium had reduced requirements for inotropic support (RR 0.44, 95% CI 0.31 to 0.64) and improved postoperative cardiac index (WMD 0.31, 95% CI 0.08 to 0.54).

In trials of infusion for glycaemic control, glucose-insulin-potassium was significantly associated with improved postoperative cardiac index (WMD 0.50, 95% CI 0.40 to 0.60). Where glycaemic control was not the aim of the infusion, glucose-insulin-potassium significantly reduced the incidence of postoperative myocardial infarction (RR 0.57, 95% CI 0.35 to 0.91) and improved postoperative cardiac index (WMD 0.38, 95% CI 0.14 to 0.63). A borderline improvement was observed in the requirement for inotropic support (RR 0.67, 95% CI 0.44 to 1.01). Meta-regression results showed no effect on the pooled results.

**Authors’ conclusions**

Use of glucose-insulin-potassium infusions was associated with reduced myocardial injury and improved haemodynamic performance in patients who underwent cardiac surgery. Patients with diabetes were shown to benefit from these infusions for the purpose of glycaemic control.

**CRD commentary**

The review addressed a clear question. Inclusion criteria were sufficiently replicable. Appropriate databases were searched for relevant studies. The authors used relevant tests to examine potential for publication bias. Steps were taken by the review authors to minimise errors and bias for quality assessment and data extraction; no such steps were reported for study selection. Study quality was not substantial and most did not score highly on individual components. A lack of complete data on statistical heterogeneity made it unclear whether combining results in a meta-analysis was appropriate. Some potential sources of heterogeneity were explored by the authors using subgroup and sensitivity analyses. The authors acknowledged some of the limitations of the review for potential confounding factors that may have influenced the results.

Reporting limitations, suboptimal included studies and uncertainty about the evidence synthesis mean that the authors’ conclusions might not be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that glycaemic control with glucose-insulin-potassium infusions might be required for patients with diabetes who were undergoing cardiac surgery.

Research: The authors did not state any implications for research.

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