Insulin-based regimens decrease mortality rates in critically ill patients: a systematic review

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CRD summary
This review evaluated the efficacy of tight glycaemic control in critically ill hyperglycaemic patients. The authors concluded that insulin-based regimens are associated with a significant reduction in morbidity and mortality among critically ill patients. The conclusions may not be generalisable since they are based on studies which included a wide variety of participants.

Authors' objectives
To determine the efficacy of insulin-based therapies in reducing morbidity and mortality among critically ill hyperglycaemic patients.

Searching
MEDLINE (1966 to December 2005), EMBASE (1980 to December 2005), and the Cochrane Library and a Cochrane Group Specialist Register were searched. Bibliographies of retrieved articles and reviews were checked and experts in the field were contacted for additional studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
To be included in the review, studies had to state that blood glucose was drawn within 24 hours of admission. Further inclusion criteria relating to the interventions were not clearly specified; however, studies evaluating insulin-based regimens in the treatment of critically ill patients seemed to be eligible for inclusion. Tight glycaemic control was obtained through various insulin regimens including insulin infused alone, insulin in combination with glucose, or as a glucose-insulin-potassium (GIK) infusion. The control treatments were placebo, dextrose solution, sodium chloride infusion, or conventional therapy with insulin.

Participants included in the review
Inclusion criteria relating to the participants were not clearly specified. The participants included were diabetic and non-diabetic patients with a diagnosis of acute myocardial infarction, acute stroke, or undergoing cardiac surgery, or were critically ill hyperglycaemic patients. Studies of children or pregnant women were excluded.

Outcomes assessed in the review
Studies had to report mortality and report follow-up for more than 80% of the participants to be eligible for inclusion. Other outcomes extracted were myocardial performance, morbidity, in-hospital and intensive care unit stay. Studies that did not report the proportions of patients who were followed up for the timing of blood glucose measurement were excluded.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies, with any disagreements resolved by discussion or by a third reviewer.

Assessment of study quality
Two reviewers independently assessed the quality of the studies, with any disagreements resolved by discussion or by a third reviewer. Quality was assessed on the basis of randomisation, concealment of allocation and intention-to-treat analysis.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The data were discussed narratively, grouped by regimen, and presented in tabular format.

How were differences between studies investigated?
Differences between the included studies were discussed in the text and presented in tabular format.

Results of the review
Sixteen RCTs (n>5,372) were included in the review.

GIK regimen (10 studies, n=1,696).

Compared with the control treatment, 5 studies found an improved myocardial performance with GIK; two of these also found shorter hospital stays. The remaining studies reported no clinical advantage or even suggested a higher mortality with the GIK therapy.

Intensive insulin-based therapy (5 studies, n>3,056).

Three of the included trials showed favourable effects of the regimen on morbidity and/or mortality, and two found no significant benefit. Among critically-ill patients, intensive insulin therapy was associated with a statistically significant reduction in intensive care mortality (4.6% versus 8.0%, \( p<0.04 \)) and in-hospital mortality (7.2% versus 10.9%, \( p=0.01 \)) in comparison with conventional insulin therapy (1 study). These benefits were observed only in the subgroup hospitalised for longer than 5 days (10.6% versus 20.2%, \( p=0.01 \)).

In a prospective, randomised controlled study of adult patients admitted to the intensive care unit, the intention-to-treat analysis showed comparable in-hospital mortality between intensive and conventional insulin therapy (37.3% and 40.0%, respectively, \( p=0.33 \)).

One RCT (n=620) evaluated an insulin-glucose infusion therapy followed by subcutaneous insulin for more than 3 months in diabetic patients with acute myocardial infarction. Compared with conventional insulin therapy, the insulin-glucose infusion was associated with a statistically significant lower 1-year mortality.

Authors' conclusions
These studies have shown that insulin-based regimens can be of benefit to intensive care or cardiac patients, but there is uncertainty as to the mechanism by which this happens. Further research is required.

CRD commentary
This review addressed a well-defined question in terms of the intervention and study design while it used a broad definition of the participants and outcomes. The authors searched three relevant databases and efforts were made to find additional published and unpublished studies. It is unclear whether language restrictions were applied, therefore language bias cannot be ruled out. The potential influence of publication bias was not evaluated. The authors attempted to minimise bias and errors during the review process by carrying out the study selection and quality assessment processes in duplicate, although the results of the quality assessment were not reported. It was unclear whether the data extraction was also performed in duplicate. The authors' decision not to pool the studies in a meta-analysis was justified given the apparent clinical and methodological differences between the studies.

The failure to report some aspects of the review process, as well as the heterogeneity of the included trials, present potential threats to the reliability and generalisability of the authors' conclusions.
Implications of the review for practice and research

Practice: The authors did not state any implication for practice.

Research: The authors stated that further studies are needed to establish the efficacy of tight glycaemic control, insulin and related regimens.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.