Glycemic control in non-critically ill hospitalized patients: a systematic review and meta-analysis

CRD summary
The authors concluded that intensive control hyperglycaemia in patients hospitalised in non-critical care settings may reduce the risk of infection but not mortality, stroke, myocardial infarction or incidence of hypoglycaemia. The quality of evidence was low and mainly derived from studies in surgical settings. This conclusion reflects the evidence presented and is likely to be reliable.

Authors' objectives
To evaluate the effect of intensive therapy to achieve tight glycaemic control in patients hospitalised in non-critical care settings.

Searching
MEDLINE In-Process and Other Non-Indexed Citations, MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, DARE, HTA database and Scopus were searched from inception through February 2010 with no language restrictions. Search terms were reported. Experts in the field were contacted.

Study selection
Randomised controlled trials (RCTs) or observational studies were eligible for inclusion if they compared the effect of intensive glycaemic control against a control group with less aggressive normalisation of glycaemic levels on adult patients with diabetes who were hospitalised in non-intensive care settings.

The outcomes of interest were mortality, stroke, myocardial infarction, incidence of infections and hypoglycaemia. Studies could include patients from both medical and surgical wards. Studies conducted in intensive care settings were excluded as were studies of patients admitted for the initiation of insulin therapy.

In the included studies the definition of "tight" and "intensive" control varied but was largely consistent with a fasting blood glucose level in the range 100 to 180mg/dL. Patients were in medical or surgical wards or presented with acute coronary syndrome or myocardial infarction. Mean ages ranged from 54 to 75 years. From 19% to 87% of participants were women. Intervention durations ranged from one day to 90 days.

Two reviewers selected studies for the review.

Assessment of study quality
Trial quality was assessed using the GRADE framework for allocation concealment, blinding and losses to follow-up for randomised trials and outcome assessment, loss to follow-up and extent of adjustment for confounders for observation studies.

Two reviewers independently carried out the quality assessment.

Data extraction
Outcomes (mortality, stroke, myocardial infarction, incidence of infections and hypoglycaemia) were extracted from each study to calculate relative risks (RR) with corresponding 95% confident intervals (CIs).

Two reviewers conducted the data extraction.

Methods of synthesis
Pooled relative risks with 95% confidence intervals (CIs) were calculated using a random-effects model. Heterogeneity across the studies was assessed with $I^2$. Subgroup analyses were planned for randomised trials versus observation studies, medical versus surgical and glycaemic target achieved versus not achieved.
Results of the review

Nineteen studies (nine randomised and 10 observational studies) were included in the review (35,425 participants, range 25 to 9,314). The quality of the randomised trials was fair: four reported allocation concealment, five reported no loss to follow-up and one reported blinding of outcome assessors. Eight out of 10 observational studies reported adequate adjustments for confounders and prognostic balance at baseline. Blinding was not reported in any of the observational studies.

Meta-analysis showed that intensive glycaemic control did not reduce the risk of death (11 studies), myocardial infarction (three studies), stroke (three studies) and hypoglycaemia (11 studies). The authors indicated that there was significant statistical heterogeneity ($I^2=60\%$) for these outcomes. Intensive glycaemic control was associated with decreased risk of infection (RR 0.41, 95% CI 0.21 to 0.77; four studies, $I^2=33\%$).

There was an increased risk of hypoglycaemia in surgical ward patients (one study) and when the glycaemic target was achieved. The remaining planned subgroup analyses did not reveal statistically significant interactions.

Authors’ conclusions

Intensive control of hyperglycaemia in patients hospitalised in non-critical care settings may reduce the risk of infection but not in mortality, stroke, myocardial infarction or incidence of hypoglycaemia. The quality of evidence was low and mainly derived from studies in surgical settings.

CRD commentary

The review addressed a clear question and was supported by appropriate inclusion criteria. The search covered a range of relevant sources and included attempts to obtain unpublished data. There were no language restrictions. Publication bias was not formally assessed. The authors were aware of the possibility of publication bias due to the small number of included studies. Two reviewers were involved in study selection, quality assessment and data extraction which minimised potential for error and bias.

A relevant quality assessment tool was applied; it appeared that the reliability of most trials was low. The authors stated that pooling data across the patients with different medical and surgical problems may not have been appropriate (for example patients who received glucocorticoid therapy had an increased risk of hyperglycaemia and patients with impaired kidney or liver function may have been at increased risk of hypoglycaemia). The result of the meta-analysis of reduced risk of infection was dominated by the patients from the surgical wards and it was unclear whether this applied to the patients in medical wards. The authors assessed the statistical heterogeneity. Differences between trials were investigated in subgroup analysis.

The authors’ conclusions reflect the evidence presented and are likely to be reliable.

Implications of the review for practice and research

Practice: The authors stated that further research was necessary before routine incorporation of intensive glycaemic control in settings with limited nursing resources and among patients at varied risk of adverse outcomes from both hyperglycaemia and treatments used to control glycaemia.

Research: The authors stated that large multicenter randomised trials with adequate protection from bias were needed as were trials in medical settings. There was a need to stratify patients according to their comorbidity and the risk of hypoglycaemia, hyperglycaemia and infection to produce practical results that would impact practice.

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