Clinical and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes

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CRD summary
This review investigated the clinical effectiveness and cost-effectiveness of insulin treatment for diabetes, by comparing continuous subcutaneous insulin infusion (from a pump) with multiple daily injections. It concluded that continuous infusion treatment resulted in a modest improvement in glycated haemoglobin levels in adults with type 1 diabetes. This was a well-conducted review and most of the conclusions are justified.

Authors' objectives
To assess the clinical effectiveness and cost-effectiveness of continuous subcutaneous insulin infusion (CSII) using insulin pumps, compared with intensive treatment with multiple daily injections (MDI), in the treatment of patients with insulin-treated diabetes.

Searching
For the clinical effectiveness review, the following databases were searched up to June 2002: the Cochrane Library, MEDLINE (from 1985), EMBASE (from 1980), PubMed (from 2001), the Science Citation Index (from 1990), BIOSIS Previews (from 1999), ISI Web of Science (from 1990), DARE and the HTA database. For the review of quality of life and cost-effectiveness, the following databases were searched up to June 2002: MEDLINE (from 1981), EMBASE (from 1980), PubMed (from 2001), PsycINFO (from 1984), CINAHL (from 1982), NHS EED and EconLit (from 1969). The searches were limited to papers written in English, and all the search terms were reported. Reference lists were checked and experts were contacted for further published and unpublished references. Industry submissions to the National Institute for Clinical Excellence were also reviewed.

Study selection
Study designs of evaluations included in the review
The inclusion criteria stated that parallel-group, randomised controlled trials (RCTs) and randomised and non-randomised crossover studies were eligible. The original review protocol was amended to include non-randomised and observational studies in areas where no eligible studies were found.

Specific interventions included in the review
The inclusion criteria specified that studies comparing CSII using insulin pumps with MDI (at least three injections per day) were eligible for the review. Studies comparing analogue and soluble insulin in CSII were also eligible. The duration of treatment had to be for 10 or more weeks.

Participants included in the review
Studies of patients with insulin-treated diabetes (type 1 or type 2) were eligible for inclusion. This included adults, children, adolescents and pregnant women. Newly-diagnosed patients were excluded. Of the 20 studies included in the review, 14 were in adults with type 1 diabetes, four included pregnant women, two included adolescents, and none included children.

Outcomes assessed in the review
Eligible studies had to report one or more of the following outcomes as the primary outcome: glycated haemoglobin, insulin dose, weight change, lipid levels, patient preference, quality of life, or adverse events. The included studies reported glycated haemoglobin levels at 10 weeks to 4 months, and at 6, 9, 12 and 24 months of follow-up.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for inclusion. Any discrepancies were resolved through discussion or in consultation with a third reviewer.
Assessment of study quality
The quality of the RCTs and crossover studies was assessed using checklists reported by the Centre for Reviews and Dissemination (see Other Publications of Related Interest no.1 The quality criteria were applied by one reviewer and checked by a second. Any discrepancies were resolved through discussion or in consultation with a third reviewer.

Data extraction
One reviewer extracted the data and a second reviewer checked the extraction. Any discrepancies were resolved through discussion or in consultation with a third reviewer. Data on study design, treatments, the numbers of patients, baseline patient characteristics, study methodology and outcomes were extracted. The mean changes from baseline in glycated haemoglobin and the mean daily insulin dose for each treatment group, along with the difference between them, were extracted. Data on patient preference, adverse events and weight change for each treatment group were also extracted.

Methods of synthesis
How were the studies combined?
The data were combined in a narrative. Where appropriate, the weighted mean difference (WMD) between CSII and MDI for glycated haemoglobin and insulin dose were combined using a random-effects model.

How were differences between studies investigated?
Details of the study settings, interventions, patients, outcomes and methods were presented in tabular format, according to the patient group assessed. Differences between the study results for glycated haemoglobin and daily insulin dose were investigated statistically using a chi-squared test.

A sensitivity analysis was also performed by excluding non-randomised crossover studies from the meta-analysis.

Results of the review
Twenty studies (n=646) comparing CSII with MDI were included. Fourteen studies assessed adults with type 1 diabetes: 4 RCTs (n=197), 7 randomised crossover studies (n=128) and 3 non-randomised crossover studies (n=119). Four RCTs assessed pregnant women (n=172) and 2 randomised crossover studies assessed adolescents (n=30).

The quality of the reporting and methodology of the included studies was generally poor.

Adults with type 1 diabetes.
After up to 4 months' treatment (5 studies), CSII was associated with an overall reduction in glycated haemoglobin of 0.64% in comparison with MDI (WMD -0.64, 95% confidence interval, CI: -1.28, 0.01); this reduction was 0.26% (WMD -0.26, 95% CI: -0.57, 0.05) after 6 months (3 studies), and 0.61% (WMD -0.61, 95% CI: -1.29, 0.07) after 12 months (2 studies). Statistically significant heterogeneity was found for the 4-month results (P=0.0035), but not at 6 or 12 months. CSII treatment also led to an overall reduction in the daily insulin dose of 12 units per day (WMD -11.9, 95% CI: -18.16, -5.63) after 4 months, although there was statistically significant heterogeneity between the individual study results (P=0.0002). The results of the sensitivity analyses, which excluded non-randomised studies, were similar. Body weight remained similar in both groups during treatment. Four of the 8 studies with results for patient preference reported that more patients preferred CSII treatment.

Pregnant women.
There was insufficient evidence from the 4 studies in pregnant women that glycated haemoglobin levels or insulin dose differed between CSII and MDI treatment.

Adolescents.
One study found a statistically significant reduction in both glycated haemoglobin (8.8% versus 9.6%, P<0.05) and the total daily insulin dose (44 versus 60 units per day, P<0.001) after 4 months of CSII treatment, compared with MDI.
The other study reported similar levels in each group at 6 months. One study also reported that patients preferred the CSII treatment.

No published randomised trials were found that compared CSII and MDI in the treatment of children.

Cost information
The additional cost of CSII, compared with MDI treatment, varied from £1,091 per year (for the cheapest pump assuming an 8-year lifespan) to £1,680 per year (for the most expensive pump assuming a 4-year lifespan). An additional cost of initial education for patients switching from MDI to CSII was estimated to be £150. It was not possible to calculate the cost per quality-adjusted life-year because of the lack of evidence on quality of life.

Authors’ conclusions
When compared with optimised multiple injection insulin therapy, CSII treatment resulted in a modest, but worthwhile, improvement in glycated haemoglobin in adults with type 1 diabetes. Its main value may be in reducing other problems, such as hypoglycaemia and the dawn phenomenon, and in improving quality of life by allowing greater flexibility in lifestyle.

CRD commentary
This review had a well-defined research question and clear inclusion and exclusion criteria. The searches were wide-ranging and covered a number of databases, although they were restricted to articles in English which may have introduced bias. The quality of the included studies was assessed using recognised criteria. Two reviewers independently selected studies, assessed quality and extracted the data, which helps minimise bias. Publication bias was not assessed. Details of the included studies were presented narratively by patient group, with the results for the primary outcomes pooled in a meta-analysis when there was sufficient data. Statistical heterogeneity between the study results was assessed, and this was further explored using sensitivity analyses. This was a well-conducted systematic review and most of the authors' conclusions are justified by the evidence presented. However, the conclusions that CSII treatment may reduce hypoglycaemic episodes and provide more lifestyle flexibility seem strong given the evidence presented in the review.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that future research should address the wider benefits of CSII treatment, such as flexibility in lifestyle, quality of life and the psychological impact of wearing a device. Research into the use of CSII in children is also needed.

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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.