Continuous subcutaneous insulin infusion in type 1 diabetes

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lives are at risk and the care is expensive, but observational comparisons, incorporating sophisticated indices of risk, can only raise hypotheses. Daly et al certainly suggest a prospective test of their hypotheses—but secure validation of the score itself (against, for example, current APACHE scoring, which has been validated) would be another prerequisite. In the end, intensive care provision at the margin of possible benefit simply has to be assessed by random allocation like everything else about which there is legitimate doubt. There is currently no substitute—unless we are to end up spending 1% of gross national product on intensive care—whatever its actual effect.

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Is beneficial in selected patients and should be more widely available

Almost 25 years ago the *BMJ* published our account of a new technique for achieving long term strict blood glucose control in type 1 diabetes. Continuous subcutaneous insulin infusion,[1] or insulin pump therapy, mimics physiological delivery by using a portable electromechanical pump to infuse insulin at a slow, basal rate throughout 24 hours, with patient activated boosts when food is eaten. Developed by us as a research tool to investigate the impact of greatly improved glycaemic control on diabetic complications, continuous subcutaneous insulin infusion is now used in everyday treatment by at least 130 000 people worldwide, more than 80 000 in the United States alone.

Personal testimony from patients shows that many can achieve better control and lead a more flexible life with a continuous insulin infusion than with other methods. Ironically, in the United Kingdom, the country of its invention, only a few hundred people use it, though there is growing pressure from patients to increase its availability. Doctors' commendable caution about an unfamiliar technique that places new demands on patients and carers has been massively reinforced by the NHS's reluctance to pay for continuous insulin infusion: funding in the United Kingdom is among the lowest in Europe. But is this modest take-up in the United Kingdom justified or are we neglecting valid indications for its wider use?

Much of the scepticism about continuous subcutaneous insulin infusion derives from misunderstandings about its effectiveness, safety, and clinical use. For example, it is often thought that continuous subcutaneous insulin infusion has not been rigorously compared with modern multiple insulin injection treatment. At least 14 randomised controlled trials compare continuous infusion with intensified injection regimens. A meta-analysis of these studies showed that glycaemic control is slightly but significantly better during insulin pump therapy, with a glycated haemoglobin percentage about 0.5% lower than on optimised injection regimens (Pickup J, Mattock M, unpublished).

As to safety, there were initial case reports of hypoglycaemic coma,[2] and the Diabetes Control and Complications Trial reported a high rate of severe hypoglycaemia during continuous subcutaneous insulin infusion (0.54 episodes per patient year).[3] However, other trials have recorded lower rates (0.1,[4] 0.22-0.39,[5] 0.24,[6] and 0.13[7] episodes per patient year), and most evidence suggests that hypoglycaemia is either no more frequent or less common during continuous infusion than on either optimised or non-optimised injection therapy.[4–8] In two recent trials severe hypoglycaemia was 84% less and nearly 50% less than on multiple insulin injection therapy.[5 6] Some studies have found less hypoglycaemia with the non-associating monomeric lispro analogue than with regular human insulin as the pump insulin.[9]

The high rates of ketoacidosis on continuous subcutaneous insulin infusion reported in early studies[10] were probably due to lack of experience; unsuitable pump insulin, with aggregation causing cannula blockage; and the use of less reliable pumps without alarms. Though the small subcutaneous depot of insulin would seem to put patients receiving a continuous infusion more at risk, with proper pump practice the frequency of ketoacidosis is the same as with injection therapy.[4–7]

Continuous subcutaneous insulin infusion can also help improve control in patients who suffer sharply raised blood glucose concentrations before breakfast (the dawn phenomenon).[11] Pumps can be programmed to increase basal infusion rates during the night to counter this dawn rise. There may be other strategies to cope with the dawn phenomenon, such as moving the evening injection of delayed action insulin

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from before supper to bedtime or using new long acting insulins (such as glargine[12]) with essentially peakless action profiles, which need formal comparison with continuous subcutaneous insulin infusion.

Reluctance to fund pump therapy may also stem from the erroneous belief that this would prove very costly. In fact, continuous subcutaneous insulin infusion is not indicated in most people with type 1 diabetes, who can achieve good control with intensified insulin therapy. Real benefits are obtained, however, in perhaps 1-2% of those with type 1 diabetes. Establishing simple clinical guidelines for using continuous subcutaneous insulin infusion will promote its wider, but selective and more rational, availability.

We suggest that a trial of continuous subcutaneous insulin infusion is indicated in patients with type 1 diabetes with frequent, unpredictable hypoglycaemia or a marked dawn blood glucose rise, whose poor control persists in spite of optimised insulin injection therapy (including educational support and attention to blood glucose self monitoring and injection technique). Some patients who lead unpredictable lives with delayed meals experience wide swings in blood glucose concentration and are particularly liable to hypoglycaemia when they try to tighten control with injection therapy. The few pregnant patients with diabetes who fail to achieve impeccable control with injections should also be considered. All candidates should be willing to learn about and undertake pump therapy and its associated procedures such as regular blood glucose monitoring; this includes patients well controlled on insulin injections who simply prefer pump therapy and are willing to pay for their pumps and supplies. People with psychological problems and major psychiatric disorders tend not to do well in meeting the demands of continuous insulin infusion. Proper facilities for pump training and medical supervision must be in place. In view of the limited numbers of patients and expertise needed, pump care should normally be delivered at specialist centres.

If clinical guidelines on the use of continuous subcutaneous insulin infusion can be agreed then NHS funding should also be committed for the relatively few patients for whom it will make a difference. For them continuous insulin infusion can substantially improve the quality of their lives and the course and outcome of their diabetes.

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Minimed, an insulin pump manufacturer, has given funds to GKT School of Medicine to support some studies and clinical activities related to insulin pump therapy.

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The *BMJ*'s ethics committee is open for business

Editors face a surprising number of ethical problems

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A paper on the workings of the ethics committee and minutes of its first meeting appear on bmj.com

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About a year ago the *BMJ* decided to form an ethics committee to help us with the increasing number of ethical problems we face.[1] The chairman and members were appointed last year,[2] and the committee met for the first time at the end of last year. Interested readers will find the minutes on bmj.com, along with a paper on how the committee works and what it does. One gratifying feature of the first meeting was that our committee endorsed broad approaches—for example, about consulting authors over ethical worries and consent—that *BMJ* editors had already adopted.

The ethics committee's business will be as transparent as possible. The manuscripts under discussion are confidential, however, so we have anonymised them to protect authors' privacy. The UK's Committee on Publication Ethics takes the same approach in its annual report.[3]

We discussed eight papers at the first meeting, all referred by *BMJ* editors concerned about some aspect of the design, conduct, or implications of a report. All but two were case reports or case series, not formal research. These kinds of papers cause particular problems because they are never submitted for ethical review, don't count as research, contain identifiable patient details, and often conclude that things could have been managed better (often by someone else). Case series reporting clinical "experimentation" with different drugs