Current topic

A decade of insulin infusion pumps

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Over the past 10 years there have been many changes in the details of diabetic management. The development of home monitoring for capillary blood glucose and widespread availability of measurements of glycosylated haemoglobin have provided direct evidence that most diabetic children have poor or very poor glycaemic control. Additionally, there has been further evidence in support of the hypothesis that poor metabolic control predisposes susceptible diabetic patients to the microvascular and macrovascular complications of the disease.¹ Frustration that glycaemic control has not improved with regimens of one, two, or more recently, three² daily injections using the new, pure, and latterly, human insulins has focused attention on alternative ways of delivering insulin in the hope of achieving improved glycaemic control.

In 1978 continuous subcutaneous insulin infusion driven by a small battery powered portable pump was introduced as a research tool for improving glycaemic control in adults with insulin-dependent diabetes mellitus.³ The infusion system provided a continuous supply of unmodified short acting insulin throughout 24 hours with supplementary boluses of insulin initiated by the patient and given before meals. The developments coincided with the introduction of other 'tools' of management such as better education, the establishment of diabetic liaison health visitors, and an improved understanding of the role of diet and exercise in the management of diabetes.⁴ Portable insulin infusion pumps seemed to be a timely technological advance.

Early studies of the euglycaemic effects of infusion pumps were encouraging.^{5–8} Have the hopes engendered by these early favourable reports been fulfilled? Has the efficacy of insulin infusion systems under conditions of tightly controlled clinical trials in specialised centres been successfully translated into general clinical practice? Put more specifically:

(1) Is insulin infusion an effective regimen that can be applied to large numbers of unselected children with insulin-dependent

diabetes mellitus ranging from infancy, through school age, to adolescence, and young adulthood?

(2) How does insulin infusion compare in terms of blood glucose control with one, two, or multiple daily injection regimens?

(3) Are the indications for and complications of insulin infusion clearer?

(4) Does insulin infusion reduce the incidence of the microvascular and macrovascular complications of diabetes?

The effectiveness of long term insulin infusion

The documented world paediatric experience is small. The total number of children reported is less than 500 with no single centre reporting experience of more than 42 children.⁹ Many reports concern highly selected and motivated children and report favourably. Reports when children are selected for other variables, such as poor metabolic control,^{6 10} tend to have poorer results with higher withdrawal rates and often little advantage in glycaemic control for infusion pump users.

(A) YOUNG ADULTS

There has been one major report of longer term experience with insulin infusion pumps in young adults: Knight reported the experience of 45 young adult diabetic patients aged from 16 to 19 years of age who were approached about the use of infusion pumps as part of the Sheffield pump feasibility project.¹¹ Thirteen (29%) young people initially chose to try the treatment but only four of the 11 who actually started infusion pump treatment continued for one year; this represents a 64% discontinuation rate. These data compare with a 30% discontinuation rate among adult diabetic patients in the same clinic. Moreover, there was a relatively high rate of ketoacidosis and other medical complications in this group of young diabetic patients.

(B) ADOLESCENTS

Since the early reports of insulin infusion in selected groups of diabetic children there have been no large feasibility studies from the United Kingdom. Reports from the United States^{10 12} and The Netherlands¹³ support the general conclusion that infusion pump systems can work on selected adolescents but that there is a variable, and usually high, discontinuation rate. The impression from recent studies is that overall, even among those who adhere to the pump regimens, there is only a modest improvement in glycaemic control. None the less within each population studied there was a small group of patients who could do well and for whom the pump was an acceptable advance in management.

(C) INFANTS

One report showed that infusion pumps can be used in the 12 month to 2 year age group.¹⁴ The pump is worn in a harness on the back, and may in selected cases provide an improvement in glycaemic control for these patients who present difficult management problems.

One recent study from The Netherlands is worth noting.¹³ Thirty four consecutive children, aged from 1·9 to 16·8 years, were randomised at diagnosis to treatment with an infusion pump or to one or two daily insulin injections. There were five withdrawals from treatment with the pump: four before the start and one after 28 months. After one year the mean (SD) glycosylated haemoglobin concentration in the group treated by infusion pump (9·5 (1·9)%) was considerably better than the conventionally treated group (11·3 (1·6)%) but still above the normal non-diabetic range.

Taken together (perhaps with the exception of the report from The Netherlands), these studies, on small numbers of young people, compare unfavourably with the large multicentre studies of adult diabetic patients where glycaemic control has been shown to improve and be sustained in the group randomised to pump compared with conventional insulin treatment for two years or more.^{15 16}

Infusion pumps have not been taken up enthusiastically by British paediatricians. The high discontinuation rate, modest improvement in glycaemic control, and lack of the necessary practical pump experience has meant that most paediatricians do not use infusion pumps. Many clinics have no children using pumps and our impression is that recruitment of new pump users in paediatric clinics has virtually ceased.

It is difficult to predict which patients will successfully use infusion pumps. Success does not seem related to intelligence, knowledge of diabetes,

parental interest, or social background.¹⁷ It is likely that patients who view the pump as a 'cure' for their diabetes will do particularly badly. The development of scales to measure 'adaptation to diabetes' may go some way towards providing an instrument to identify children who will do well on one or other particular regimen.

Comparison with intensified insulin regimens

In the early 1980s there was a series of reports comparing insulin infusion with intensified, three or four times a day, injection regimens. The report of Schiffrin *et al* provided the most information on the largest group of children, and it showed an improvement in glycaemic control for both intensified insulin regimen and insulin infusion.⁸ In her study the insulin pump provided better glycaemic control. The intensified insulin regimen was administered using conventional syringes and needles.

More recently the development of portable injection devices such as the Penject (Beckett-Dickinson Ltd), NovoPen (Novo Laboratories PLC), and Insuject (Nordisk UK Ltd) has meant that multiple daily injection regimens are easier to administer. There has as yet been no properly organised, prospective, and randomised, large scale comparison of an intensive portable injection insulin regimen compared with an infusion pump regimen. Such a study would be a difficult and expensive undertaking. It would have to address the decision to use pumps or pens as a contest between alternative regimens. Motivated and compliant patients, however, will probably improve on either regimen and the challenge lies in identifying which patients will do best on which regimen.

Indications and complications of insulin infusion

There are no absolute indications for insulin pump use in either adult or paediatric practice. Certain patients want to use infusion pumps because of their apparent convenience and potential flexibility: allowing them to alter or omit meals or snacks and to exercise at will. Children and parents may be seduced by the novelty and technology of the infusion system and believe that the pump will easily achieve improved control.

After a decade of experience it is recognised that there is an increased incidence of diabetic ketoacidosis in infusion pump users. This particular risk, however, seems to lessen as the clinic becomes more used to using pumps and patient education improves.^{18 19} It is now clear that children should test their urine for ketones when the stability of glycaemic control is stressed—for example, during infections.

Hypoglycaemia is probably no more common among pump users than in children on conventional insulin treatment, but information on which to assess this risk with any precision is not available. Mild hypoglycaemia, with a blood glucose concentration in the order of 3.2 mmol/l, causes variable symptoms, particularly a delay of reaction time, in diabetic patients.²⁰ The nature of the insulin pump system means that unless the subject senses hypoglycaemia the insulin continues to be infused—a situation that then becomes frankly dangerous.

Cognitive unawareness is traditionally thought to occur in patients with a long duration of disease. It has been reported, however, in those who have had diabetes for only five years and who have otherwise normal selected cardiovascular tests of autonomic function.²⁰ The dangers of hypoglycaemia may be potentiated by improved glycaemic control, which has been shown to reduce the plasma glucose threshold at which glucose counter-regulatory hormones are released thus theoretically reducing the level at which hypoglycaemic awareness is detected by the patient.²¹

Infusion site infection is uncommon but needs to be guarded against by frequent (say twice weekly) changes of infusion catheter and site. Some 10% of children have developed recurrent small subcutaneous abscesses that are unsightly and potentially life threatening. One death has been reported in an adult patient from endocarditis after such an infection.²²

Pump size and performance have been given as objections to the continuation with insulin infusion treatment. The pump may become physically or psychologically unsightly. System failure is common. Insulin aggregates in the cannula or needle or the cannula leaks. While the pumps themselves are mechanically reasonably reliable, patients may run out of supplies of insulin, cannulae, batteries, or blood glucose testing equipment.

Reduction of the complications of diabetes

Insulin infusion can improve glycaemic control but not all the metabolic abnormalities of diabetes are rectified.²³ The improvement in glycaemic control, however, has been sufficient to improve retinopathy, nephropathy, and neuropathy in adult patients.¹ In paediatric populations the modest improvement in glycaemic control has not proved adequate to reduce increased albumin excretion or reduce a raised creatinine clearance towards more normal levels.¹⁰ Thus the hope that improved glycaemic control would reduce the incidence of the complications of diabetes has not yet proved feasible for adolescent patients. Longitudinal studies are

urgently required to evaluate different insulin regimens against early markers of latent diabetic complications.

Conclusions

The advent of intensified insulin regimens over the past 10 years has coincided with other improvements in the management of patients with diabetes. These developments have drawn attention to the difficulties many diabetic adolescents face and have thus stimulated further exploration of insulin regimens, metabolic regulation, subtle physiological abnormalities, and psychological function. Intensive insulin regimens will expose deficiencies in the organisation of clinics and staff. Repair of these deficiencies is to the good of all patients but poses difficult questions about the use of resources. The infusion pump has in one sense been a false prophet and has not lived up to expectations in paediatric practice.

Insulin pens are being enthusiastically promoted and used in many clinics. The pens have a different but rational insulin delivery system and seem to be relatively safer than infusion pumps. There is, however, one preliminary report of rapid metabolic decompensation associated with pen use. (SM MacRury, AB Boal, KR Paterson. Diabetic ketoacidosis during NovoPen therapy. Poster 53. British Diabetic Association, Medical and Scientific Section Autumn Meeting, Cardiff, 1986). It is obvious that no insulin regimen is suitable for all users. The urgency remains to seek new strategies of management and to settle for nothing short of ultimate cure and prevention of diabetes. Insulin pumps have, however, clarified the reality of poor glycaemic control, the need for health education in diabetes, and the magnitude of the task ahead.

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