Clinical application of insulin pumps in the management of insulin dependent diabetes

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SUMMARY Seven volunteers aged 12.0 to 17.9 years participated in a trial to compare conventional insulin treatment with continuous open loop (pump) insulin infusion. After 6 weeks of conventional treatment followed by 6 weeks of insulin pump treatment, 4 children chose to manage their diabetes permanently by means of the insulin pump. The mean blood glucose concentration (based on home blood glucose monitoring) while on conventional insulin treatment showed no appreciable change during the 6 weeks' treatment on an insulin pump. Compared with conventional treatment, however, the mean 24 hour blood glucose profiles of the patients on pump insulin showed less variation in the blood glucose throughout the day, together with an appreciably lower peak after breakfast. These improvements occurred despite increased dietary flexibility while on pump insulin. The insulin pump seems to be an acceptable form of treatment for some children and young adults with diabetes mellitus and gives near physiological control of blood glucose.

Insulin pumps have been used successfully in the management of diabetes mellitus in the past few years.¹ There have been published reports of their use in younger adults² but their main clinical application has been in the management of the older patient (mostly in research trials)³ and in patients who have clinically unstable diabetes.⁴ The introduction of pumps has been widespread in the United States where it is estimated that between 4000 and 5000 diabetic patients use them.⁵ In the United Kingdom, however, their use has been more limited.

We investigated the use of insulin pumps in children and young adults, noting their acceptability and influence on blood glucose control. We report the results of this study, carried out in the Oxford Paediatric Diabetic Clinic over the past 12 months.

Patients and methods

We were interested primarily in insulin pumps in the management of the 'average child' with diabetes. We did not choose preferentially patients with 'brittle diabetes', although some of our patients had had periods of appreciable clinical instability. Twenty three likely candidates (8 girls, 15 boys) attending the paediatric clinic were approached as potential insulin pump users. All were aged 10 years and over, and during discussions in the clinic had

expressed an interest in the pump. In the event only 7 patients volunteered for the trial; all were boys aged 12 to 17.9 years (mean 14.6 years) and the duration of their diabetes ranged from 3.5 to 7.1 years (mean 5.7 years) (Table). They came from various socioeconomic backgrounds—social class I(2), II(1), III(4) (Office of Population Censuses and Surveys). Three patients were receiving twice daily

Table Characteristics of the 7 patients in the study group

Age (years)	
Mean	14.6
Range	12.0-17.9
Duration of diabetes (years)	
Mean	5.7
Range	3.5-7.1
Insulin treatment	Once daily (n=5) Twice daily (n=2)
Insulin dose (units/kg)	
Conventional treatment	
Mean	0.99
Range	0.6-1.37
Pump treatment	
Mean	0.83
Range	0.5-1.12
Weight gain (kg)	
Mean [†]	1.7
Range	0-4.0

injections of Actrapid and Monotard insulin: (Novo Laboratories) the remaining 4 were on Actrapid and Monotard once daily. Informed consent was given by the patients and parents and the study was approved by the health district ethical committee.

The study protocol was 6 weeks of conventional treatment followed by 6 weeks of insulin pump treatment. Control of blood glucose concentrations throughout the study was achieved by home blood glucose monitoring and appropriate adjustment of insulin dose. Home blood glucose monitoring was done at least once daily and on successive days tests were staggered to sample at different times of the day. Twice each month a 7 test profile of blood glucose estimations was also performed. Blood glucose measurement was by Dextrostix and Glucometer system (Miles Laboratories Ltd). Venous blood samples were taken at the end of each 6 week period for measurement of glycosylated haemoglobin (ion-exchange chromatography (BioRad Ltd)).

Pump specifications. Five children used the Autosyringe AS6C model (Travenol Ltd), and 2 used a Graseby Dynamics MS26 model. Both systems provided a continuous insulin infusion, together with preprandial bolus doses of insulin that were given manually. With the Autosyringe system either U40 or U80 insulin was used, depending on the total dose. One child used the 1 ml U100 Autosyringe model with U100 Human Actrapid insulin (Novo Laboratories). With the Graseby Dynamic MS26 model both patients used U100 Human Actrapid. The infusion system was the Autosyringe Microvolume Infusion set with a 27 gauge needle placed into the anterior abdominal wall. No skin preparation was used and the needle was secured by a small piece of adhesive tape. At first the infusion sets were changed daily, mostly before going to sleep, but subsequently the same needle was re-used, allowing 1 needle every 4 days. The pumps were powered by either rechargeable batteries or standard 9V batteries.

Diet and exercise. At first the children were advised to remain on their prescribed carbohydrate diet. For mild exercise, which was encouraged, the pump and infusion system were kept in place. The pump was detached before and replaced after vigorous exercise such as football or swimming and the children were allowed up to 2½ hours without the pump. Although this time was selected intuitively, strict blood glucose testing during these periods showed that it was safe, and in most cases exercise lasted much less than 2½ hours.

Insulin dose. The initial insulin dose on the pump

was calculated on the basis of the patient's conventional treatment. Half of this was given as a continuous basal infusion and the remainder divided into preprandial bolus doses. A bolus dose was given only for a meal or snack with a carbohydrate content equal to or greater than 20 g. Despite the slightly lower carbohydrate content of breakfast compared with other daily meals, approximately 40% of the day's bolus insulin was given before breakfast (this is because the blood glucose concentration is usually at its highest after breakfast—an observation noted on various conventional insulin regimens).^{6,7} Before lunch 30% of the day's bolus insulin was given and the remaining 30% before the main evening meal. During sleep the pump remained on, delivering the continuous basal infusion. In the first 2 weeks on pump treatment the basal rate and bolus doses were adjusted to individual requirements assessed by the home blood glucose monitoring results.

Results

The 7 patients were on conventional insulin for 6 weeks followed by insulin pump for a minimum of 6 weeks. The mean of all home blood glucose measurements and glycosylated haemoglobin values obtained on conventional and pump treatment are shown in Fig. 1. The blood glucose concentration of the 7 patients on conventional insulin treatment (mean (SD) 9.0 (1.4) mmol/l (162.16 (25.23) mg/100 ml)) showed improvement during the 6 weeks on pump treatment (mean (SD) 8.1

Fig. 1 Mean blood glucose and glycosylated haemoglobin concentrations on conventional insulin and insulin infusion pump treatment.

Conversion: SI to traditional units—blood glucose 1 mmol $\approx$ 18.01 mg.

(1.6) mmol/l (145.95 (28.83) mg/100 ml). This was not, however, statistically significant. Likewise, the glycosylated haemoglobin value on conventional treatment (mean (SD) 10 (1.0)%) showed improvement during the 6 weeks on pump treatment (mean (SD) 9.2 (1.7)%) but again this was not statistically significant. In 5 patients there was a fall in both the mean blood glucose and glycosylated haemoglobin values. In 2 patients, the mean blood glucose and glycosylated haemoglobin values rose on changing from conventional to pump treatment.

On conventional treatment there were the expected peaks and troughs in the 24 hour blood glucose profiles.⁶ In all 7 children on pump treatment the peaks and troughs were reduced and the SD of the blood glucose value fell at each of the 7 selected points in the day. There was a significant difference between conventional treatment and pump treatment in the post-breakfast blood glucose peak—conventional, mean (SD) 13.4 (3.9) mmol/l (241.44 (70.27) mg/100 ml); pump, mean (SD) 7.9 (1.9) mmol/l (142.34 (34.23) mg/100 ml); $P < 0.01$, Student's *t* test (Fig. 2). The 24 hour insulin dose did not change appreciably between conventional and pump treatment.

All children made substantial alterations to their diet on changing to pump insulin with the omission of morning and afternoon snacks and variation in the timing of the carbohydrate content of the main meals but there was no appreciable change in weight on either treatment. All children said they felt better and healthier while on the pump and this was confirmed by their parents.

Fig. 2 Twenty four hour blood glucose profiles comparing conventional treatment with insulin pump treatment. Each point represents the mean (SD) of 7 patients: in each patient at least 20 blood glucose estimations were performed for each point in the day over each 6 week period.

One patient developed a small area of cellulitis at the infusion site which resolved on resiting the needle, but there were no serious episodes of hypoglycaemia or diabetic ketosis on either treatment. One child aged 12 years was admitted to hospital 2 weeks after starting pump treatment because of erratic blood glucose control, but this improved with further instructions on using the pump.

Discussion

This study confirms to some degree the published reports that improved control in adults can be achieved by insulin pump treatment^{1,2} and that pumps are acceptable to children and young adults. Although patients were not randomly divided into 2 groups according to which form of treatment came first, equal effort was made to optimise blood glucose control in each period. Two of the children who had clinically unstable diabetes before entering the trial achieved more stable metabolic control together with an overall improvement in their general health. Insulin pump treatment produced a 'flatter' 24 hour blood glucose profile with a reduction in the post-breakfast peak (Fig. 2).

The main clinical benefit of the insulin pump reported by the children was flexibility in the daily routine, particularly diet. Meals were omitted or delayed and as confidence in the use of pumps grew, preprandial insulin dosage was adjusted depending on the carbohydrate content of the meal. With similar changes in dietary routine on conventional treatment, blood glucose control would be expected to deteriorate.

The basal infusion rate was adjusted according to the pre-breakfast blood glucose concentration. Limited data of blood glucose values at 3 am suggested that this was satisfactory as nocturnal hypoglycaemia was avoided. The 3 am and pre-breakfast blood glucose values were in the upper range of normal—6.1 mmol/l (109.91 mg/100 ml) and 8.1 mmol/l (145.95 mg/100ml) respectively. These concentrations, similar to those recommended by Unger⁵ in his cautionary note on possible dangers associated with meticulous control of diabetes by insulin infusion pump, were suggested to avoid severe nocturnal hypoglycaemia, a factor implicated in a report from the United States^{8,9} on 12 deaths in diabetic adults using insulin infusion pumps.

The complications with insulin pumps were minimal. One patient had mild cellulitis that was treated by removal of the needle; 1 child required a second hospital admission to improve his understanding of the pump system. All of the children passed through a phase of disenchantment with the

pump in the first 2 weeks, but by the end of the 6 weeks were at ease with the management of their diabetes in this way. Four patients, aged 12, 15, 16, and 17 years, chose to continue with their pumps.

Several imperfections in the systems were noted by all the children. Particularly noteworthy was the overall size of the pump, with bulk rather than weight causing problems. This was overcome to some extent in 2 children who used the Graseby Dynamic pump by wearing the system in a shoulder holster. There were no mechanical errors or pump failures but on 2 occasions there was breakage of the insulin syringe at the point of connection with the infusion systems. On 5 occasions the needle became dislodged at the infusion site in the abdominal wall; mild hyperglycaemia, detected by the children themselves, resulted. There were no difficulties with attachment of the machine by day or night and sleeping was not a problem. Attendance at school was unaffected as were all other everyday activities.

Several objections have been raised to the widespread clinical use of insulin pumps. Cost is obviously an important consideration: the machines are expensive to buy, and their running costs are high compared with conventional treatment. Despite this, the parents of 4 diabetic children expressed a desire to purchase their own systems.

Another important consideration is the burden placed on clinic staff by the extra care and advice required to convert large numbers of patients safely to insulin infusion pumps. The patients require a clear understanding and must be prepared to monitor their diabetes closely by measuring blood glucose at home.

Despite these reservations this study has shown that insulin pump systems are an acceptable treatment for young adults and children with insulin dependent diabetes mellitus. They offer near physiological control of blood glucose while releasing the child from some of the rigidity of the

daily routine. It is envisaged that developments in pump technology will result in new generations of less expensive and more compact machines.

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References

- 1 Pickup JC, Keen H, Viberti GC, *et al.* Continuous subcutaneous insulin infusion in the treatment of diabetes mellitus. *Diabetes Care* 1980; **3**: 290-300.
- 2 Tamborlane WV, Sherwin RS, Genel M, Felig P. Out-patient treatment of juvenile onset diabetes with a preprogrammed portable subcutaneous insulin infusion system. *Am J Med* 1980; **68**: 190-6.
- 3 Viberti GC, Pickup JC, Jarrett RJ, Keen H. Effect of control of blood glucose on urinary excretion of albumin and B₂ microglobulin in insulin-dependent diabetes. *N Engl J Med* 1979; **300**: 638-41.
- 4 Willms B, Talaulicar M, Franetzki M. Treatment of brittle diabetics with portable insulin infusion systems. In: Owens DR, ed. *New approaches to insulin therapy*. Proceedings of the 2nd Vienna-Lainz Diabetes Symposium. Lancaster: MTP Press, 1981: 79.
- 5 Unger RH. Meticulous control of diabetes: benefits, risks and precautions. *Diabetes* 1982; **31**: 479-83.
- 6 Werther GA, Turner RC, Jenkins PA, Baum JD. Twenty-four hour profiles of plasma C-peptide in Type I (insulin dependent) diabetic children. *Diabetologia* 1982; **22**: 245-9.
- 7 Schmidt MI, Hadji-Georgopoulos A, Rendell M, Margolis S, Kowarski A. The dawn phenomenon, an early morning glucose rise: implications for diabetic intraday blood glucose variation. *Diabetes Care* 1982; **4**: 579-85.
- 8 Centers for Disease Control: Deaths among patients using continuous subcutaneous insulin infusion pumps. *Morbidity and Mortality Weekly Report*. 1982; **31**: 80-7.
- 9 Anonymous. Deaths in diabetes using insulin infusion pumps. *Lancet* 1982; **i**: 636.

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