Insulin pump therapy

NEALE COHEN FRACP

It is becoming more frequent for patients with type 1 diabetes to present with a request to go on an insulin pump. Here is an overview of insulin pumps and the capabilities of the latest models.

Insulin pump therapy is becoming increasingly popular in patients with type 1 diabetes. Continuous subcutaneous insulin infusion pumps have been evolving over the past 20 years, becoming progressively smaller in size and more complex in function. In the last five to 10 years, insulin pump therapy has become an important treatment option for patients with brittle type 1 diabetes and for those wanting more flexibility in the treatment of their diabetes. It should, however, be considered only after a trial of multiple daily injections (MDI) therapy with a long-acting insulin analogue (detemir [Levemir], glargine [Lantus]).

Insulin pump therapy is an intensive form of therapy and is best managed in specialist diabetes centres where diabetes nurse educators and dietitians are available as well as physicians.

This article focuses on the current use of this relatively new technology in the treatment of type 1 diabetes and the potential benefits to outcomes, including improvement in diabetic control, and to lifestyle and costs.

What is an insulin pump?

An insulin pump is a computerised device designed to deliver a continuous subcutaneous insulin infusion at different rates and also bolus doses according to a patient's needs. Insulin pumps are mostly external devices, worn 24 hours a day, with temporary subcutaneous cannulae that are replaced by patients every three days. Insulin pump therapy, generally requires frequent finger prick glucose testing, and in this respect is similar to the intensive insulin therapy, MDI therapy. Only rapid-acting insulins (aspart [NovoRapid], lispro [Humalog], glulisine [Apidra]) are used in pumps and insulin pump therapy is indicated only for the treatment of type 1 diabetes.

The most recent insulin pumps in Australia include the Deltec Cozmo (Medical Specialties Australia), DANA Diabecare IISG (DiaCare International), MiniMed Paradigm REAL-Time System (Medtronic), Animas 2020 (Australian Medical and Scientific) and D-Tron, Accu-Chek Spirit and H-Tron (Roche Diagnostics). The capabilities of the latest pumps are discussed in the box on page 69.

Permanent insulin pumps, which are implanted surgically, are being developed. However, as they are not available for general use, they will not be discussed further here.

Rationale for pump use

The erratic nature of type 1 diabetes is in part caused by variation in insulin absorption. The more modern insulin analogues detemir and glargine have less variable absorption than the older insulins such as isophane, which they have now largely replaced.[1]

There is a small proportion of patients with type 1 diabetes who continue to have large fluctuations in blood glucose levels despite MDI therapy and the use of the new insulin analogues. Continuous insulin infusion reduces fluctuations in insulin absorption and blood glucose levels and is a suitable alternative therapy for these patients.

There have been many studies investigating pump therapy and its clinical outcomes and it is now generally accepted that pump therapy improves glycaemic control compared with MDI therapy. Meta-analyses show an improvement in HbA_{1c} of 0.5 to 1.2% with pump therapy compared with MDI therapy.[2,3] However, many of the studies in these analyses use old pump technology and old insulin. More recent prospective trials show improvement in HbA_{1c} of 0.4 to 1.4% with pump therapy compared with MDI therapy. There are some studies comparing pump therapy and MDI therapy using the long-acting insulin analogues, but these are small in size and duration and more work is needed in this area.[4-7]

One of the most important aspects of pump therapy is that it reduces the numbers of hypoglycaemic episodes. Most recent studies of pump therapy show reduction in hypoglycaemia and this is impressive considering that most treatments that improve HbA_{1c} mostly increase hypoglycaemia.[8] This reduction varies according to the patient population being studied but has been described as an up to 80% reduction.[8] In terms of patient quality of life, this is one

Dr Cohen is Director of Clinical Services, International Diabetes Institute, Caulfield, Vic.

of the most important benefits to the patient.

Patient groups

GPs play an important role in identifying patients with type 1 diabetes who may be appropriate for insulin pump therapy. Between 5 and 10% of patients with type 1 diabetes have unstable or brittle diabetes, resulting in poor control and frequent hypoglycaemia. In this setting, pump therapy should be considered if trials with intensive MDI and the new insulin analogues have not been successful in achieving good control. Patients with hypoglycaemia unawareness and those experiencing severe hypoglycaemia with loss of consciousness or fitting should also be considered for insulin pump therapy.

Pumps are becoming more popular in paediatric and adolescent groups with type 1 diabetes. These patients often require greater flexibility in insulin doses and have the greatest fluctuation in day to day diet, exercise and lifestyle. Hypoglycaemia is also a serious management issue in young patients, and causes much anxiety in parents managing their children's condition. Most recent paediatric studies show a reduction in hypoglycaemia rates with pump therapy.

Pregnant women with type 1 diabetes need to achieve optimal diabetic control for the best pregnancy outcomes. Insulin pump therapy provides the most aggressive form of treatment in this group and some centres provide it as a temporary treatment for the duration of the pregnancy.

Diabetic gastroparesis is a complex management issue in type 1 diabetes. This neuropathic complication, which gives rise to delayed gastric emptying and absorption of gastric contents, is often associated with recurrent vomiting and therefore requires careful adjustment of meal-time insulin doses. Most new pumps have the capability of adjusting bolus doses to a prolonged bolus, allowing slow administration of bolus insulin doses to cover the extended time of raised blood glucose resulting from the slow digestion in gastroparesis.

Some patients will simply choose to use an insulin pump for lifestyle issues and flexibility in terms of timing of doses with the ability to skip doses, eat at variable times or give extra doses of insulin. It is becoming more frequent for patients to present with a request to go on a pump.

Costs

Insulin pumps are expensive but the running costs are generally small. In Australia, the current cost of about $8000 for a pump is covered by most private health insurance policies with hospital cover. Tubing costs are about $15.00 per month as the infusion sets are now available on the National Diabetes Services Scheme (NDSS), which is administered for the Commonwealth by DiabetesAustralia(www.diabetesaustralia.com.au/ndss/index.html). The continuous glucose monitor attachment in the new Medtronic pump system is more than $1000, and is very expensive to run (more than $4000 per year if used all the time). Battery costs vary according to the type and model of pump used.

Capabilities of the latest insulin pumps

Insulin pumps administer continuous insulin at basal rates that are adjustable from hour to hour according to the patient's requirements. In general terms, basal insulin constitutes about 50% of a patient's total daily insulin requirements. Infusion rates are varied throughout the day and are determined by the treating physician, the diabetes educator and the patient over an initial stabilising period according to general blood glucose trends. It is possible to set up many different infusion rates for most modern pumps. It is also possible to set up different basal insulin profiles, such as a sick day profile or a profile for days on which a lot of exercise is done.

Pumps also deliver bolus doses of insulin, under the control of the patient. Mostly these are given as pre-meal boluses but correction boluses are given for blood glucose levels that are not in the required range. The most recent pumps are capable of calculating appropriate bolus doses according to the information provided. For example, a pre-meal bolus dose will be calculated based on the carbohydrate load of the meal about to be consumed and the current glucose measurement; and a correction bolus will be calculated taking into account the current blood glucose measurement and the timing of the most recent insulin dose. Most of the current pumps have the capability to individualise doses according to the patient's insulin sensitivity (the expected blood glucose lowering effect of a unit of insulin) and his or her response to carbohydrate (number of units of insulin required per amount of carbohydrate consumed). Current pumps are also able to set target blood glucose levels. All these settings can be easily adjusted by patients and medical staff. Many pumps also have bolus shaping capabilities that allow slower administration of bolus doses, which is of use in patients with gastroparesis.

Some pumps are able to download data for analysis, including blood glucose profile, basal and bolus insulin profiles and total daily insulin use. The most recent Medtronic insulin pumps, the MiniMed Paradigm 522 and 722, can be combined with a continuous glucose monitoring system that monitors blood glucose levels every five minutes and transmits this information to the pump – the MiniMed Paradigm REAL-Time System. With this capability, it is possible for a patient to get a 'real-time' continuous glucose reading and respond to it without having to monitor their blood glucose by frequent finger prick testing.

Costs to the community for insulin pump therapy have been studied in the United Kingdom and, more recently, in Australia.[9,10] These studies showed good cost effectiveness compared with MDI therapy for type 1 diabetes. They took into account the long-term complications of diabetes projected over a lifetime as well as lifetime costs of pump therapy and the large amount of medical and paramedical time involved in the initiating of pump therapy. Results were comparable to many of the current pharmaceutical agents that have been approved for use on the PBS system. The Australian study showed that in most poorly controlled groups of patients with type 1 diabetes the cost per life-year gained was about $76,000.[10] The greatest cost effectiveness was therefore in groups who would be expected to achieve an HbA_{1c} reduction of 1.2% or more.

Initiation of pump therapy

Pump therapy is an intensive form of treatment requiring time and effort on the part of the patient and the medical staff. Before commencing therapy there is an education process involving appointments with a diabetes educator, physician and dietitian; this may take up to several months. Pump therapy may be initiated as an outpatient or with a brief hospital stay. Insulin doses are calculated according to previous total insulin requirements and divided into basal insulin and bolus doses. Stabilisation occurs over a period of a few weeks with close and regular monitoring by medical staff.

Complications of pump therapy

The main complications of insulin pump therapy include insertion site infections and pump malfunctions. These are infrequent in our experience and rarely lead to discontinuation of pump therapy.

In the case of pump site infections, patients must remove the cannula and reinsert it in a different location. These infections may relate to subcutaneous haematoma formation or leaving the cannula *in situ* for longer than the advised three days.

In the case of pump malfunctions, patients must have adequate access to medical staff. Line blockages may occur, resulting in an unexpected rise in blood glucose; these are best treated with removal and replacement of the cannula. In the case of pump failure, most insulin pump companies are able to provide a replacement pump within 24 hours. Very occasionally patients may need to revert back to regular insulin injections for the interim period until a replacement pump becomes available.

The incidence of diabetic ketoacidosis with modern pump therapy is generally thought to be similar to the rates with MDI therapy.

Summary

Insulin pump therapy is a cost-effective treatment for unstable type 1 diabetes and is currently used in about 5 to 10% of patients with type 1 diabetes. It provides improved glycaemic control compared with MDI therapy, and also reduces the incidence of hypoglycaemic episodes.

Pump therapy should be considered only after a trial of MDI therapy with the new long-acting insulin analogues. Patient groups in whom insulin pump therapy is appropriate include patients with severe hypoglycaemia, hypoglycaemia unawareness, brittle diabetes and diabetic gastroparesis. MT

References

1. Fulcher GR, Gilbert RE, Yue DK. Glargine is superior to neutral protamine Hagedorn for improving glycated haemoglobin and fasting blood glucose levels during intensive insulin therapy. Intern Med J 2005; 35: 536-542.
2. Weissberg-Benchell J, Antisdel-Lomaglio J, Seshadri R. Insulin pump therapy: a meta-analysis. Diabetes Care 2003; 26: 1079-1087.
3. Pickup J, Mattock M, Kerry S. Glycaemic control with continuous subcutaneous insulin infusion compared with intensive insulin injections in patients with type 1 diabetes: meta-analysis of randomised controlled trials. BMJ 2002; 324: 705.
4. Doyle EA, Weinzimer SA, Steffen AT, Ahern JA, Vincent M, Tamborlane WV. A randomized, prospective trial comparing the efficacy of continuous subcutaneous insulin infusion with multiple daily injections using insulin glargine. Diabetes Care 2004; 27: 1554-1558.
5. Bruttomesso D, Pianta A, Crazzolara D, et al. Continuous subcutaneous insulin infusion (CSII) in the Veneto region: efficacy, acceptability and quality of life. Diabet Med 2002; 19: 628-634.
6. Fahlen M, Eliasson B, Oden A. Optimization of basal insulin delivery in type 1 diabetes: a retrospective study on the use of continuous subcutaneous insulin infusion and insulin glargine. Diabet Med 2005; 22: 382-386.
7. Linkeschova R, Raoul M, Bott U, Berger M, Spraul M. Less severe hypoglycaemia, better metabolic control, and improved quality of life in type 1 diabetes mellitus with continuous subcutaneous insulin infusion (CSII) therapy; an observational study of 100 consecutive patients followed for a mean of 2 years. Diabet Med 2002; 19: 746-751.
8. Bode BW, Sabbah HT, Gross TM, Fredrickson LP, Davidson PC. Diabetes management in the new millennium using insulin pump therapy. Diabetes Metab Res Rev 2002; 18 Suppl 1: S14-S20.
9. Roze S, Valentine WJ, Zakrzewska KE, Palmer AJ. Health-economic comparison of continuous subcutaneous insulin infusion with multiple daily injection for the treatment of type 1 diabetes in the UK. Diabet Med 2005; 22: 1239-1245.
10. Cohen N, Minshall ME, Sharon-Nash L, Zakrzewska K, Valentine WJ, Palmer AJ. Continuous subcutaneous insulin infusion versus multiple daily injections of insulin: economic comparison in adult and adolescent type 1 diabetes mellitus in Australia. Pharmacoeconomics 2007; 25: 881-897.

DECLARATION OF INTEREST: None.