Clinical Focus:

Insulin Pump Therapy

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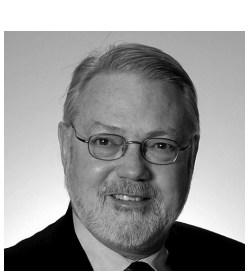

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Advances in management options for insulin-dependent patients

The insulin pumps of the 1970s were bulky and heavy, offering little flexibility in the rate of basal insulin delivery and with few safety features. Improvements in pump technology have fuelled a dramatic increase in pump use with about 300,000 individuals worldwide now using pump therapy.

Today's pumps deliver insulin via a subcutaneously inserted infusion set and provide a wide range of basal and bolus delivery options. Continuous glucose monitoring systems (CGMs) and downloadable data have added more value to pump therapy and further expanded its role in diabetes management.

For insulin-dependent patients, today's pumps come closer than ever to approximating physiological insulin secretion, thus enabling a more "normal" lifestyle and improving users' quality of life and sense of well-being.

That said, pump therapy may not be the best solution for all insulin-dependent patients, as it requires a level of motivation that not all patients are willing or able to achieve. It is important for clinicians to understand which patients are best suited for pump therapy.

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PERSPECTIVE

The paradigm shift in diabetes management began in the early 1990s when The Diabetes Control and Complications Trial (DCCT) conclusively demonstrated that improved glycemic control with intensive insulin therapy leads to reductions in microvascular complications in patients with type 1 diabetes. The DCCT's follow-up trial, Epidemiology of Diabetes Interventions and Complications, showed that intensive insulin therapy also reduced cardiovascular mortality and morbidity. Other studies suggest that intensive insulin therapy may have similar benefits for insulin-dependent patients with type 2 diabetes.

"Intensive insulin therapy" describes a pattern of insulin administration that approximates physiologic responses, i.e., basal insulin to cover background needs, supplemented by premeal boluses.

Patients on intensive insulin management must choose one of two regimens: multiple daily injections (MDI) or continuous subcutaneous insulin infusions (CSII), i.e., insulin pump therapy. While patient preference and lifestyle play into this decision, it is fair to say that the pump offers a new level of freedom and flexibility to motivated patients. The pump also comes closest to reproducing "normal" insulin response.

In terms of glucose control, some studies have shown that insulin pump therapy may have an edge over MDI, though the difference may be modest. In one study of 107 type 1 diabetes patients initially treated with MDI, switching to the pump caused glycosylated hemoglobin (A1C) levels to decline by a mean of 0.5 percent (from 7.6% to 7.1%). Pumps that incorporate CGM technology, which alerts users to potential highs and lows in glucose levels, further enhance glucose control.

Other studies have generally confirmed clinicians' anecdotal observations that specific patients have very positive experiences with the pump, which lead to improved glycemic control and quality of life. To date, there is no reliable way to predict which patients will benefit most from pump therapy, though certain baseline characteristics suggest better outcomes than others.

A notable advantage of pumps is the reduction in variability of glucose levels. Compared to MDI, pump therapy can reduce severe hypoglycemic episodes by as much as fourfold, without any appreciable reduction in glucose control. Many patients on pump therapy also report an increase in the warning signals of hypoglycemia. In fact, asymptomatic hypoglycemia has become an accepted indication for the initiation of pump therapy.

Pump therapy and type 2 diabetes

Insulin pump therapy can be considered in type 2 diabetes patients who require large doses of insulin or who have inadequate control on MDI therapy. When such patients inject large doses of insulin, a subcutaneous pool or "depot" can linger and, when mobilized, lead to unexpected hypoglycemia. Pumps deliver insulin in slow controlled pulses, leading to more uniform and predictable insulin absorption. Insulin requirements may decrease by an average of 15% to 20% in type 2 patients and use of oral agents may also decrease.

To succeed at pump therapy, patients with type 2 diabetes must be able to monitor blood glucose three to six times a day, determine their premeal insulin needs and tolerate a device that reminds them they have diabetes. They must also have the motivation to achieve glucose control, and they must have a reasonable level of psychological stability.

FEATURES OF PUMP THERAPY

Insulin delivery

Unlike the MDI approach, which combines rapid-, intermediate- and long-acting insulin injections, insulin pump therapy requires only rapid-acting insulin because the insulin is delivered continuously. Pumps can deliver basal insulin at variable and programmable rates – a mode of delivery that cannot be matched by intermittent injection of longer-acting insulin.

This feature enables the pump to mitigate the "dawn phenomenon," the abrupt increase in glucose levels that occurs in the early-morning hours in many patients with diabetes. The dawn phenomenon is not caused by antecedent hypoglycemia and can present a significant challenge to diabetes management. To counteract it, pump users can increase their basal insulin delivery rate prior to the dawn hours. Other patients find they have higher or lower insulin needs on weekends than on

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Perspective

The DCCT showed that achieving and maintaining glucose levels as close to normal as possible can prevent or delay microvascular complications in people with type 1 diabetes. The trial also found that the cohort using CSII systems maintained better glucose control than those on MDI.

The years following the DCCT saw a rapid increase in the use of insulin pumps, and numerous studies (notably, those comparing pumps to MDI) have shown that pumps help maintain glucose levels as close to normal as safely possible. Short-acting insulin analogues with greater responsiveness to the immediate physiologic environment further enhance the pump's effectiveness.

Today's pumps can be programmed to vary the basal insulin delivery to accommodate changing insulin needs in response to patients' individual patterns. Variable bolus patterns mean bolus insulin can be delivered more quickly or stretched out over a longer period of time, in an attempt to approximate the normal pancreatic secretion of insulin.

Benefits & Drawbacks

Insulin pumps have proved successful both in clinical trials and in daily clinical practice. The benefits of insulin pump therapy include:

- More precise insulin dosing and elimination of daily multiple injections
- Improved insulin absorption with continuous delivery (more closely approximating pancreatic delivery in people without diabetes)
- Better ability to manage illness, varying activity levels, and the dawn phenomenon
- Reduced "peaks and valleys" in glucose levels
- Ability to reverse hypoglycemia unawareness
- Better management of delayed food absorption (by adjusting the bolus delivery to match food absorption)
- Stabilization of A1C levels
- Ability to follow a flexible eating regimen, including the guiltless enjoyment of special-occasion foods
- Ability to exercise safely, as basal insulin rates can be reduced or temporarily stopped as needed
- Ability to travel with ease, as basal insulin rates can be adjusted to the destination time zone

Insulin pumps require some motivation and vigilance, and are not suited for every insulin-dependent patient. Patients must monitor their glucose levels frequently (four to eight times a day), learn to count carbohydrates, and exercise consistent attention to their insulin needs. Costs are considerable: several thousand dollars for the pump and about $200 to $300 per month for supplies. Many private insurers, realizing the benefits of pump therapy, will pay for at least a portion of these costs if patients provide a certificate of medical necessity from their physician. Provincial health plans in Ontario, Saskatchewan, Newfoundland and Quebec cover pumps or pump supplies for certain people, usually in pediatrics. Since coverage policies may change, it's worth verifying the current status with the appropriate authorities.

Another potential drawback is the possibility of infection at the infusion site, but this complication can be prevented in most cases with proper attention to hygiene. Infusion system failures, generally due to blockages or leaks that interrupt the flow, may also occur, though they are less common with today's systems.

Because pump users do not take long-acting insulin, ketonemia and diabetic ketoacidosis can develop more rapidly and frequently if the flow of short-acting insulin is interrupted for any reason.

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weekdays – a discrepancy the pump can readily accommodate.

The bolus mealtime insulin doses can also be accurately tailored to the meal size and content, preprandial glucose levels, and anticipated activity levels, in increments as small as 0.1 unit (compared to 1 or 2 unit increments with pens and syringes). Mealtime boluses can be delivered over a longer period of time when appropriate. Such "square wave" or "dual wave" boluses are useful for stretched-out meals, such as buffets or barbecues.

Using rapid-acting insulin can circumvent some of the problems associated with long-acting insulin. Specifically, the large doses of long-acting insulin required to deliver reasonable basal levels can lead to weight gain and raise the risk of prolonged hypoglycemia. Longer-acting insulin injections also vary widely in their effects, even when the same dose is given to the same person on successive days. Pump delivery sidesteps this problem, thus yielding more predictable glucose control.

Overall, these features combine to fine-tune glucose control, to reduce total insulin requirements by as much as 30%, and to reduce the risk of both daytime and nighttime hypoglycemia. Since even a 0.1% decrease in A1C levels translates to a reduction in diabetes complications, any strategy that can nudge A1C levels downward deserves due consideration.

To provide the maximum benefits, intensive insulin therapy should be started as early as possible after the diagnosis of type 1 diabetes. Patients must be aware that this approach requires greater effort and vigilance, and carries a greater risk of hypoglycemia than conventional insulin therapy.

To mitigate the risk of hypoglycemia, I generally start new pump users on a somewhat lower dose of insulin than I think they may ultimately require, and titrate upward as needed. Working backwards from the patient's previous regimen, I may start with a total daily insulin dose of 30% to 40% less than their previous total, particularly if their needs have been high.

Continuous glucose monitoring

A continuous glucose-monitoring system is a device that records glucose levels throughout the day and night. A number of technologies are being tested, but only one is currently approved. The device features a subcutaneous sensor that measures tissue glucose levels every 10 seconds and sends the information to a monitor attached to a belt or waistline. The monitor calculates average glucose values every five minutes for up to three days.

Doctors or other health professionals can download this information and see the levels in graph or chart form, view patterns in glucose levels, and make

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Treatment considerations

Most patients with type 1 diabetes are candidates for insulin pump therapy. The use of pumps in insulin-dependent patients with type 2 diabetes is somewhat more controversial, as these patients may still be producing some endogenous insulin, which complicates the task of establishing a pump regimen.

In my practice, about half of my patients with type 1 diabetes – particularly younger people – are using insulin pumps. To be considered for pump therapy, my patients must meet one or more of the following criteria:

- Diagnosed type 1 diabetes as documented by a family doctor, pediatrician or endocrinologist
- Wide fluctuations in blood glucose levels
- History of severe hypoglycemia or hypoglycemia unawareness
- Inability to achieve optimal diabetes control as per the Canadian Diabetes Association guidelines (A1C < 7% and, if safely achievable, < 6%)
- Difficulty coping with multiple daily injections

It is also preferable if candidates for pump therapy meet at least some of the following behavioural and psychosocial criteria:

- Self-monitoring blood glucose levels at least 4 times a day
- Consistent recording of results in a logbook
- Motivation to strive for optimal diabetes control
- Adequate support base (family, friends or community agency)
- Adequate financial resources or support to sustain long-term pump therapy
- Recognition of, and treatment for, concomitant medical conditions

The total insulin delivered from the pump divides about evenly between basal and bolus. Pumps with integrated glucose sensors provide a moment-to-moment record of glucose levels, enabling a more accurate analysis of glucose excursions. By reviewing these pump records, clinicians can trace peaks or valleys in glucose levels to basal or bolus problems and make concomitant dosage adjustments.

The importance of education in pump use cannot be overstated. Patients are given instruction in the benefits of intensive diabetes management, in carbohydrate counting, and in adjusting insulin doses in response to food intake. With the proper education and support, pump patients generally self-manage effectively.

It should be emphasized that most family doctors do not have enough candidates for pump therapy to become experts in the fine points of pump use. For patients who may be suited for the pump, the family doctor's key role is referral to the appropriate specialist(s).

CDE Commentary

As a certified insulin pump trainer, I am quite passionate about the benefits of insulin pumps. At the diabetes centre where I work, patients are listed and selected according to readiness. We used to take patients on a first-come first-serve basis, but we soon realized that not all patients were ready to start the pumping experience.

Not everybody is expected to know the nuts and bolts of insulin pumps. If a family doctor has a patient who appears a good candidate for an insulin pump, it is important to refer that patient to the appropriate specialist(s).

Q: How do you prepare patients for insulin pump therapy?

A: Just as with driving a car, using the pump requires some advance knowledge and mental preparation. Candidates meet with a dietitian for instruction on carbohydrate counting and insulin dose adjustment. Reassurance is important, as many patients are anxious and overwhelmed with new information. They need to know their feelings are normal.

Q: What are some of the things that can go wrong with the pump, and how to prevent them from happening?

A: Because the pump uses only shorter-acting insulin, it carries a greater risk of diabetic ketoacidosis (DKA). Pump users can minimize the risk of DKA by monitoring blood glucose routinely throughout the day to ensure insulin is flowing without disruption. If blood glucose rises above 14 mmol/L, patients can monitor their blood ketones with a specially designed precision meter.

Another potential problem with insulin pumps is poor glucose control. Of course, this problem can also occur with other treatment strategies. To pursue the car analogy, glucose monitoring is essential to keep the "car" from veering into hyper- or hypoglycemic terrain. At our centre, pumpers can download the data from their pumps and meters, which allows us to help them identify strategies to improve glucose control. We can identify pump management gaps such as forgetting to bolus, not checking blood glucose in a timely manner, or improper carbohydrate counting.

Q: How can a diabetes management team assist insulin pump users?

A: Because pump users need to count carbohydrates, the dietitian plays a vital educational role. Social workers can advocate for financial assistance for patients for whom cost may pose a barrier. A certified pump trainer can provide the bulk of teaching and follow-up care. Pump trainers liaise with the rest of the medical team to ensure a smooth flow of communication. I believe that effective communication between the trainer and the patient's family doctor can make pump therapy an exciting and positive experience for both parties.

At our clinic, we have a 24/7 advice line, which all pump users can call if they need medical advice. Patients can also attend group educational sessions to share their problems and concerns.

adjustments in basal and/or bolus doses as needed. The device is now available for day-to-day or intermittent use. Both clinical studies and reports from my patients have been extremely encouraging. One patient has compared current glucose monitoring recommendations to buying a watch that tells the correct time four times per day. My patients who have incorporated continuous glucose-sensing technology report an increased sense of safety and control.

TREATMENT CONSIDERATIONS

Patient selection

Some clinicians recommend pumps only after MDI fails to provide euglycemia, while others consider it for motivated patients whose lifestyle may not lend itself very easily to MDI. In my practice, I occasionally (though infrequently) start patients on the pump before a trial of MDI. Patients who exercise should not be discouraged from using the pump, as it is fully compatible with exercise. Some of my pump-using patients are even marathon runners.

Diabetes care requires sustained effort and attention, and pump therapy may further increase these requirements. Stress, mental health and emotional issues may impact patients' ability to use the pump effectively, so these psychological aspects must be taken into consideration when selecting patients.

Depression is about three times more common in people with diabetes than in the general population, but often goes unrecognized and untreated. A number of brief screening instruments can be used to identify depression, stress and quality of life in patients considering the use of a pump. Failure to take into account an undiagnosed depression may adversely affect a patient's chance of success with pump therapy.

Model of care

The traditional, authoritarian model of medical care may not be appropriate for pump users. An empowerment model, which shifts the primary management responsibility to the patient while providing ample support, facilitates learning and tames normal fears in new pump users. In this model, patients freely choose their behavioural changes, and research has shown that freely chosen changes are more likely to be maintained than those mandated by others.

Pumps for children

Many young patients find it easier and more convenient to take their multiple daily doses of insulin via the pump than with a syringe or insulin pen. The pump also allows for quick and accurate compensations for the often-erratic eating patterns of children. On the other hand, the level of knowledge and vigilance required by pump users precludes the unsupervised use of pumps in children. The pump should only be considered in children who are closely monitored by a parent or other adult willing and able to learn how to manage all aspects of pump therapy. This requirement may be easier to meet in preschool children, as most schools do not have on-site personnel who can assume this responsibility.

Patient satisfaction

While the literature sometimes reports high rates of discontinuation of pump therapy, my own experience has been that properly selected and educated patients rarely seek to go off the pump. In my practice, pump users report a consistently high level of satisfaction.

Future directions

Pump technology is constantly evolving. Current research and development efforts are leading toward fully automated pumps. The pumps of the future will likely feature moment-by-moment sensors that instantaneously translate glucose readings to insulin output. ●

RESOURCES

For physicians

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Continuous Subcutaneous Insulin Infusion. American Diabetes Association 2004 position statement. www.overcome-diabetes.com/diabetes-prevention/insulin-infusion.htm

Bode BW, *et al*. Insulin pump therapy in the 21st century. Postgraduate Medicine 2002; 111(5). www.postgradmed.com/issues/2002/05_02/bode3.htm

Lloyd C. Psychological aspects of pumps and patient selection. Conference paper (2000). www3.interscience.wiley.com/cgi-bin/fulltext/ 85007436/HTMLSTART?CRETRY=1&SRETRY=0

Schorr AB. Pump therapy now becoming a type 2 thing. Diabetes Health 2001. www.diabeteshealth.com/read/2001/02/01/2134.html

Diabetes: continuous glucose monitoring. http://diabetes.webmd.com/continuous-glucose-monitoring

For patients

Conway R. All about insulin pumps. Diabetes Clinic website. www.diabetesclinic.ca/english/print_pages/Information_for_Professionals/prof_pumps.htm

Product information (sponsor's website) www.minimed.com: In addition to product information, this website has a page dedicated to healthcare professionals, featuring trial updates and links to continuing medical education programs. For people living with diabetes, Medtronic also sponsors this bilingual website: www.pumptherapy.ca.

1 Case Study:

BRIAN IS A 49-YEAR-OLD CAUCASIAN MAN WHO DEVELOPED TYPE 1 DIABETES IN CHILDHOOD. CONTROL OF HIS DIABETES OVER THE YEARS HAS BEEN SUBOPTIMAL AND HE HAS BEEN DIAGNOSED WITH MILD RETINOPATHY AND HAS EXPERIENCED SOME ERECTILE DYSFUNCTION. HE ALSO HAS A HISTORY OF ASYMPTOMATIC HYPOGLYCEMIA, INCLUDING A RECENT SERIOUS EPISODE THAT REQUIRED A BRIEF HOSPITALIZATION. HIS BMI IS 26 KG/M², MAKING HIM OVERWEIGHT BUT NOT OBESE. HIS CURRENT MEDICATIONS INCLUDE NPH AND RAPID-ACTING INSULIN, ALONG WITH A STATIN.

His most recent laboratory testing results are as follows:

- A1C: 8.5%
- Total cholesterol: 6.3 mmol/L
- LDL cholesterol: 4.7 mmol/L
- HDL cholesterol: 1.17 mmol/L
- Triglycerides: 2.2 mmol/L
- Creatinine: 79.2 µmol/L
- Microalbumin: 4 µg

Brian's records reveal a pattern of mid-afternoon hyperglycemia. You refer him to a dietitian specializing in diabetes care who adjusts his insulin regimen and teaches him how to calculate his mealtime dose of rapid-acting insulin, based on the amount of carbohydrates in the meal and his preprandial blood glucose level. Despite following this new regimen, over the ensuing month he experiences two more episodes of severe hypoglycemia, following which he comes to see you again. (You had started him on ACE inhibitor therapy as well as modifying his LDL-lowering therapy.)

His subjective experience of hypoglycemia is not reliable. Carbohydrate counting and insulin adjustments have helped, but have not adequately controlled his hypoglycemic episodes. As well, he has begun to experience diabetes complications. You suggest he consider insulin pump therapy. His initial reaction is positive, as he admits to finding it a nuisance to "carry all these different types of insulin" with him.

The equipment is ordered. Brian visits his endocrinologist to discuss his therapy and undergoes a training session with his dietitian, who is also a certified pump trainer. His basal insulin rate is set at 0.7 units per hour starting at midnight and 1.1 units per hour from 5 a.m. to 8 a.m. At 8 a.m., he switches to 0.8 units per hour and continues this rate until the following midnight. He experiences some early problems with elevated blood glucose levels, but a bent-needle infusion set (to improve absorption) resolves these problems.

Six months after starting the pump (and attending regular educational workshops), Brian's laboratory values have reached target ranges. His A1C has stabilized at just under 7%. He has recovered a physical sense of impending hypoglycemia and has been free of serious hypoglycemic episodes since starting the pump. He feels more hopeful than ever about his ability to control his diabetes, and expresses a desire to begin an exercise program in order to shed 10 pounds. ●

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