Canadian Diabetes

Le diabète au Canada

Volume 20, Number 3 Autumn 2007

Intensive Diabetes Management: A New Paradigm for a New Era

Robin Conway MD, Sara Meltzer MD FRCPC

Editor's Note

Management of diabetes has evolved dramatically over the last 20 years. The results of the Diabetes Control and Complications Trial (DCCT) (1) and the United Kingdom Prospective Diabetes Study (UKPDS) (2) have shown conclusively that normalization of blood glucose values can greatly reduce, if not eliminate, the devastating microvascular complications of diabetes. If we heed these lessons, then we can hope to banish diabetes-induced blindness, kidney failure and neuropathy to the history books. Evidence is accumulating that even minor abnormalities in blood glucose levels are associated with an increased risk of cardiovascular disease and that good glucose control is clearly beneficial (3). Thus, the recommended goals for glucose control have been brought closer and closer to normal. Attainment of these goals is now more achievable due to improvements in home glucose monitoring, new insulin analogues, insulin administration devices and management tools such as carbohydrate counting, as well as computer-assisted decision making. The concept of intensive diabetes management and its advantages cannot be overlooked. The term "intensive management" may be a misnomer: what has happened is a paradigm shift from fixing an insulin dose and then adjusting meals and lifestyle to fit that dose; to putting the patient in control and adjusting the insulin to fit the patient's lifestyle and food intake. We might better label this as "flexible management" or "physiologic management."

It has been shown that patients who are involved with their own treatment are more likely to adhere to treatment plans, and as a result obtain better glucose control and higher quality of life. The benefits of "intensive management" are no longer thought to be limited to people with type 1 diabetes. The UKPDS (2) shows us that people with type 2 diabetes also benefit from intensive management. The education required for this approach is relatively straightforward and simple because it follows physiologic principles.

In type 2 diabetes, for those who still manage well with diet and oral agents, there may be a role for minor adjustments of oral agent dosages related to changes in diet or activity, particularly with medications that stimulate insulin release. As the need for insulin supplementation increases as the pancreas progressively deteriorates, intensifying treatment early on with basal insulins allows achievement of much better control. Even with further islet cell loss over time, the need for mealtime insulin becomes evident. Many people with type 2 diabetes appreciate the flexibility and degree of control achievable with mealtime fast-acting insulins. The use of algorithms for adjusting prandial insulin increases flexibility and glycemic control (4). As endogenous insulin production decreases to a point where both basal and bolus insulin needs have to be addressed, patients with type 2 diabetes need to start using intensive (or flexible) treatment plans that are the same as those used in the treatment of type 1 diabetes.

The new insulin analogues, when used appropriately, allow us to mirror the action of the functioning pancreas. Intermediate insulin (NPH), or the extended long-acting insulin analogues such as glargine and detemir, provide for the basal insulin, while short-acting insulins such as aspart and lispro can provide the insulin needed for meals and rapid correction of hyperglycemia. For patients who experience nocturnal hypoglycemia on NPH or poor immediate glucose control after a meal with later hypoglycemia, the appropriate analogues present solutions.

The value of continuous subcutaneous insulin infusion (CSII) was proven by the DCCT but it took the advent of the new short-acting insulin analogues and microprocessor technology to bring the promises to fruition. Insulin pumps are finding more acceptance as management tools, particularly since some provincial health ministries have started to pay for pumps in the pediatric population. Insulin pumps are still best initiated by healthcare professionals familiar with the details and process, but family physicians should also have some basic knowledge, since they will be seeing more and more pump users and will also be asked to assist in selecting candidates to pump programs. These devices have become much more sophisticated and now may calculate the remaining active insulin after a bolus, to allow for more precise corrections while decreasing the risk of hypoglycemia.

Patients on pump therapy should have a solid understanding of their insulin doses

Continued on page 10

In This Issue

HOW ARE WE GOING ABOUT IT?

For more than 100 years, Merck Frosst has been striving to advance the frontiers of medical knowledge. Working in collaboration with healthcare professionals, our researchers have developed innovative medicines that continue to be used in the ongoing battle against disease.

This same innovation and commitment is also being aimed at diabetes. On behalf of the many Canadians living with this disease, we at Merck Frosst are striving to make medical history.

Like your diabetes patients, each and every day, we put ourselves to the test.

PLEASE VISIT OUR WEBSITE AT **www.merckfrosst.com**

MERCK FROSST

Discovering today
for a better tomorrow.

Merck Frosst Canada Ltd., Kirkland, Quebec

Intensive Diabetes Management: Ready for Prime Time

Jackie Leithoff MSc, Ellen L. Toth MD FRCPC
Department of Medicine, University of Alberta, Edmonton, Alberta
Heritage Medical Research Centre, University of Alberta, Edmonton, Alberta

INTRODUCTION

Intensive diabetes therapy, as defined by the United Kingdom Prospective Diabetes Study Group (UKPDS) (1) aims to achieve optimum glycemic control using whatever management techniques are needed. Most healthcare professionals consider the term to apply more specifically to advanced techniques in insulin therapy, self-monitoring of blood glucose (SMBG), and nutrition and behavioural sciences (2).

In 2007, it is generally accepted that, in most patients, intensive diabetes therapy† may not only be optimal but also cost effective. It is nearly 15 years since the results of the Diabetes Control and Complications Trial (DCCT) demonstrated that near normalization of blood glucose (BG) levels in type 1 diabetes could significantly delay the onset and slow the progression of diabetes complications (2). Similarly, it will be 10 years since the UKPDS showed that intensive BG control, with either oral therapy or insulin, decreased microvascular complications in patients with type 2 diabetes (1). However, in reality, glycemic (or non-glycemic) goals may not be easy to achieve in patients, for a variety of reasons, including economic or psychological factors, limited access to physicians or other professionals who are knowledgeable in diabetes management, patient nonadherence, undesirable side effects and limitations of the currently available pharmacologic agents, limitations of current insulin delivery devices and drawbacks of the current glucose measurement devices.

The DCCT showed that for patients with type 1 diabetes, optimal management involved intensive insulin therapy including ≥3 insulin injections daily or use of an insulin pump (2). The results of both the DCCT (type 1 diabetes) and the UKPDS (type 2 diabetes) demonstrated that tight glycemic control can decrease the incidence of microvascular complications (retinopathy, nephropathy and neuropathy) by at least 25% (1,2). Intensive insulin therapy can also be optimal for many patients with type 2 diabetes, who may have insulin deficiency and therefore require insulin supplementation. These patients are often older and some have had the disease for a long period of time. For all patients, therapy must be individualized in order to attain and maintain an appropriate goal and reduce the incidence of side effects or adverse reactions. Based on the available evidence (which is strongest for the avoidance of microvascular complications), most countries' diabetes associations recommend achieving and maintaining a glycosylated hemoglobin (A1C) level of lower than 7.0%. European guidelines recommend <6.5% A1C (3), while the Canadian Diabetes Association clinical practice guidelines recommend ≤7.0%, and <6.0% for those in whom it can be safely achieved (Table 1) (4). In addition, targets for postprandial BG are suggested, since higher postprandial BG has been shown to be related to cardiovascular risk.

RATIONALE FOR INTENSIVE DIABETES MANAGEMENT

The benefits of intensive management extend beyond the achievement of clinical targets. People with diabetes who use intensive management may enjoy a more flexible lifestyle, less hypoglycemia, and a more positive quality of life due to fewer complications.

Intensive therapy should be considered early in the course of the disease in order to decrease complications, as two-thirds of the costs of diabetes management are currently for complications of diabetes, which often involve inpatient care (5).

Although beneficial effects on the prevention of macrovascular complications are not proven, evidence suggests the value of intensive therapy during and after acute myocardial infarction in patients with diabetes (6). Other studies have shown the importance of maintaining normoglycemia during severe infections, cerebral ischemia or perioperative periods (7).

An intensive comprehensive approach is

Table 1. Recommended targets for glycemic control in adults with diabetes* (4)

	A1C (%)	FPG/pre-prandial PG (mmol/L)	2-hour postprandial PG (mmol/L)
Target for most patients	≤7.0	4.0–7.0	5.0–10.0
Normal range (consider for patients in whom it can be achieved safely)	≤6.0	4.0–6.0	5.0–8.0

*Treatment goals and strategies must be tailored to the patient, with consideration given to individual risk factors. Glycemic targets for children <12 years of age and pregnant women differ from these targets.

A1C = glycosylated hemoglobin FPG = fasting plasma glucose PG = plasma glucose

†*The phrases "intensive diabetes management" and "intensive diabetes therapy" are used interchangeably in this paper.*

particularly important during the early course of the disease, when the greatest clinical benefits have been noted. The metabolic memory hypothesis proposes that long before the advent of hyperglycemia, events occur that scar cells, laying the groundwork for the development of both microvascular and macrovascular complications of diabetes. With time, the effects of metabolic "scarring" becomes less amenable to reversal by intensive metabolic control (8).

COST-EFFECTIVENESS OF INTENSIVE DIABETES MANAGEMENT

Intensive management of diabetes is associated with higher "upfront costs" of labour, medications and supplies, but this investment has shown to be effective in reducing morbidity and mortality as well as minimizing later expenditures for costly long-term complications. The cost benefit of tight glucose control is most pronounced in young patients, who in general will have a longer duration of life during which the complications of diabetes could develop. Both the DCCT and UKPDS analyzed the costs of treating type 1 and type 2 diabetes, respectively, with intensive treatment strategies. In the DCCT, the cost was $4014 (US)/year, which was 2.4 times that of conventional therapy ($1666 [US]/year) (2). However, this cost was in a research setting. Outside the DCCT study, in physician practices, the intensive therapy was much less expensive—only $2337 (US)/year (9). The difference is primarily due to less frequent and less prolonged use of hospital services and a lower cost for outpatient visits.

In the UKPDS, intensive management in type 2 patients was also found to make as much sense economically as medically. As part of the study, a simulation model of disease progression revealed that patients with diabetes who receive intensive treatment live 5.1 years longer than those receiving conventional therapy. In addition, with further consideration of the reduction in complications (blindness, end stage renal disease and lower extremity amputation) that decrease quality of life, the study noted that the incremental cost per quality-adjusted life year gained is relatively inexpensive in relation to other commonly accepted medical therapies. The improved glycemic control in patients with type 2 diabetes is associated with improved quality of life, higher retained employment, greater productive capacity and less absenteeism (1).

Consideration of these factors suggests the cost of intensive therapy is offset by even greater economic benefit. When the patient is committed to learning diabetes self-management and the diabetes team is dedicated to teaching the patient the appropriate techniques and the rationale for them, intensive diabetes management is the logical course both for individual patients and for society.

METHODS TO ACHIEVE INTENSIVE DIABETES MANAGEMENT

All practitioners can work toward intensifying diabetes management; however, the complexity of intensive insulin therapy and management is usually beyond the scope of the sole practitioner. In order for intensive management to be clinically successful, a systematic multi-faceted approach is required, including appropriate glycemic goals, an established frequency of glucose monitoring, choice of pharmacologic or therapeutic management regime, lifestyle changes and access to treatments. In addition to ensuring patient adherence to any therapy, careful follow-up to monitor progress toward individualized goals is required to support and reinforce the patient's management skills (10).

The diabetes team

Intensive therapy requires a core group of skilled professionals with diverse roles: an interdisciplinary team with the patient at the centre. The team includes physicians, nurses, dietitians and behavioural scientists, all of whom should have special interest and training in the management of diabetes so they can assist and support the person with diabetes in attaining the goal of self-management. This core membership reflects the basic requirements of diabetes treatment: self-management, self-monitoring and nutrition. Teams may also extend to healthcare professionals who can help meet special needs, such as podiatrists, exercise physiologists, ophthalmologists, pharmacists, and geriatric and pediatric diabetes specialists. Specific dietary counselling is necessary to teach individuals how to change or alter insulin doses for varying food intakes. Behavioural scientists can provide counselling services regarding adjustment to chronic illness and stress management, diagnose psychiatric illness and screen for learning disorders that might interfere with patient comprehension.

Canadian Diabetes
Le Diabète au Canada

Autumn 2007

Canadian Diabetes/le Diabète au Canada is published four times a year by the Canadian Diabetes Association. All articles published in *Canadian Diabetes* are the sole opinions of the authors and are not necessarily endorsed by the Canadian Diabetes Association.

Change of address notices to:
Canadian Diabetes Association
1400-522 University Avenue
Toronto, Ontario M5G 2R5

The publication of *Canadian Diabetes/ le Diabète au Canada* is made possible by the contribution of Merck Frosst Canada Ltd., Kirkland, Quebec, Canada.

Canada Post Publication agreement number 40063447.

ISSN0841-9388

CANADIAN DIABETES ASSOCIATION | ASSOCIATION CANADIENNE DU DIABÈTE

Nutrition and exercise

Diabetes therapy is complex and specific to the disease type of each patient. The plan for treatment of type 1 diabetes should include intensive insulin therapy integrated with diet, exercise and glucose monitoring. Similarly, type 2 treatment should include diet and/or weight management, oral pharmacologic therapy and/or insulin and glucose monitoring.

The importance of nutrition and exercise programs in both type 1 and type 2 diabetes has been inadequately emphasized, and the result has been unsatisfactory patient adherence. The DCCT demonstrated that patients who were able to adjust their food intake and insulin dose achieved lower A1C values (2). However, it may often be unreasonable to expect the patient to maintain a consistent meal plan and insulin regimen. The technique of carbohydrate counting allows knowledgeable patients to determine varying pre-meal doses of rapid-acting insulin, which also need to be adjusted according to the activities planned (11). Patients with type 2 diabetes who are overweight or obese are encouraged to decrease calorie consumption, since weight loss results in a decrease in insulin resistance. Even without weight loss, patients can improve their glucose results by a pattern of eating that minimizes insulin requirements—small, balanced meals (at least 3 to 4 food groups per meal) spaced out throughout the day, with the carbohydrate in the meal preferably from a food that is high in fibre and slowly absorbed.

Surprisingly, patients do not need to achieve an ideal body weight to improve control of BG, hypertension and lipid levels. Loss of as little as 5% of body weight may lead to significant improvements in insulin resistance, but the weight loss must be maintained and exercise programs must be ongoing (12). Low-fat and low-carbohydrate diets have their advocates; however, controlled trials have shown little difference with respect to weight loss (13). The key is the caloric intake relative to the caloric output. Exercise prescriptions should be tailored to the individual patient's capacity and co-existent conditions. Patients with type 2 diabetes should be encouraged to exercise 3 times per week, for at least 30 minutes per day, targeting all major muscle groups. Studies have shown that resistance exercise done at least 3 times a week improves insulin sensitivity to about the same extent as aerobic exercise (14).

Pharmacologic agents

During the early stages of type 2 diabetes, the cornerstones of therapy remain proper nutrition, exercise and education. However, the disease is characterized by progressive insulin resistance and insulin deficiency. About 50% of beta-cell function has been lost by the time a patient with type 2 diabetes has been diagnosed, and this function will continue to decline over time. While insulin resistance may occur independently of diabetes, insulin deficiency is always a core defect of diabetes. Pharmacologic treatments are then often required, with the biguanide metformin remaining the mainstay of initial treatment (15). Over the course of the last few years, drugs in several new classes have been approved, including thiazolidinediones, meglitinides, alpha-glucosidase inhibitors, incretins and DPP-IV inhibitors. All of these agents have tissue-specific sites of action and can be used in combination.

It is generally accepted that, in most patients, intensive diabetes therapy may not only be optimal but also cost effective.

With this array of options, treatment regimens have become increasingly complex and confusing. There is little evidence from good-quality randomized clinical trials that any single drug or drug combination is better than another, with the exception of metformin in obese patients (1). Thus, safety profiles and cost should be primary considerations in prescribing, but in fact prescribing decisions are often influenced by marketing campaigns for newer drugs that may have potential advantages, but have not been truly tested in regards to long-term outcomes (16). In the meantime, many patients with type 2 diabetes are prescribed medications with insufficient attention being paid to the optimal intensive therapeutic use of nutrition and physical activity, and with insufficient patient education. Additionally, misguided emphasis may be placed on the performance of SMBG in patients whose therapy involves only diet or oral agents, a subpopulation in which the usefulness of self-monitoring is not proven (17). Finally, it is not uncommon to see a spiralling of treatment with up to 3 or 4 drugs being added to therapy with little resulting improvement. As the disease continues to progress, maximal doses of drugs are often insufficient to achieve the recommended A1C target of ≤7.0%. Typically, between 5 to 10 years after diagnosis, insulin therapy is needed in a majority of individuals with type 2 diabetes (18).

Introduction of insulin in type 2 diabetes

When glycemic control can no longer be achieved with1 or 2 oral agents, insulin should be added to significantly improve glycemic control. Table 2 outlines available insulins in Canada (4).

While insulin is indicated in many patients with type 2 diabetes, its use is often delayed. Reluctance to initiate insulin therapy ranges from patients' fear of weight gain and needles, to concerns about hypoglycemic events, cardiovascular complications and cost. Many of these reasons for reluctance have now been invalidated by new clinical evidence and better technologies. The availability of finer needles and insulin pens has made injections much less painful. Hypoglycemic events are much less frequent in patients with type 2 diabetes, because of the greater variety of insulins now available (19). Other studies have shown no increase, or even a decrease, in cardiovascular disease in patients treated with intensive insulin (6). Furthermore, insulin is less expensive than many oral agents. This evidence suggests that the major barrier to insulin initiation is provider reluctance.

When oral antihyperglycemic agents no longer maintain glycemic control, adding basal insulin has been shown to lower the entire 24-hour fasting glucose profile (20). This would be started by using insulin with an intermediate duration of action (NPH) at bedtime. To initiate bedtime insulin, patients must begin to monitor their BG levels, if they haven't already been doing so. A simple regimen may be to start at 8 to 12 units the first night, and increase by 1 to 2 units every 2 to 4 days if fasting glucose remains >6.0 mmol/L. If fasting glucose is <4.5 mmol/L even once, lower their dose at night by 2 units. This algorithm can be adjusted to higher or lower limits, as appropriate for the individual patient. In fact,

Table 2. Types of insulin available in Canada (4)

Insulin type/action (appearance)	Brand name (generic name)	Basal/bolus	Dosing schedule
Rapid-acting analogue (clear) Onset: 10–15 minutes Peak: 60–90 minutes Duration: 4–5 hours	Humalog (insulin lispro) NovoRapid (insulin aspart)	Bolus	Usually taken right before eating, or to lower high blood glucose levels
Short-acting (clear) Onset: 0.5–1 hour Peak: 2–4 hours Duration: 5–8 hours	Humulin-R Novolin ge Toronto	Bolus	Taken about 30 minutes before eating, or to lower high blood glucose levels
Intermediate-acting (cloudy) Onset: 1–3 hours Peak: 5–8 hours Duration: up to 18 hours	Humulin-N Novolin ge NPH	Basal	Often taken at bedtime, or twice a day (morning and bedtime)
Extended long-acting analogue (clear and colourless) Onset: 90 minutes Peak: none Duration: 24 hours	Lantus (insulin glargine) Levemir (insulin detemir)	Basal	Usually taken once or twice a day
Premixed (cloudy) A single vial contains a fixed ratio of insulins (the numbers refer to the ratio of rapid- or short-acting to intermediate-acting insulin in the vial)	Humalog Mix 25 Humulin (20/80, 30/70) Novolin ge (30/70, 40/60, 50/50)	Combination of basal and bolus insulins	Depends on the combination

patients who become more successful with nutrition and exercise regimens may be able to reduce their dose over time. Also, patients may become capable of adjusting their dose once they have learned how to take the insulin.

Hypoglycemia is the main risk in starting insulin therapy; however, if insulin is started at a low dose and titrated up slowly, hypoglycemia is rarely a problem. A slow titration also helps to decrease the risk of excess weight gain, as it minimizes the need to "eat up to the insulin dose" and maintains the lowest effective dose.

Adding basal insulin to prior oral treatment is successful for many patients, although the oral dose may require reduction if it is an insulin secretagogue. However, if the A1C target of <7% is not achieved or is no longer achieved, at least 1 injection of prandial insulin should also be started. The dose can be titrated in accordance with SMBG values measured either 2 hours after the start of a meal, 2 hours before the next meal, or at bedtime (if the injection is administered before the evening meal) (21). If A1C remains elevated, the next step will be insulin taken with each meal.

A fully intensified basal-bolus regimen represents the most physiological insulin replacement therapy. The prandial insulin doses can be adjusted independently to limit postprandial hyperglycemia without affecting basal insulin action. The use of this approach facilitates transition to a full basal-bolus regimen as the disease progresses; it may be suitable for patients who are initially reluctant to accept full intensive insulin replacement therapy (22).

Prandial insulin is best matched to intake using the system of carbohydrate counting, in which carbohydrate intake at each meal is estimated and then a sufficient bolus (short-acting insulin analogue) is given to balance the carbohydrate. A usual serving of a starch, fruit, carbohydrate-rich vegetable, or milk or milk equivalent basically represents about 15 g of carbohydrate. Often a carbohydrate-to-insulin ratio of 10 to 15 g carbohydrate for each unit of insulin will often serve as a good starting point. If a high glucose value is found at mealtime, adjustments should be given to correct for the hyperglycemia. An opposite correction may be required if the pre-meal glucose is low.

"Pumpers" use a term called the Insulin Sensitivity Factor (ISF). This represents the expected blood glucose drop in mmol/L obtained with 1 unit of insulin. It is often calculated by dividing the total daily dose into the number 90 (e.g. for a total daily insulin dose [TDD] of 45 units [90 ÷ 45 = 2], about 1 unit of insulin would be required to decrease BG by 2 mmol/L). Another "pumper calculation" is the insulin-to-carbohydrate ratio. For this, the total daily dose is divided into 450, i.e. 450 ÷ TDD. (In the example used above, 450 ÷ 45 units TDD = a carbohydrate-to-insulin ratio of 10:1, i.e. 10 g of carbohydrate ingested would need a dose of 1 unit of insulin.)

BLOOD GLUCOSE MONITORING

As noted above, the role of SMBG in improving glycemic control in type 2 patients who are using oral agents has not been demonstrated. However, SMBG is a critical component of overall diabetes management for patients taking insulin. Daily self-monitoring is especially important to check for asymptomatic hyperglycemia and hypoglycemia. The intensity of the monitoring required corresponds to the intensity of the insulin therapy (SMBG ≥3 times per day when multiple doses of insulin are administered in 1 day) (23).

Unfortunately, many patients with diabetes are not convinced, or are unaware, of the value of self-monitoring. Data from the National Health and Nutrition Examination Survey (NHANES) found that the great majority of patients with type 2 diabetes who were included in this study monitored their BG rarely, if at all, and although some patients may be diligent in testing their BG on a regular basis, they may not necessarily benefit in terms of glycemic control (24). Several reasons have been suggested for this finding. It may be that patients are testing but are not using the information to make adjustments to their therapy. Some patients find using a lancet device to be quite painful, and this can increase the psychological burden. In some cases, patients will find testing demoralizing, especially if results are outside the target range (17).

With new technologies and the advent of smaller monitors (which provide results in seconds, require smaller blood samples, and allow for the use of alternative test sites), patient technique becomes less of an issue, since many of the aspects of monitoring relate to ease of use. For example, if patients have difficulty handling small strips, they may insert the strips into meters improperly, causing false readings. New monitors have incorporated disc systems that eliminate the need to handle small strips. A more

ergonomic design can also alleviate pain for patients with arthritis or other musculoskeletal concerns. Optimally designed monitors are small and easy to grip, fit into the palm of the hand or rest on the tabletop. Several of these monitors also have large, easy-to-read displays, which are beneficial for visually impaired patients. Memory and data-management software allows monitors to hold up to 3000 readings, which are stored in an electronic logbook. Some monitors now have underfill detection features that alert patients if insufficient blood has been placed on the test strip. This lessens the risk of false-low readings, decreases waste and reduces expense to patients.

When used correctly, glucose monitoring plays a pivotal role in motivating patients and their healthcare providers to interpret BG levels and to assist in the optimization of nutrition, activity and/or insulin levels (25).

Continuous glucose monitoring systems

Even with frequent daily SMBG, the achievement of normal glycemic levels and the avoidance of hypoglycemia have remained elusive for many patients. Frequent fingerstick measurements offer a static picture at any given point, but do not provide a measurement of the magnitude and duration of glycemic excursions. The recent availability of continuous glucose monitoring systems (CGMS) provides an opportunity to match the demands of intensive therapy with intensive glucose monitoring. This system continuously measures subcutaneous interstitial glucose levels, on average, every 5 minutes.

Data provided by these monitors can help identify periods of previously undetected nocturnal hypoglycemia, and also allows patients and clinicians to make specific changes in the timing and dosing of insulin, as well as dietary and physical activity alterations (26). Preliminary clinical evidence with both type 1 and type 2 diabetes patients suggests that using CGMS data to make therapeutic adjustments results in an overall lowering of BG levels, and may even translate into a reduction in healthcare costs (27,28).

However, these devices are not yet useful for routine use in patients with diabetes, for a number of reasons. First, the sensor must be removed and reinserted in a different area every few days. In addition, patients must continue to measure their BG levels with a traditional monitor several times a day to ensure that the continuous glucose monitor is correctly calibrated. Also, the continuous glucose sensors currently available are not as accurate as most BG monitors. When BG concentrations are rapidly rising, or if levels are in the low range, there may be a difference between interstitial fluid glucose (measured by the sensor) and BG (measured by the capillary glucose), so confirmation of BG levels by fingerstick test may still be required. One benefit of CGMS is that trend arrows on the glucose sensor will show the direction that BG is moving and the speed of movement; this information is often as valuable as the actual BG value.

The cost of CGMS alone is about $2000 (US), which may make it unaffordable for some patients, but many diabetes clinics provide this service at a cost of $50 to $100 for 3 days.

Intensive therapy requires a core group of skilled professionals with diverse roles: an interdisciplinary team with the patient at the centre.

As well as stand-alone CGMS systems, some insulin pumps also have a built-in ability for continuous glucose monitoring.

Insulin delivery

Subcutaneous insulin injection has been the route of choice for the last several decades, but the inconvenience of multiple injections for type 1 patients needing intensive management, and the reluctance of type 2 patients to start insulin therapy, has spurred the development of non-invasive, needle-free delivery methods. Today, continuous subcutaneous insulin infusion pumps (CSII) are used primarily by type 1 patients. According to MiniMed Inc., the major supplier of pumps in the United States, there has been a more than 10-fold increase in the number of patients under 20 years of age starting on insulin pumps since the publication of the DCCT in 1993 (26). Insulin administered by pump provides a better day-to-day reproducibility, more reliable insulin action and fewer unexpected fluctuations in glycemic control. However, there are several requirements that patients need to fulfill to successfully use this therapy. They must be willing to monitor their BG several times daily, and must learn to count carbohydrates for accurate insulin adjustment of food intake. The use of a pump also requires patients to be sufficiently motivated to use problem-solving skills and be able to apply a glucose correction algorithm.

Funding agencies and provincial governments are gradually recognizing the potential benefits of pump therapy in improving glycemic control and decreasing complications, particularly in pediatric patients. The provinces of Ontario, Saskatchewan and Newfoundland now have programs that cover the full cost of an insulin pump and provide a monthly subsidy for pump supplies. Quebec has a pilot project to assess the costs and benefits of such a program.

Although there are potential metabolic advantages to CSII therapy in patients with type 2 diabetes, there have been very few controlled studies to determine if it leads to improved glycemic control (29).

Insulin pumps are considered "smart" as new features are added to their design. Software options can keep track of the insulin remaining in the bloodstream, calculate the dose for the next insulin bolus, and monitor activity during specific times of the day and then alert the user if an expected activity did not occur (e.g. missed lunch). For people with visual impairments, there are tactile features. Also, new pumps can interface with personal computers to simplify record keeping with diabetes management software, and can upload those records to the Internet. Perhaps the most interesting advancement in the integration of insulin pumps with glucose monitoring is that some pumps can receive glucose readings from an integrated monitor via infrared (IR) or radio frequency (RF) communication (30). There are currently no algorithms to automatically control insulin delivery based on biofeedback of BG level, although there have been abstracts indicating studies that are currently underway. If the loop were closed, the system would function as an artificial pancreas.

Other technological developments in this field may allow subcutaneous insulin administration to be supplemented or replaced by other modes of delivery such as

inhaled insulin; oral, buccal or dermal modalities; and intra-peritoneal delivery systems. Inhaled insulin delivers effective doses in a less painful and, for many, more acceptable manner, which may improve patient compliance; however, long-term pulmonary safety data are needed. At this point, neither Pfizer (which markets the product as Exubera) nor Health Canada is able to suggest when it will be available in Canada. It is currently approved for use in the US and Europe (31). Other oral, buccal and dermal modalities need more studies in order to demonstrate the long-term safety, tolerability and efficacy of these methods. The initial high cost of these novel insulins will price them out of the reach of the majority of people with type 2 diabetes.

Intra-peritoneal insulin holds considerable promise because of a more physiologic delivery of insulin into the portal circulation, and the ability to inhibit hepatic glucose production. Insulin is placed in disk-shaped infusion systems/pumps, then fully implanted in the abdominal subcutaneous tissue using general anesthesia. The pumps deliver regular insulin through a free-moving peritoneal catheter. Sufficient insulin is stored in the pump reservoir for 2 to 3 months' use. Pumps are refilled in hospital via a skin puncture that allows access to the reservoir. Rates of insulin delivery are modulated by the patient, according to the results of SMBG, using an external programmer that sends radio-wave signals to the electronic command unit of the pumping mechanism. The method has been used with some success in type 1 patients in France, but has not yet been approved for use in North America (32). Due to the invasive nature of their implantation into the abdominal cavity and the associated morbidity and costs, it is unlikely that this method will find widespread acceptance among patients with type 2 diabetes.

REFERENCES

1. United Kingdom Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. *Lancet*. 1998;352:837-853.
2. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329:977-986.
3. European Diabetes Policy Group 1999. A desktop guide to type 2 diabetes. *Diabet Med*. 1999;16:716-730.
4. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2003 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes*. 2003;27(suppl 2):S19.
5. American Association of Clinical Endocrinologists Medical Guidelines for the Management of Diabetes Mellitus: the AACE system of intensive diabetes self-management – 2002 update. *Endocr Pract*. 2005;8:41-65.
6. Malmberg K. Prospective randomized study of intensive insulin treatment on long term survival after acute myocardial infarction in patients with diabetes mellitus. DIGAMI (Diabetes Mellitus Insulin Glucose Infusion in Acute Myocardial Infarction) Study Group. *BMJ*. 1997;314:1512-1515.
7. Raucoules-Aimé M, Lugrin D, Boussofara M, et al. Intraoperative glycaemic control in non-insulin-dependent and insulin-dependent diabetes. *Br J Anaesth*. 1994;73:443-449.
8. LeRoith D, Fonseca V, Vinik A. Metabolic memory in diabetes – focus on insulin. *Diabetes Metab Res Rev*. 2005;21:85-90.
9. Herman WH, Dasbach EJ, Songer TJ, et al. The cost effectiveness of intensive therapy for diabetes mellitus. *Endocrinol Metab Clin North Am*. 1997;26:679-695.
10. Bayless M, Martin C. The team approach to intensive diabetes management. *Diabetes Spectrum*. 1998;11:33-37.
11. Gillespie S, Kulkarni K, Daly A. Using carbohydrate counting in diabetes clinical practice. *J Am Diet Assoc*. 1998;98:897-905.
12. Watts N, Spanheimer R, DiGirolano M, et al. Prediction of glucose response to weight loss in patients with non-insulin dependent diabetes mellitus. *Arch Intern Med*. 1990; 150:803-806.
13. Stern L. The effects of low carbohydrate vs. conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. *Ann Intern Med*. 2004;140: 178-185.
14. Cuff D, Meneilly G, Martin A, et al. Effective exercise modality to reduce insulin resistance in women with type 2 diabetes. *Diabetes Care*. 2003;26:2977-2982.
15. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2003 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes*. 2003;27(suppl 2):S1-S152.
16. American Diabetes Association. Glaxo's Avandia raises heart-death risk: Study. Available at: http://www.reuters.com/article/healthNews/idUSL2170925720070521?feedType=RSS. Accessed August 24, 2007.
17. Mitchell C, Bowker S, Majumdar S, et al. Lack of correlation between patient-reported outcomes and glycemic control in type 2 diabetes not managed by insulin. *Can J Diabetes*. 2004;28:362-368.
18. Wright A, Burden A, Paisley R, et al. Sulphonylurea inadequacy: efficacy of addition of insulin over 6 years in patients with type 2 diabetes in the United Kingdom Prospective Diabetes Study (UKPDS 57). *Diabetes Care*. 2002;25:330-336.
19. Cryer P, Davis S, Shamoon H. Hypoglycemia in diabetes. *Diabetes Care*. 2003;26:1902-1912.
20. Hirsch I, Bergenstal R, Parkin C, et al. A real world approach to insulin therapy in primary care practice. *Clin Diabetes*. 2005;23:78-86.
21. Arshag D, Mooradian A. *Internist's Hand book of Endocrinology, Diabetes and Metabolism*. St. Louis, MO: Saint Louis University; 1998.
22. Raccah D, Bretzel R, Owens D, et al. When basal insulin therapy in type 2 diabetes mellitus is not enough – what next? *Diabetes Metab Res Rev*. 2007;23:257-264.
23. Graham R. Self monitoring of blood glucose (SMBG) considerations for intensive diabetes management. *Pharm Ther*. 2005; 30:3-15.
24. Harris M. Frequency of blood glucose monitoring in relation to glycemic control in patients with type 2 diabetes. *Diabetes Care*. 2001;24:979-982.
25. Briggs A, Cornell S. Self monitoring blood glucose (SMBG); now and the future. *J Pharm Practices*. 2004;17:29-38.
26. Medtronic Diabetes website. Available at: http://www.medtronicdiabetes.com. Accessed August 24, 2007.
27. Skyler JS. The economic burden and the benefits of improved glycemic control: the potential role of a continuous glucose monitoring system. *Diabetes Technol Ther*. 2000;2(suppl 1):S7-S12.
28. Kaufman F, Gibson LC, Halvorson M, et al. A pilot study of the continuous glucose monitoring system: clinical decisions and glycemic control after its use in pediatric type 1 diabetic subjects. *Diabetes Care*. 2001;24:2030-2034.
29. Wittlin S. Treating the spectrum of type 2 diabetes, emphasis on insulin pump therapy. *Diabetes Educ*. 2006;32:39.
30. Medline Plus Medical Encyclopedia. Insulin pump. Available at: http://www.nlm.nih.gov/medlineplus/ency/imagepages/18035.htm. Accessed August 24, 2007
31. Canadian diabetics await inhaled insulin approval. Available at: http://www.cbc.ca/health/story/2006/07/13/insulin-inhaled.html. Accessed August 24, 2007.
32. Renard E. Implantable closed-loop glucose-sensing and insulin delivery: the future for insulin pump therapy. *Curr Opin Pharmacol*. 2002;2:708-716.

Canadian Diabetes *Readership Survey* – 2007

Thank you for taking the time to complete this survey about *Canadian Diabetes*, the quarterly newsletter that advances the practice of diabetes care and education through the distribution of current information to Canadian Diabetes Association members and primary care physicians across Canada.

By completing this brief survey, you will help us create a professional newsletter that best meets the needs of you – the reader. In addition, your name will be entered into a draw to win a one-year professional membership with the Canadian Diabetes Association (Diabetes Educator Section or Clinical & Scientific Section). Benefits of membership include receipt of Association publications, a reduced rate to attend the annual professional conference, opportunities for career development, and more.

Deadline for entry: November 1, 2007

Fax your survey to (416) 363-7465

Attention: *Canadian Diabetes* Readership Survey

1. *Canadian Diabetes* is published four times per year (March, June, September, December). How many issues per year do you read?

- O One
- O Two
- O Three
- O Four

2. How thoroughly did you read the most recent issue of *Canadian Diabetes*?

- O Read it completely
- O Read selected articles
- O Scanned it
- O Didn't read

3. When you finish reading *Canadian Diabetes*, do you usually:

- O Save it
- O Pass it along to someone else to read
- O Discard it

4. What do you think of the four times per year publication schedule for *Canadian Diabetes*?

- O It's just right
- O I would like to receive this newsletter more often than four times a year
- O It's too often

5. Do you have any suggestions for specific topics to be covered in *Canadian Diabetes*?

_____

_____

_____

_____

6. Would you be interested in *(please check all that apply):*

- O Writing a referenced paper
- O Writing about projects/programs relevant to diabetes education
- O Acting as an information contact for Canadian Diabetes Association publications

N.B. if you are interested in participating in Canadian Diabetes Association publications please fill in the contact information below.

7. Would you like to receive information on joining the Canadian Diabetes Association?

- O Yes O No

8. Please tell us your overall impression of *Canadian Diabetes*, or provide suggestions that you feel would help us improve the newsletter:

_____

_____

_____

9. Do you read or receive other publications from the Canadian Diabetes Association?

- O Yes, *Canadian Journal of Diabetes*
- O Yes, *The Diabetes Communicator*
- O Yes, *Diabetes Dialogue*
- O Yes, other (please specify): _____
- O No

10. Can you name the sole sponsor of *Canadian Diabetes*?

_____

To qualify for the draw to win a one-year professional membership with the Canadian Diabetes Association, please provide your contact information (optional):

NAME:	E-MAIL ADDRESS:	PHONE NUMBER:	FAX NUMBER:

(Please note that all personal information is held confidential according to the Canadian Diabetes Association's privacy policy. Visit http://www.diabetes.ca/section_main/privacy.asp for further information.)

For more information on the Canadian Diabetes Association's professional memberships, please visit http://www.diabetes.ca/professionals.

Fax your survey to (416) 363-7465
Attention: *Canadian Diabetes* Readership Survey

Thank You!

Suite de la page 12
aussi d'une prise en charge intensive. La formation nécessaire est relativement simple, car elle est fondée sur des principes physiologiques.

En présence de diabète de type 2, le besoin d'insuline exogène augmente à mesure que le pancréas se détériore. Si on intensifie le traitement tôt en prescrivant une insuline de base, on obtient un bien meilleur contrôle. Lorsque la détérioration du pancréas atteint un certain degré, le besoin d'insuline prandiale devient évident. Dans ce cas, de nombreux patients atteints de diabète de type 2 apprécient la souplesse et le degré de contrôle que leur procurent les insulines prandiales à action rapide. L'usage d'algorithmes pour l'adaptation des doses d'insuline prandiale améliore la souplesse du traitement et le contrôle de la glycémie[4]. Lorsque la sécrétion endogène d'insuline diminue au point où les besoins d'insuline de base et de bolus d'insuline sont évidents, les patients atteints de diabète de type 2 doivent amorcer un régime thérapeutique intensif (ou souple) comme celui des patients atteints de diabète de type 1.

Les nouveaux analogues de l'insuline, s'ils sont utilisés correctement, reproduisent le fonctionnement normal du pancréas. L'insuline semilente (NPH) ou les analogues de l'insuline à très longue durée d'action, telles les insulines glargine et detemir, comblent les besoins d'insuline de base, tandis que les insulines à courte durée d'action, telles les insulines aspart et lispro, peuvent répondre aux besoins d'insuline au moment des repas et corriger rapidement une hyperglycémie. Chez les patients qui présentent une hypoglycémie nocturne lorsqu'ils reçoivent de l'insuline NPH ou un mauvais contrôle de la glycémie immédiatement après un repas suivi d'une hypoglycémie, l'administration d'un analogue de l'insuline convenable est une bonne solution.

L'utilité de la perfusion sous-cutanée continue d'insuline a été établie au cours de l'essai DCCT, mais il a fallu l'avènement des nouveaux analogues de l'insuline à action rapide et des microprocesseurs pour que les promesses se réalisent. Les pompes à insuline sont de mieux en mieux acceptées comme outils de prise en charge, surtout depuis que certains régimes d'assurance maladie provinciaux ont commencé à en rembourser le coût chez les enfants. Il est encore préférable que le traitement par une pompe à insuline soit amorcé par un professionnel de la santé qui s'y connaît, mais les médecins de famille devraient avoir des connaissances élémentaires, parce qu'un nombre croissant d'utilisateurs de pompe à insuline se présenteront au service des urgences ou au cabinet de leur médecin et ils devront contribuer au choix des patients pouvant recevoir une pompe à insuline. Ces dispositifs sont de plus en plus perfectionnés et peuvent maintenant afficher la quantité d'insuline active restante après l'administration d'un bolus. Les corrections sont donc plus précises et le risque d'hypoglycémie, moindre.

Les patients qui portent une pompe à insuline doivent bien comprendre la détermination de leurs doses d'insuline et sont probablement les mieux placés pour les adapter en présence d'une maladie aiguë : ils pourraient devoir augmenter les doses d'insuline de base et adapter le «facteur de correction pour l'hyperglycémie», car les hormones anti-insuline peuvent accentuer l'insulinorésistance. Ainsi, une personne qui utilise habituellement 1 unité d'insuline pour réduire sa glycémie de 4 mmol/L pourrait avoir besoin de 1 unité pour réduire sa glycémie de 2 mmol/L si elle est malade. Le rôle du médecin de famille ou du service des urgences peut être de rappeler ces renseignements aux patients. Si un patient est trop malade pour gérer sa pompe, le renseignement clé dont le médecin traitant a besoin est sa dose quotidienne totale, car cette dose sera la base du traitement à l'hôpital et pourra être administrée sous forme de bolus avant les repas et d'insuline NPH ou d'une autre insuline de base au coucher s'il n'est pas réaliste de se servir de la pompe.

Non seulement la prise en charge intensive du diabète donne-t-elle aux patients plus de souplesse au quotidien, mais elle leur donne plus de jours pour profiter de cette souplesse. Du point de vue de l'assureur, il est avantageux d'investir dans la prévention, soit de fournir des pompes à insuline et d'autres ressources maintenant, si justifié, car elles préviennent les complications à long terme et les coûts connexes. Puisqu'une pandémie de diabète de type 2 se pointe à l'horizon, il serait prudent pour tous les médecins qui traitent de tels patients de se familiariser avec les avantages de la prise en charge intensive du diabète. Dans quelques années, les patients et le système de soins de santé nous en remercieront.

RÉFÉRENCES (voir 3e colonne)

Editor's Note…continued from page 1
and are likely best at adjusting their insulin in acute illnesses; they may need to increase basal rates in situations of illness as well as making adjustments to their "high glucose correction factor," since the anti-insulin hormones may make them more insulin resistant than normal. This would mean that individuals who can usually use 1 unit of insulin to lower their glucose by 4 mmol/L may need 1 unit for a 2 mmol/L excess if they are ill. The role of the family doctor or emergency room physician may be to remind them of these things. In patients who are very ill and cannot manage their pumps, the key information that the treating physician needs is their total daily dose (TDD), since this dose will form the basis of therapy in hospital if needed, and can be applied as pre-meal bolus and overnight intermediate NPH or other basal insulin if pump use cannot be realistically applied.

Not only does intensive diabetes management allow patients more flexibility in their day-to-day lives, it will grant them more days in which to enjoy that flexibility. From the perspective of the insurer, it is advantageous to invest in prevention – by supplying insulin pumps and other resources now, when warranted – knowing that doing so will prevent long-term complications and inherent costs. As a type 2 diabetes pandemic looms on the horizon, it would be prudent for all physicians treating such patients to become familiar with the advantages of intensive diabetes management. Years from now, our patients and the healthcare system will thank us.

REFERENCES

1. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med.* 1993;329: 977-986.
2. United Kingdom Prospective Diabetes Study (UKPDS) Group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. *Lancet.* 1998;352: 837-853.
3. Diabetes Control and Complications Trial/ Epidemiology of Diabetes Interventions (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med.* 2005;353:2643-2653.
4. *Practical Diabetes Management: Clinical Support for Primary Care Physicians.* Toronto, ON: Canadian Diabetes Association; 2004.

LAISSER NOTRE EMPREINTE DANS L'HISTOIRE DU DIABÈTE

DIA-06-CDN-34500124-JA-F

OÙ EN SOMMES-NOUS RENDUS ?

Depuis plus de 100 ans, Merck Frosst tente de repousser les frontières de la médecine. En collaboration avec les professionnels de la santé, nos chercheurs ont mis au point des médicaments novateurs toujours utilisés dans la lutte incessante contre la maladie.

Ce même esprit novateur et notre engagement sont mis à contribution pour contrer le diabète. Pour les nombreux Canadiens atteints de cette affection, Merck Frosst tente de réécrire l'histoire de la médecine.

Comme pour vos patients, la lutte contre le diabète fait partie de notre quotidien.

MERCK FROSST

Découvrir toujours plus.
Vivre toujours mieux.

Merck Frosst Canada Ltée, Kirkland, Québec

VEUILLEZ CONSULTER NOTRE SITE WEB : **www.merckfrosst.com**

Canadian Diabetes

Le diabète au Canada Volume 20 N° 3 Automne 2007

Prise en charge intensive du diabète : un nouveau paradigme pour une nouvelle époque

Robin Conway, M.D., et Sara Meltzer, M.D., FRCPC

Note de la rédaction

La prise en charge du diabète a énormément évolué en 20 ans. Les résultats de l'essai DCCT (*Diabetes Control and Complications Trial*)[1] et de l'étude UKPDS (United Kingdom Prospective Diabetes Study)[2] ont irréfutablement démontré que la normalisation de la glycémie peut réduire considérablement, sinon éliminer, les complications microvasculaires dévastatrices du diabète. Si nous tenons compte de cette conclusion, il ne sera question de cécité, d'insuffisance rénale et de neuropathies causées par le diabète que dans les manuels d'histoire. Il existe de plus en plus de données indiquant que mêmes des anomalies légères de la glycémie sont associées à une hausse du risque de maladie cardiovasculaire et qu'un bon contrôle de la glycémie est nettement avantageux[3]. Par conséquent, les objectifs glycémiques recommandés se sont petit à petit rapprochés des valeurs normales. Ces objectifs sont maintenant davantage réalisables grâce aux améliorations des méthodes de surveillance de la glycémie à domicile, aux nouveaux analogues de l'insuline, aux dispositifs d'administration de l'insuline et aux outils de prise en charge tels le compte des glucides et la prise de décision assistée par ordinateur. On ne peut faire abstraction du concept de prise en charge intensive du diabète et de ses avantages. Le terme «prise en charge intensive» pourrait être inexact; en fait, on a changé le paradigme et au lieu d'établir la dose d'insuline puis d'adapter les repas et le mode de vie en conséquence, on charge le patient d'adapter la dose d'insuline à son mode de vie et à son apport alimentaire. Il serait peut-être plus juste de parler de «prise en charge souple» ou de «prise en charge physiologique».

On a démontré que les patients qui prenaient part à leur propre traitement étaient plus susceptibles de s'y conformer, ce qui aboutit à un meilleur contrôle de la glycémie et une meilleure qualité de vie. On ne croit plus que les avantages de la «prise en charge intensive» sont limités aux patients atteints de diabète de type 1. L'étude UKPDS[2] a révélé que les patients atteints de diabète de type 2 bénéficient

Suite à la page 10

CANADA POSTES
POST CANADA
Postage paid Port payé
Publications Mail Poste-publications
40063447