Diabetes Technologies and Their Role in Diabetes Management

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ABSTRACT

The 1993 Diabetes Complications and Control Trial (DCCT) showed that controlling blood glucose prevents and delays the progression of long-term complications of diabetes. New diabetes technologies can make control of diabetes possible and safer. This paper reviews these technologies used to monitor blood glucose, administer insulin and evaluate effectiveness of therapy. Self-monitoring of blood glucose has been a standard of care for several decades. Today, patients and practitioners can gain great benefit from data that can be provided by using Continuous Glucose Monitoring (CGM). Current physiologic insulin therapy regimens have improved blood glucose control capabilities. Insulin therapy devices, including pens and pumps are reviewed. Advantages of insulin pump therapy and features of the latest ‘smart’ pumps are described. Children with diabetes, and their families, have many challenges as well as many opportunities to employ new technologies in diabetes management plans. The ability of school and caregivers to support children can impact the overall success of any diabetes therapy regimen.


INTRODUCTION

The control of diabetes and its effects on long-term morbidity are well known. Many new ideas and modalities have been explored that target improved methods to monitor blood glucose and deliver insulin to achieve better metabolic control. Over the years, technological advances in these areas have made it possible to improve blood glucose control. This review addresses these newer technologies such as:

- Blood glucose (BG) monitoring
- Real time continuous glucose monitoring (CGM)
- Insulin delivery with insulin pens and pumps
- The closed loop system (artificial pancreas)
- Blood Glucose Monitoring

Blood glucose monitoring as a means of assessing diabetes control has been used since the 1970s and is an essential clinical tool in day-to-day diabetes management. The Diabetes Control and Complication Trial clearly has shown that good control of BG improves short- and long-term microvascular complications. Because of technological advances, the devices that monitor blood glucose are more accurate and efficient than ever before.

BG monitoring is done using two methods: blood glucose meters for checking blood glucose levels at discrete times, most commonly used for day-to-day diabetes management; and continuous glucose monitoring.

Blood glucose meters. Self-monitoring of blood glucose (SMBG) is the essence of day-to-day diabetes control. SMBG enables patients and their health care providers to make medication adjustments that achieve and maintain optimal glycemia. Over the
last decade, glucose meters have dramatically improved in their ease of use, in time required to perform the test and in volume of blood required.

**Technology of the glucose meters.** All glucose meters use enzymes that oxidize the glucose in the blood sample. Electrons released from the glucose by this reaction generate an electrochemical current that is measured as a digital value displayed on a screen. The amount of current released is proportional to the glucose concentration. Most of the meters use this method for glucose measurement. Though most of the meters contain sensors that adjust and correct to the outside temperature, glucose strips used for meters may give inaccurate readings in extreme hot or cold weather. It is advisable to wait before testing to assure that strips are at room temperature, to eliminate errors.

**Accuracy and precision.** All glucose meters in use today are reasonably accurate, with blood glucose values being within 5% (5mg/dl <100mg/dl) of the lab value if done with capillary blood from the finger. There is also good reproducibility, with blood glucose results from the same drop of blood on two separate occasions having little variability, differing by only 2% to 3%. The difference in readings between two meters using the same drop of blood has been shown to be less than 4%.

Most meters need only about 0.3 to 10 µl of blood to function. Most current meters are calibrated for capillary blood from finger tips. There is an increasing demand for testing at alternate sites because of the discomfort of the frequent finger pricking. Some meters are FDA approved for alternate site testing with the forearm being the most popular site, though the abdomen, thigh and other areas of the body may be used. However, there are limitations to the use of alternate sites. There is lag time between the actual blood/capillary glucose (finger prick) to that of interstitial (other sites), resulting in delayed recognition of hypoglycemia. Accuracy of the level is affected for the samples obtained after exercise and one-hour post-prandial (after a meal), especially if glucose levels are low.

**Data storage and reproducibility.** All meters are equipped with memory of data storage in many different formats. In addition to the blood glucose data, other information such as food and exercise data can be stored. These stored data can be imported into patient’s charts using software for uploading, transmitted to insulin pumps and communicated to health care providers via web-based programs. The computer data displays are used to estimate the glucose trends; average and standard deviations that help to identify insulin adjustment needs. The new glucose meters are easy to use resulting in improved patient acceptance and motivation to improve diabetes control.

### CONTINUOUS GLUCOSE MONITORING (CGM)

Continuous glucose monitoring recently has been approved by the FDA and provides an additional tool for diabetes management. These monitoring devices are approximately the size of a cellular phone and are worn on a belt or in a pocket. A sensor is inserted through a plastic cannula under the skin, in the subcutaneous tissue. Glucose values are displayed on a digital screen every few minutes with arrows or other indicators of blood glucose trends, allowing the adjustment of food or insulin early to prevent low or high blood glucose levels. Several FDA approved devices are available commercially for continuous glucose monitoring. However, these devices are complex, and specially trained diabetes care personnel are needed to teach patients how to use them.

**Technology of CGM.** All commercial CGM devices measure glucose from the interstitial subcutaneous tissue. The sensors generally are stable and functional for 3 to 7 days. The system consists of a transmitter which provides the energy for the sensor and facilitates the transfer of the glucose signal to a receiver. The sensor takes time to generate an accurate signal after insertion, and it is important to recalibrate if the sensor is detached for any reason. Currently there are four such CGM devices (Table 1).

All sensors can be programmed for low and high alarms that are set by parents, and all indicate that action must be taken. Glucose values are recorded every five minutes. Sensors measure a wide range of glucose levels, from 20mg/dl to 500 mg/dl. All involve wireless transmission of data to a receiver.

**Accuracy of the sensor data.** Because the glucose levels that these sensors measure are of the interstitial tissues, readings from the BG meter differ from the sensor glucose levels by 8mg/dl to 18 mg/dl. There is a time lag between measurements—the sensor value reading lagging behind the meter reading. Whenever rapid or wide fluctuations in blood glucose levels occur, there is an even greater difference between the sensor value and finger stick BG value. For these reasons, calibration should not be performed following meals or during hypoglycemia. Sensors should be calibrated using the capillary levels obtained on the glucose meter a few times over a 24-hour period.

The most useful information that the sensor provides is about trends of glucose excursions, which can be used to make appropriate changes in insulin dosing, food intake and physical activity. Sensors have been tested in studies to test patient acceptance, ability to lower HgbA1c and ability to detect hypoglycemia. A large study is underway to test the effect of these sensors on diabetes control.

**Sensor and hypoglycemia.** Avoidance of clinically significant hypoglycemia is important because low blood glucose levels have negative effects on health. CGM has helped in identifying and reducing the frequency and degree of hypoglycemia. To detect low BG values, the sensor alarm can be set for specific glucose levels and for the glucose level rate of fall. Thus, based on the rate of fall of glucose, potential hypoglycemia can be prevented. Patients who use the sensor feel that it helps decrease the frequency of hypoglycemia and gives them additional information for adjusting insulin doses. The CGM devices store all blood glucose data and include software that allows the information to be downloaded. This information can be inter-phased with the insulin delivery history from an insulin pump and used to make insulin dose adjustments.
CGM is an excellent tool for patients with diabetes who are motivated and who want to optimize their control. It gives peace of mind to parents of young patients who have frequent episodes of hypoglycemia or have hypoglycemia unawareness. More experience is needed to establish its efficacy in improving diabetes control. Its use is limited to centers that have trained personnel who can teach patients to use it.

**NEWER INSULIN DELIVERY SYSTEMS**

Insulin delivery is now most commonly performed using insulin pens and pumps. More and more children and their families are opting for use of these alternate methods of insulin delivery over conventional insulin syringes. Pens and pumps free the patient from the need to carry and store the paraphernalia needed for traditional modes of insulin injection.

### Insulin Pens

There are both pre-filled disposable and reusable pens with pre-filled cartridges. An advantage of insulin pens is that they do not need refrigeration and are accepted well by patients, especially teenagers, as the device truly looks like a pen; thus, the stigma of using a syringe and needle is avoided. Because of the pens’ easy use, caretakers other than parents (school personnel, baby sitters) can be taught to be comfortable in dialing up the insulin dose.

### Insulin Pumps (Continuous Subcutaneous Insulin Infusion [CSII])

The advent of insulin pumps has revolutionized insulin delivery. Continuous subcutaneous insulin infusion mimics physiological insulin secretion by providing basal insulin to inhibit glucose production by the liver. Mealtime boluses can be determined by a pre-programmed algorithm and delivered by manually pressing a button on the pump. Since its introduction in the 1970s, there have been many technological advances in delivery of the insulin with the pumps. The pumps currently in use are called “smart pumps,” as they have programmable features that are built-in and enable the patient to tailor their insulin delivery more precisely to achieve fine tuning of blood glucose levels. Pumps have greatly facilitated diabetes management, allowing a more flexible lifestyle than was dictated by fixed insulin regimens, in which the timing and composition of meals had to coincide with peak action of insulin to avoid hypoglycemia and fluctuations in blood glucose levels. This single modality has made living with diabetes easier.

### Technology

All pumps have an insertion set, in which a plastic cannula is inserted into

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**Table 1. Continuous Glucose Monitoring Devices**

<table>
<thead>
<tr>
<th>Features</th>
<th>Medtronic MiniMed Guardian</th>
<th>Medtronic MiniMed Real Time Insulin Pump</th>
<th>DexCom</th>
<th>Freestyle Navigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication</td>
<td>Wireless receiver</td>
<td>Insulin pump receiver</td>
<td>Wireless receiver</td>
<td>Wireless receiver</td>
</tr>
<tr>
<td>Distance</td>
<td>6 feet</td>
<td>6 feet</td>
<td>5 feet</td>
<td>10 feet</td>
</tr>
<tr>
<td>Sensor life</td>
<td>3 days</td>
<td>3 days</td>
<td>7 days</td>
<td>5 days</td>
</tr>
<tr>
<td>How BG data are obtained</td>
<td>Manual or linked to glucometer</td>
<td>Same as the Guardian</td>
<td>Cable link to One Touch Ultra or manual</td>
<td>Freestyle meter built into the receiver</td>
</tr>
<tr>
<td>Number of calibrations</td>
<td>2 to 4 / day</td>
<td>2 to 4 / day</td>
<td>2 to 4 / day</td>
<td>4 / 5 days</td>
</tr>
<tr>
<td>Predictive high/low alarm</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Range of glucose display (mg/dl)</td>
<td>40 to 400</td>
<td>40 to 400</td>
<td>40 to 400</td>
<td>20 to 500</td>
</tr>
<tr>
<td>Display updated</td>
<td>Every 5 minute</td>
<td>Every 5 minutes</td>
<td>Every 5 minutes</td>
<td>Every 1 minute</td>
</tr>
<tr>
<td>Events that can be entered</td>
<td>Insulin, meals, exercise</td>
<td>Insulin, meals, exercise</td>
<td>None</td>
<td>Insulin, meals, exercise, health, other</td>
</tr>
<tr>
<td>Computer software</td>
<td>Insulin, meals, exercise, Carelink personal software</td>
<td>Carelink personal software integrates with Paradigm pump download</td>
<td>DexCom DM, consumer data manager DM 2, professional data manager</td>
<td>Freestyle CoPilot software</td>
</tr>
</tbody>
</table>
the subcutaneous (SQ) tissue using a needle

guide. In general, the cannula is connected
to the pump by flexible tubing. The sole

exception is the Omnipod pump, in which

no tubing is needed, as the catheter is part of

the Omnipod itself and inserts directly into

the SQ tissue. All pumps share many basic

features, with some minor differences:

• Compact and easy to wear

• Programmable dosing calculators for car-

bohydrates and for correction of high BG

• Alarm settings for battery life and insulin

volume

• Child safety locks

• Many types of boluses to suit the meal

content

• 24-hour technical support

• Bolus history tracking

Additional features of the newer smart

pumps include:

• Automatic communication with the BG

meter

• Bolus onboard feature to avoid stacking

(cumulative effect) of insulin

• Food data information and capability to

add new foods

• Waterproof feature

• Variable basal patterns

• Communication with CGM

• Software for downloading all information

Commercially available insulin pumps

are shown in Table 2.

Advantages of using CSII. Rapid acting

insulin analogues are more physiological and

more effective in controlling meal-related

hyperglycemia than are older insulins.10

Rapid acting insulin can be given using mul-

tiple doses of insulin (MDI) per day to cover

meals. This at times may create problems

with acceptance and adherence. One of the

main barriers to optimal diabetes control

to teens has been the unwillingness to give

insulin injections every time they eat.

CSII provides the freedom and flexibility

of lifestyle and produces better coping and

acceptance of the rigors of daily diabetes care,

with improved quality of life and greater

adherence to recommendations.11 Freedom

from restrictions of timing and number of

meals is an important issue among teenag-

ers. Use of insulin pumps eliminates that

restriction and provides greater satisfaction

with diabetes management.12 As glucose

variability is lessened with basal rate adjust-

ments, the fear of hypoglycemia diminishes,

and may even be eliminated.

Metabolic advantages. CSII not only pro-

vides improvement in patient satisfaction

and better acceptance of diabetes, but offers

better glycemic control. Reduction of serious

hypoglycemia associated with seizures and

coma is significant, from 37% to 24% (Fig-

ure 1). CSII also has improved meal-related

hyperglycemia and decreased the frequency

of post-prandial hyperglycemia. Because

HgbA1C is the standard measure of diabetes

control, the effect of CSII on HgbA1C has

been studied extensively. Improvement of

HgbA1C has been shown in studies compar-

ing MDI with CSII. At baseline (Figure 2) the

levels were not significantly different. At 16

weeks, the CSII (pump) group had signifi-

cantly lower levels compared to baseline.

Glucose variability and CSII. Glucose

variability has been receiving more attention

as an important indicator of metabolic con-

trol. Great variability in BG causes oxidative

damage to the endothelium, and hence, leads
to long-term morbidity. This effect is consid-
ered to be as damaging as exposure to hyper-
glycemia.13 With CSII, insulin delivery can be

adjusted to decrease or even to eliminate this

variability. To reduce the degree or frequency

of blood glucose variability further, it is now

possible to incorporate the data from some

CGM devices into the pump’s memory,

with the goal of having the pump adjust

the settings based on the BG numbers and
trends. This adjustment is done by the use of

algorithms. One such algorithm was devel-

oped by the DirecNet study group.14 DATA

(DirecNet Applied Treatment Algorithm)

provides guidelines that help the CSII/CGM

Table 2. Comparative Features of Insulin Pump Varieties

<table>
<thead>
<tr>
<th>Features</th>
<th>Animas IR2020</th>
<th>Medtronic Paradigm</th>
<th>Accu-Chek Spirit</th>
<th>Insulet Omnipod</th>
<th>Sooil/USA diabecareIIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Battery life</td>
<td>6 wks to 8 wks</td>
<td>3 wks</td>
<td>3 wks</td>
<td>4 wks</td>
<td>8 to 10 wks</td>
</tr>
<tr>
<td>Reservoir size</td>
<td>200 units</td>
<td>300 units</td>
<td>176 or 300 units</td>
<td>200 units</td>
<td>300 units</td>
</tr>
<tr>
<td>Basal increment</td>
<td>0.025 U</td>
<td>0.05 U</td>
<td>0.05 U</td>
<td>0.05 U</td>
<td>0.01 to 0.1 U</td>
</tr>
<tr>
<td>Bolus increment</td>
<td>0.05 U</td>
<td>0.05 U</td>
<td>0.1 U</td>
<td>0.05 U</td>
<td>0.1 U</td>
</tr>
<tr>
<td>BG meter link</td>
<td>Manual entry Link with Ultra Ping</td>
<td>Manual entry Link with Ultra</td>
<td>Link with Ultra</td>
<td>Link with Ultra</td>
<td>Link with Ultra</td>
</tr>
</tbody>
</table>
user to modulate the pump settings for more accurate insulin dosing and to reduce blood glucose variability.

CLOSED LOOP SYSTEM (ARTIFICIAL PANCREAS)

With technological advances, combining of CGM and the newer programmable external pumps, along with a built-in algorithm that automatically adjusts the insulin delivery based on BG readings from the sensor, constitutes the “closed loop” or “artificial pancreas.” This insulin delivery system more closely reproduces normal beta cell function in achieving near normal glycemia. However, as the glucose readings obtained from CGM lag behind blood glucose concentrations, and subcutaneous insulin delivery lags behind the physiologic portal delivery route, the ability of the closed loop system to lower post-prandial hyperglycemia is not yet ideal. However, it is superior to other currently available alternatives. The future of this concept of closed loop artificial pancreas is being explored further under the JDRF Artificial Pancreas Project.

SUMMARY

The discovery of insulin dramatically changed management of diabetes. Since then many new modalities have improved both short-term and long-term diabetes care. Newer technological strategies and tools have not only made living with diabetes easier, but have improved metabolic outcomes. In the future, further refinement of glucose monitoring and insulin delivery systems will pave the way for improved access of the latest technologies to all patients with diabetes, ultimately leading to development of a true artificial pancreas.

REFERENCES


