Intraoperative Management of Diabetes Mellitus: Whats new?

Zulfiqar Ahmed, MBBS, FAAP
Department of Anesthesiology
Children's Hospital of Michigan Detroit, MI

This refresher course is designed to discuss the recent advances in diabetes mellitus management. We will discuss the new types of insulins in the market, their use along with the new types of monitoring methods available to the patients and the physicians. Also we will review the new methods of insulin administration to the patients[1]. This topic has important implications on peri operative management of diabetic patients.

New Insulin Types

Insulins currently available are classified on the basis of onset of action, peak effect, and duration of action[2]. Three analogs of human insulin for intravenously administered insulin along with an inhalational form are now available by prescription. They include: insulin lispro and aspart as rapid acting and glargine as long-acting, when given subcutaneously. Exubera is an inhalational form of insulin, is now available in the market

Insulin Lispro

Insulin lispro was the first true rapidly acting insulin produced by recombinant DNA technology. Regular insulin, when injected subcutaneously, produces hexamers and dimers, slowing the absorption. This aggregation is diminished with lispro, so it is more rapidly absorbed and has a shorter duration of action. The effect peaks in 30 min to 1 h and lasts from 3 to 4 h. Thus, the critical time during which hypoglycemia may develop is 0.5 to 1.5 h after administration. Insulin lispro is commonly used in continuous subcutaneous insulin pumps.

Insulin Aspart

Insulin Aspart (Novolog) has a single substitution of proline by aspartic acid at B-28; the kinetics are similar to lispro.

Insulin Glargine

Insulin glargine[3] is a long-acting recombinant human insulin analog. It may be compared to, and considered as, a replacement for NPH, Lente, and Ultralene. It has a longer duration of action with no pronounced peak. With once-daily use, it is similar to twice-daily human NPH insulin in tolerability and glycemic control. Results of trials have shown that insulin glargine can be used as a baseline in Type I and 2 DM in concert with other drugs, including short-acting insulin, insulin lispro, and oral hypoglycemic drugs in Type 2 patients. Glargine is not physically compatible with other insulin and therefore requires a separate injection.

Inhaled Insulin

FDA recently approved inhaled insulin (Exubera™). It is available in a blister pack and is delivered via an inhaler as aerosolized powder into the oral cavity. The onset if inhaled insulin is as fast as subcutaneous injection of the insulin analogues. The duration of action of Exubera™ is longer then insulin analogues and comparable to subcutaneously administered regular insulin.

The clinical efficacy of Exubera™ administered three times a day before meals along with a single night time injection of Humulin was comparable to multiple subcutaneous injection regimens.

Figure-1
Inhaler for Exubera

New Monitoring Methods

Home Monitoring

Although home monitoring is not new, present technology allows the multiple, rapid, and accurate daily analysis that is crucial for optimum disease control. Technology allows for an almost painless collection of a blood sample. Home monitors require very small amounts of blood and yield results in seconds. BG readings help the patient to adjust his or her dose of insulin and allow the information necessary to program an insulin pump to be obtained. Perioperative monitors, like the i-STAT System, (Abbott Laboratories, North Chicago, IL) provide clinicians an on-site, portable, nearly instantaneous blood analysis that is reliable and accurate.

Glycosylated Hemoglobin

Hb-A_{1c} is a measure of the percent of hemoglobin (Hb) that has been non-enzymatically glycosylated by glucose on the ß chain. A normal level is 4%–6%. The ADA recommends values of <7% to <8.5% depending on the age of the patient. Although not diagnostic, increased levels suggest existing diabetes or poor control of BG levels during the previous 1–3 months. Periodic measurements allow for the assessment of the long-range effectiveness of glucose control.

Urinary Ketones

Commercially available reagent strips are used by patients if they develop symptoms of a cold, flu, vomiting, abdominal pain, polyuria, or on finding an unexpectedly high glucose level. Blood ketone testing is also available and is recommended for patients with persistent, rapid and marked fluctuations in their degree of hyperglycemia.

Methods of Medication Administration

As proven unequivocally by Diabetes Complications and Control Trial[4], the first objective of diabetes management is to maintain BG levels as close to normal as possible. The long-term complications of DM, such as atherosclerosis, neuropathy, nephropathy, and retinopathy, can be delayed or minimized by rigid BG control. Multiple methods of insulin administration have been suggested.

Multiple Subcutaneous Injections

Multiple subcutaneous injections involve the administration of 25% of the total dose as intermediate or long-acting insulin at bedtime with additional doses of a rapid-acting preparation before each meal (four dose regimens). Type I patients may require intermediate or long-acting insulin in the am, as well as the evening, for coverage throughout the day. They will also require

rapid-acting insulin with each meal or snack. Patients adjust the dose in concert with recommendations of their provider by evaluating BG levels. Insulin is now available in multiple-dose insulin injection pens. These pens provide insulin in a variety of combinations, including lispro (Humalog), aspart (Novolog), NPH, and fixed mixtures of regular or rapid-acting analog and NPH. Pens may make multiple injection prescriptions more convenient for patients because they eliminate the need for carrying vials of insulin and syringes. The fixed mixtures are generally not used in T1DM.

Insulin Pumps

It is now possible to use an external pump connected to a subcutaneous catheter to administer insulin continuously[5]. (MiniMed, Insulin Pump (Medtronic MiniMed, Northridge, CA.) Delivery is through a specially developed 25-gauge catheter placed under the skin. The site is changed every 2–4 days to ensure adequate delivery: detachable catheters allow patients to bathe. Insulin pumps can program multiple different 24-h delivery rate patterns and are adjusted to achieve a normal or near-normal BG level. Usually rapid-acting insulin is used in these pumps and the requirement is dictated by the previous insulin regimen of the patient. There is a basal rate as well as a bolus mode for preprandial deliveries. They are programmable to give a variable basal insulin rate with the capability for boluses at appropriate times.

Implantable Pumps

Implantable insulin pumps are not currently available. Mini-med pumps (in development) are disk-shaped, titanium-cased devices, and the infusion rate can be adjusted by a hand-held remote controlled programmer. They are placed subcutaneously and the catheter floats freely in the peritoneum. Refill is accomplished subcutaneously via injection. The proximal portion has a port through which the catheter can be flushed when blocked. The advantage is that the intraperitoneal insulin is completely absorbed into the portal circulation and 50% of the dose is extracted by the liver in the first pass effect. Absorption of insulin is more predictable intraperitoneally than subcutaneously. The higher portal circulation and lower systemic circulation mimics physiology and with hypoglycemia, lower systemic circulation inhibits the counter-regulatory hepatic glucose production less than would otherwise occur. The degrees of glycemic control and glycated Hb concentration achieved with peritoneal absorption are similar to those obtained with intensive subcutaneous insulin treatment but with less risk of hyperglycemia from subcutaneous catheter interruptions.

Continuous Subcutaneous Glucose Monitors

Still in development, these monitors can be used for short-term monitoring in the pediatric population. Although they are not sufficiently accurate to use for immediate insulin determination, they can identify glucose trends. Thus, changes in BG can be monitored very closely and changes in glucose dynamics can be detected early. These monitors document incidences of asymptomatic hypoglycemia of 30%–60%.

Perioperative Management

Guidelines for perioperative BG management for patients on insulin pumps are listed[1] in Figure-2. With frequent glucose determinations (hourly or more often), subcutaneous continuous insulin administration with an insulin pump is safe and provides more consistent BG levels. On arising, before surgery, the patient will have BG measured and be given clear liquids with or without sugar depending on the BG level. The basal insulin infusion continues as programmed. The pump can be used to administer subcutaneous insulin boluses if directed.

Regardless of the method chosen to administer insulin in the perioperative period, frequent BG monitoring is essential to guide management. Surgical stress may alter the expected BG requiring intraoperative adjustments in insulin or glucose administration to maintain the BG in the desired range. Obviously, a glucose infusion is indicated if the BG decreases to less than 80 mg/dl.

Table-2
Perioperative blood sugar management for a patient on an insulin pump (CSII).

1. Maintain basal insulin infusion rate.
2. Eliminate postprandial boluses of insulin.
3. Measure hourly (or more frequently) blood sugar level.
4. Note the typical bolus to decrease the blood sugar by 50 mg/dl.
5. When possible resume preoperative diet schedule.

Discussion

Anesthesiologists can expect to see more patients using continuous subcutaneous insulin infusion pumps[1]. Subcutaneous absorption of both insulin lispro and aspart are more rapid than regular insulin. For elective procedures, these patients most often present with well regulated glucose levels and in a relatively stable state. During emergencies, patients may not be stable before surgery, but the same guidelines for insulin, glucose, and electrolyte infusion and frequent monitoring should be followed to allow the required procedures to proceed. Unstable patients will require more intensive management and both young and very ill patients will continue to pose challenges.

Postoperative nausea and vomiting (PONV) with resultant delay in oral intake may disrupt normal patterns of insulin administration. Vigorous and preemptive anti-PONV treatment should be initiated in the operating room. Elective surgery for TIDM patients should usually be scheduled for the first case of the day.

Whether using new or old technology and drugs, the objective remains the same: maintaining a safe BG level in the diabetic patient during the perioperative period. New forms of insulin and new technology can make this task easier for the anesthesiologist with improved BG control for the patient.

References

1. Ahmed Z, Lockhart CH, Weiner M, Klingensmith G: Advances in diabetic management: implications for anesthesia. Anesth Analg 2005; 100: 666-9
2. Lorenz RA: Modern insulin therapy for type 1 diabetes mellitus. Prim Care 1999; 26: 917-29
3. Campbell RK, White JR, Levien T, Baker D: Insulin glargine. Clin Ther 2001; 23: 1938-57; discussion 1923
4. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, Raskin P, Zinman B: Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med 2005; 353: 2643-53
5. Maniatis AK, Klingensmith GJ, Slover RH, Mowry CJ, Chase HP: Continuous subcutaneous insulin infusion therapy for children and adolescents: an option for routine diabetes care. Pediatrics 2001; 107: 351-6