Continuous subcutaneous insulin infusion during general anesthesia: A case report

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Care of the patient with diabetes mellitus presents numerous challenges to the anesthesia practitioner. There is no perfect way to care for these patients nor are any 2 patients with diabetes exactly alike. With the advent of subcutaneous insulin pumps, the anesthesia practitioner has another tool to assist him or her in giving high quality care.

This case study describes the anesthesia care provided to a patient with type 1 diabetes who wore his continuous subcutaneous insulin infusion (CSII) pump during general anesthesia for surgical repair of a herniated lumbar disk. Importantly, the anesthesia plan involved a collaborative effort with the patient. Blood glucose levels were stable throughout the perioperative period. Little or no extra work was required of the CRNA.

This case showed that the CSII could be used to minimize perioperative fluctuations in blood sugar. Postoperatively, the patient expressed a high degree of satisfaction with the anesthetic.

Key words: Continuous subcutaneous insulin infusion, diabetes mellitus, general anesthesia, insulin lispro.

Currently in the United States 18.2 million people have diabetes mellitus.[1] Diabetes mellitus is a common medical condition affecting 6% of Americans younger than 50 years and 10% to15% of those older than 50 years. Because of the complications of the disease (eg, cardiac, vascular, ophthalmologic, renal), and by virtue of their absolute numbers, persons with diabetes frequently interface with surgical and anesthetic care. Nearly 50% of individuals with diabetes undergo surgery at some time in their lives.

During the perioperative period, optimization of blood glucose levels is an important task for those who provide anesthesia care. Since their introduction in 1978, continuous subcutaneous insulin infusion (CSII) pumps have offered an attractive option for glucose regulation in this challenging patient population. About 100,000 people in the world currently use CSII pumps.[2]

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs (Table 1).[3] For example, heart disease is the leading cause of diabetes-related deaths. The risk of stroke is 2 to 4 times higher among people with diabetes. Diabetes is the leading cause of new cases of blindness among adults. Diabetes also is the leading cause of end-stage renal disease. About 60% to 70% of people with diabetes have some form of nervous system damage. As a final example, diabetes that is poorly controlled before conception and during pregnancy can cause major birth defects or spontaneous abortions. The total direct and indirect cost of diabetes in the United States is estimated to be $132 billion per year.[1]

Table 1. Comorbibity associated with diabetes mellitus

Heart disease
Stroke
Blindness
Kidney failure
Hypertension
Peripheral and autonomic neuropathy
Amputations
Stiff joint syndrome
Hyperosmolar nonketotic coma
Ketoacidosis
Abnormal lipid metabolism
Periodontal disease
Pregnancy complications
Sexual dysfunction
Psychosocial dysfunction
Accelerated aging

High blood glucose levels cause glycosylation reactions that lead to formation of abnormal proteins. Abnormal glycosylation of elastic and connective tissues leads to stiff joint syndrome, fixation of the atlanto-occipital joint, poor collagen formation, and poor tensile strength of deep surgical wounds.[4]

It is knowledge of these serious short-term and long-term complications that leads some surgical patients with diabetes to actively regulate blood glucose levels to the fullest extent possible, thus they desire to continue CSII during the perioperative period. The following case summary describes the successful anesthetic management of one of the growing number of patients who use CSII to administer their insulin.

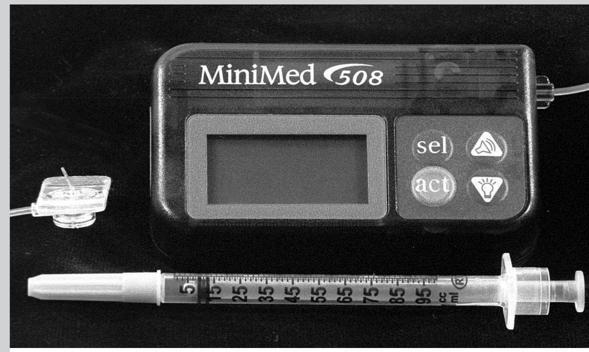
Case summary

A 43-year-old, ASA physical status III, 185-cm, 77-kg male patient with type 1 diabetes mellitus (insulin-dependent) presented for surgical correction of L5-S1 disk herniation to relieve right leg and back pain. In spite of his pain, the patient was physically fit, with a resting heart rate of 58 beats per minute and a blood pressure of 126/66 mm Hg. Except for diabetes, this patient's medical history was unremarkable. During childhood, he had undergone uncomplicated tonsillectomy and adenoidectomy. He was very knowledgeable about diabetes mellitus, the importance of diet and exercise, glucose monitoring, and about the use of the insulin pump (Medtronic Minimed 508, Medtronic MiniMed, Northridge, Calif; Figure). After confirming consent for surgery and anesthesia, an 18-gauge intravenous catheter was inserted and the following medications were given intravenously: midazolam, 2 mg; ranitidine, 50 mg; metoclopramide, 10 mg; ketorolac, 30 mg; and cefazolin, 2 g.

In the preoperative holding area, the patient's laboratory values were normal with the exception of the blood glucose concentration, which was 64 mg/dL. At this time, the patient ingested one 4-g glucose tablet; he was then moved to the operating room. Throughout the course of the anesthetic, his insulin pump was set to infuse 0.3 U/h of ultrashort-acting recombinant insulin lispro (Humalog). See Table 2 for a more thorough description of this patient's usual daily insulin infusion rates.

Once in the operating room, monitors were applied, preoxygenation was performed, and a remifentanil infusion of 0.375 µg/kg per min was begun with the patient still on the gurney. For induction of general anesthesia and tracheal intubation the remifentanil infusion was increased to 0.5 µg/kg per min. Rapid sequence induction with cricoid pressure was performed, using propofol, 60 mg, and succinylcholine, 140 mg. A 7.0-mm cuffed tracheal tube was inserted without difficulty. Following intubation, sevoflurane, 0.8%, was started and the remifentanil infusion was decreased to 0.125 µg/kg per min. The tracheal tube was secured and the patient then was carefully placed in the prone position on a Wilson frame. Care was taken not to dislodge the catheter or disable the insulin pump during the position change. Proper positioning and adequacy of ventilation were again confirmed.

Figure. Medtronic Minimed 508 insulin pump (Medtronic MiniMed, Northridge, Calif)



Note catheter tip in left of photograph. An insulin syringe is included to show size.

Table 2. Patient's typical daily insulin infusion rates*

Time	U/h
Midnight - 4:30 AM	0.3
4:30 AM - 5:30 AM	0.9
5:30 AM - 8:00 AM	1.0
8:00 AM - 11:00 AM	0.3
11:00 AM - 1:00 PM	0.2
1:00 PM - midnight	0.3

* Insulin lispro, 100 U/mL

Throughout the 66-minute operation, the patient's vital signs remained within normal limits. General anesthesia was maintained with sevoflurane, 0.75% to 1% in 50% oxygen with nitrous oxide. The remifentanil infusion was titrated between 0.125 and 0.50 µg/kg per min. During the course of the operation, the blood glucose level was measured and found to be 118 mg/dL. No adjustments were made in the basal insulin infusion rate.

Microscopic dissection of the bulging disk proceeded uneventfully. At the direction of the surgeon, the patient was given dexamethasone, 20 mg, intravenously. Thirty minutes before the end of the case, he was given morphine, 5 mg, and ondansetron, 4 mg, by the intravenous route. Ketorolac, 30 mg, also was given intramuscularly at this time at the surgeon's request in order to provide postoperative analgesic and anti-inflammatory effects. (Note: this patient demonstrated no evidence of renal disease.) Following completion of the surgery, the patient was returned to the supine position and upon return of spontaneous ventilation and purposeful movement the tracheal tube was removed. The total dose of remifentanil given during the case was 2 mg.

The patient was transferred to the postanesthesia care unit where he recovered without incident, requiring no additional analgesics. At this time, his blood glucose concentration was 158 mg/dL. Following transfer to phase 2 recovery, he ate lunch and self-administered an insulin bolus of 1.8 units. A final glucose measurement was made revealing a concentration of 185 mg/dL. One hour later, the patient was discharged to home.

Discussion

The rationale behind CSII is that a continuous, controllable baseline insulin infusion with intermittent larger boluses at mealtimes more closely mirrors physiologic secretion of insulin by the pancreas, which follows a diurnal rhythm. Such a pattern of insulin administration is more likely to result in normoglycemia throughout the course of the day.

Normal insulin secretion peaks in the early morning. This "dawn phenomenon" reflects a concomitant rise in blood glucose concentration following accelerated glucose production that occurs in response to early morning peaks in growth hormone and cortisol levels.[5] In the type 1 diabetic patient, the dawn phenomenon results in hyperglycemia, since there is no insulin surge to accompany the increase in glucose production and release. The normal blood glucose concentration in a person who has not eaten a meal within 3 to 4 hours is about 70 to 90 mg/dL. After a meal containing large amounts of carbohydrates, the glucose level seldom rises above 140 mg/dL unless the person has diabetes mellitus.[6] In the nondiabetic person, this rapid response in insulin secretion to alterations in blood glucose concentrations provides an important feedback mechanism for glucose regulation.

Although there is no consensus in the literature regarding precise intraoperative glucose levels during anesthesia and surgery, most recommendations target glucose levels between 80 to 150 mg/dL. These values are slightly higher than those of persons without diabetes.

The long-term health benefits of CSII for people with diabetes are significant. A recent meta-analysis found that CSII therapy was associated with sustained decreases in both glycohemoglobin and mean blood glucose levels.[7] At least 3 major longitudinal studies have demonstrated the value of careful glycemic control in reducing the risk of microvascular and macrovascular diabetic complications.[8-10]

Table 3. Advantages of perioperative normoglycemia

- Reduced wound infections
- Improved wound healing
- Improved neurologic outcome after cerebral ischemia
- Validates patient's belief in "tight" control

Table 4. Patient characteristics for successful continuous subcutaneous insulin infusion (CSII)[10]

- Motivation to achieve normoglycemia using self-management skills
- Individual has accepted self-care responsibilities associated with diabetes
- Intellectual ability to learn, retain, and process information
- Technical ability to accurately perform blood glucose monitoring and to operate the insulin pump
- Effective coping patterns
- Availability of support systems
- Access to financial resources to cover the cost of CSII therapy

Anyone receiving exogenous insulin administration by any method is at risk of developing hypoglycemia. Such periods of hypoglycemia have been associated with myocardial ischemia and have even been implicated in fatal automobile crashes.[11] Importantly, CSII has been shown to decrease the frequency of hypoglycemic episodes in persons with diabetes.[12] Intensive therapy with CSII also has been shown to reduce the risk of developing retinopathy, nephropathy, and neuropathy in these patients.[8] These complications reduce wellness and often lead to major morbidity and mortality.

During the perioperative period, CSII offers short-term benefits in glycemic control that reduce the risk of hyperglycemia or hypoglycemia and thus simplify anesthetic management (Table 3). A significant benefit to the patient of maintaining glucose levels within the normal range during anesthesia and surgery is that normoglycemia is associated with improved wound healing and a reduced incidence of surgical wound infections (a benefit that also applies to nondiabetic patients).[13,14]

Since patients with insulin pumps are usually quite knowledgeable about the use of their pumps, it is often desirable to incorporate these individuals into the provision of their own care (Table 4). The anesthesia practitioner, in collaboration with the patient and others, can appropriately select an insulin infusion rate to be used during the anesthetic. The patient also can demonstrate how to change or suspend the insulin infusion rate, how to determine that the pump is working properly, and how to reapply the infusion catheter if it becomes detached.

The anesthesia provider may find that maintaining CSII during the course of the operation simplifies "tight" glycemic control. An anesthetic technique incorporating CSII is likely to keep blood glucose levels within the desired range without the need for separate intravenous lines, dextrose infusions, insulin infusions, or intravenous infusion pumps.

Insulin lispro, the type of insulin used by the patient in the present case study, is an insulin analog with improved pharmacokinetic characteristics compared to regular human insulin. Insulin lispro differs from human insulin by inversion of the beta-chain amino acids proline and lysine at positions 28 and 29, respectively. These changes result in a reduced capacity for self-association compared to human insulin.[12,13]

Self-association of insulin to higher molecular weight forms has been the rate-limiting step in achieving a biologic response. The modifications present in insulin lispro confer monomeric behavior, resulting in more rapid absorption after subcutaneous injection, an earlier peak effect, and a shorter and more consistent duration of action relative to regular human insulin. These characteristics mimic plasma insulin dynamics in nondiabetic subjects in response to meals. Because insulin lispro has a shorter duration of action than regular human insulin, loss of glycemic control may occur quickly if CSII is interrupted.[12,15,16]

Human insulin and insulin lispro are equipotent. Pharmacokinetic differences between the two are the result of more rapid absorption of insulin lispro from the subcutaneous tissue injection site.[12] Subcutaneous administration of 1 unit of either variety of insulin reduces blood glucose concentrations by about 30 to 50 mg/dL.[17] All of the properties of insulin lispro just described make it the most suitable type of insulin for continuous infusion.

Currently, 3 companies market insulin pumps in the United States: Medtronic Minimed, Northridge, Calif; Disetronic Medical Systems, Inc, Fishers, Ind; and Animas Corporation, Westchester, Pa. These devices are similar in design to the programmable syringe infusion pumps that anesthetists commonly use; that is, they each consist of a syringe-like reservoir that releases insulin into a delivery tubing when its plunger is depressed by a motor-driven lead screw.

Insulin is delivered from the pump to the patient via a plastic tubing through a 6-mm to 9-mm subcutaneous catheter. This catheter is a disposable catheter-over-needle device that pierces the skin, usually at the waist, and is held in place by an affixed adhesive pad. Should the catheter become detached, another one can easily be applied without stopping the pump. If insulin delivery is halted, the patient's glucose levels will rise above the desired upper limit within 90 minutes.

Potential problems that the anesthesia practitioner may encounter when delivering anesthesia care to patients with insulin pumps include intraoperative hypoglycemia, catheter occlusion, and catheter dislodgement. To reduce the likelihood of hypoglycemia, the patient should enter the operating room with a normal blood glucose level, the intravenous fluids should not contain dextrose, and the insulin pump should be set at a basal infusion rate. Regardless of whether the diabetic patient uses CSII or not, the intraoperative blood glucose level should be measured every hour to determine that neither a hypoglycemic nor a hyperglycemic state exists. The pump and its delivery system should be examined periodically during the anesthetic to determine that they continue to function properly.

Conclusion

More and more people with diabetes mellitus are using CSII for around-the-clock glycemic control. Such patients who present for surgery often desire that "tight" glycemic control be continued during the perioperative period, since normal blood glucose concentrations reduce the likelihood of surgical wound infection and improve wound healing. Chronic complications of diabetes also may be minimized through the normoglycemia that the perioperative use of CSII provides. All these benefits are provided by a device that is simple for the anesthesia provider to use.

REFERENCES

1. National Diabetes Fact Sheet. National Estimates on Diabetes. Available at: http://www.cdc.gov/diabetes/pubs/factsheet.htm. Accessed January 2, 2004.
2. Walsh J, Roberts R. *Pumping Insulin: Everything You Need for Success with an Insulin Pump.* 3rd ed. San Diego, Calif: Torrey Pines Press; 2000:1.
3. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus: committee report. *Diabetes Care.* 2002;25:S5-S20.
4. Roizen MF. Anesthetic complications of concurrent diseases. In: Miller RD, ed. *Anesthesia.* 5th ed. Philadelphia, Pa: Churchill Livingstone; 2000:906-907.
5. Koivisto VA, Yki-Jarvinen H, Helve E, Karonen S-L, Pelkonen R. Pathogenesis and prevention of the dawn phenomenon in diabetic patrients treated with CSII. *Diabetes.* 1986;35:78-82.
6. White NH, Henry DN. Special issues in diabetes management. In:

Haire-Joshu D, ed. *Management of Diabetes Mellitus: Perspectives of Care Across the Life Span.* St Louis, Mo: Mosby Year Book; 1992:291.

7. Weissberg-Benchell J, Antisdel-Lomaglio J, Seshadri R. Insulin pump therapy: a meta-analysis. *Diabetes Care.* 2003;26:1079-1087.
8. The Diabetes Control and Complications Trial Research Study 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.
9. Klein R. Hyperglycemia and microvascular and macrovascular disease in diabetes. *Diabetes Care.* 1995;18:258-268.
10. Reichard P. Are there any glycemic thresholds for the serious microvascular diabetic complications? *J Diab Comp.* 1995;9:25-30.
11. Desouza C, Salazar H, Cheong B, Murgo J, Fonseca V. Association of hypoglycemia and cardiac ischemia: a study based on continuous monitoring. *Diabetes Care.* 2003;26:1485-1489.
12. Garg SK, Carmain JA, Braddy KC, et al. Pre-meal insulin analogue insulin lispro vs Humulin R insulin treatment in young subjects with type 1 diabetes. *Diabet Med.* 1996;13:47-52.
13. Golden SH, Peart-Vigilance C, Kao WHL, Brancati FL. Perioperative glycemic control and the risk of infectious complications in a cohort study of adults with diabetes. *Diabetes Care.* 1999;22:1408-1414.
14. Levetan C. Controlling hyperglycemia in the hospital: A matter of life and death. *Diabetes Care.* 2000;18:17-24.
15. Howey DC, Bowsher RR, Brunelle RL, Woodworth JR. [Lys(B28), Pro(B29)]-human insulin. a rapidly absorbed analogue of human insulin. *Diabetes.* 1994;43:396-402.
16. Howey DC, Bowsher RR, Brunelle RL, et al. [Lys(B28), Pro(B29)]-human insulin: effect of injection time on postprandial glycemia. *Clin Pharmacol Ther.* 1995;58:459-469.
17. Davidson PC. Bolus and supplemental insulin. In: *The Insulin Pump Therapy Book: Insights from the Experts.* Fredrickson L, ed. Los Angeles, Calif: MiniMed Technologies; 1995,65.

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