

Successful Management of Inadvertent Insulin Overdose during Laparoscopic Cholecystectomy in a Diabetic Patient

—A case report—

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We present here a case of inadvertent insulin overdose (500 units) during surgery in a 51-year-old DM (diabetes mellitus) patient, but the patient recovered without complications after a tightly monitored glucose infusion. Five milliliters (500 units) of insulin instead of 5 units were injected inadvertently to a 51-year-old diabetic patient and the event was detected without delay at the post-anesthesia care unit (PACU). Although the patient was alert and extubated, we cautiously and intensively monitored the vital signs, plasma glucose level, arterial pH, the electrolytes and the fluid intake and output in the PACU. We administered intravenous glucose for 16 hours to avoid hypoglycemia in accordance with the plasma glucose level. The patient was sent to the intensive care unit (ICU) 8 hours after the event, and the patient was discharged at the next day from the ICU. Insulin should be administered with great care in DM patients undergoing surgery, and glucose infusion is an effective method to maintain the blood glucose level during treatment of hypoglycemia patients. (*Korean J Anesthesiol* 2006; 51: S 24~7)

Key Words: anesthesia, diabetes mellitus, glucose, insulin overdose.

Patients with DM (diabetes mellitus) should be fully evaluated and controlled plasma glucose level during the pre-operative period,¹⁻⁵⁾ especially in cases of pregnancy,⁶⁾ cardiopulmonary bypass⁷⁾ and cerebrovascular disease.⁸⁾ Strict plasma glucose control can be achieved when the plasma glucose level is checked and controlled with hypoglycemic agent such as insulin regularly and frequently, and helps prevent acute and chronic complications of DM. Stress caused by surgery and anesthesia induces hyperglycemia,⁹⁾ causing higher blood glucose levels in DM patients who underwent surgery than in patients who did not have surgery. Longstreth et al.¹⁰⁾ reported that a high plasma glucose level correlated with a poor neurologic recovery score in 430 patients after cardiopulmonary resuscitation. Even if consciousness is restored, neurologic deficit may remain in hyperglycemic patients. Therefore it is important to maintain an adequate plasma glucose level (120-180 mg/dl) during anesthesia as well as in the pre-operative period.¹¹⁾

When plasma glucose was controlled with insulin, careful titration of insulin is required. In this paper, we present a case of inadvertent insulin overdose (500 units) during laparoscopic cholecystectomy in a 51-year-old DM patient who recovered without complications after a tightly monitored glucose infusion.

CASE REPORT

A 51-year-old man was scheduled for a laparoscopic cholecystectomy for acute cholecystitis with gallstones. He had a 10-year history of DM and was treated intermittently with oral hypoglycemic agents. His fasting blood glucose level, HbA1c, and c-peptide were 470 mg/dl, 13.8%, and 0.5 ng/ml, respectively in the emergency room, and electromyography showed polyneuropathy. Electrocardiography, chest X-ray, and other laboratory data did not show significant abnormalities, except for glucosuria in the urinalysis.

We monitored the patient's plasma glucose level 4 times per day for 7 days preoperatively (Table 1). During this time, his plasma glucose level decreased from 500 mg/dl to 120 mg/dl with insulin Humalog[®] (Eli Lilly, Houten, Netherlands) 18-40

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Table 1. Preoperative Plasma Glucose Levels and Insulin Dose

	HD 1	HD 2	HD 3	HD 4	HD 5	HD 6	HD 7
6 AM glucose (mg/dl)		262	79	350	350	302	121
10 AM glucose (mg/dl)		290	253	331	276	192	180
3 PM glucose (mg/dl)	> 500	399	359	203	248	189	161
8 PM glucose (mg/dl)	> 500	209	294	263	279	341	167
Insulin dose (units/day)	18	24	26	28	34	38	40

HD: hospital day, HD 7: the day before operation.

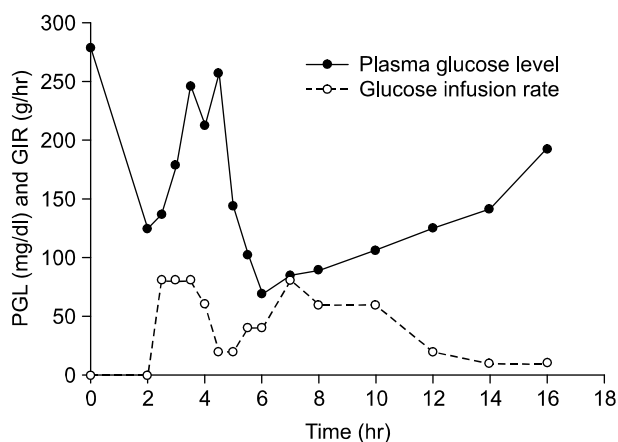


Fig. 1. Changes in plasma glucose level and glucose infusion rate after the inadvertent insulin injection. PGL: plasma glucose level, GIR: glucose infusion rate.

units. After 10 hours of fasting for laparoscopic cholecystectomy, his plasma glucose level was 132 mg/dl. The patient was sent to the pre-anesthetic preparing room. As premedicant glycopyrrolate 0.2 mg and midazolam 2.0 mg were injected intravenously. General anesthesia was induced with fentanyl 50µg, propofol 80 mg with lidocaine 20 mg, and rocuronium 40 mg. After intubation, general anesthesia was maintained with sevoflurane 1.5-2.5%, N₂O 1 L/min in O₂ 1 L/min. Thirty minutes after the induction of general anesthesia, the plasma glucose level was 278 mg/dl, and the senior resident ordered an anesthetic intern to inject the patient with “insulin 5”. Two hours after the intravenous insulin was injected, the patient was transferred to the post-anesthetic care unit (PACU) after extubation without realizing that the anesthetic intern injected 5 ml of insulin instead of 5 units of insulin.

We discovered an empty insulin vial on the anesthetic cart in the operating room 30 minutes after the patient was transferred to the PACU. We called the intern to confirm whether

he injected 5 ml (500 units) instead of 5 units of insulin and realized that he misunderstood the order “insulin 5” as “insulin 5 ml”. The blood pressure, pulse rate, and plasma glucose level were 100/55 mmHg, 85 beats/min, and 124 mg/dl, respectively at the PACU. The mental status of the patient was alert at the PACU. Electrocardiograph, pulse oxymeter and radial artery cannulation were applied for intensive monitoring and multiple blood sampling. An endocrinologist was called for the management of the insulin overdose. Arterial blood gas analysis (ABGA) showed; pH 7.42, PaCO₂ 39 mmHg, PaO₂ 224 mmHg (FiO₂ 0.4), HCO₃⁻ 25.3 mM/L, BE 0.8 mM/L, O₂ saturation 100%, Na⁺ 139 mM/L, K⁺ 3.1 mM/L and Ca²⁺ 4.45 mM/L.

The left external jugular vein was cannulated with an 18 G catheter and an infusion of 80 g/hr glucose in 50% D/W was started. We infused an additional 20 mEq KCl mixed with normal saline. Then, we checked the patient’s blood glucose level every 30 minutes and ABGA every hour (Fig. 1). After the inadvertent insulin injection, it took 8 hours to reduce glucose infusion rate (< 20 g/hr). The patient remained alert and comfortable with stable vital signs. We transferred the patient to the intensive care unit (ICU) for further observation. On admission to the ICU, vital signs were stable: blood pressure 100/60 mmHg, pulse rate 70 beats/min, and blood glucose level 89 mg/dl, Na⁺ 140 mM/L and K⁺ 4.0 mM/L. Glucose infusion was discontinued 16 hours after the inadvertent insulin injection (Fig. 1).

The patient was transferred to the general ward the next day without any signs of hypoglycemia. The patient started to eat a DM diet with insulin and an oral hypoglycemic agent at the ward 1 day after the operation and was discharged 10 days later without significant problems.

DISCUSSION

It is well known that glucose administration is needed in case of hypoglycemia. But, few physicians know well that how

much and how long glucose infusion is needed to prevent hypoglycemia due to insulin overdose and what kind of monitoring is needed.

In our case, insulin was injected intravenously after induction because the patient's plasma glucose level was 278 mg/dl. We detected the insulin overdose 2 hours after injection. Early detection of insulin overdose is essential to prevent complications of hypoglycemia.¹²⁾ We were able to avoid the severe complications of hypoglycemia by our relatively early detection of the event. The treatment goal of insulin overdose is to maintain an appropriate plasma glucose level. Glucose replacement is the best regimen for achieving this goal, although oral glucose, glucagons and excision of subcutaneous tissue at the insulin injected site are recommended by some authors.^{13,14)} We frequently checked the electrolyte balance as well as plasma glucose level during the insulin therapy in the PACU. Sodium decreased by 1.6 mEq/L, which was equal to the blood glucose level increase of 100 mg/dl. The most dangerous electrolyte imbalance in insulin therapy is potassium. A total of 300 mEq potassium replacement is required to maintain a serum potassium level in the range of 3.5-4.5 mEq/L in cases where 2,400 units of insulin were injected as a suicide attempt.¹⁵⁾ When glucose and fluid are administered, both should be carefully titrated and monitored. The half-time of disappearance of insulin following 0.1 units/kg of regular insulin in normal individuals was approximately 3 to 7 minutes. In cases of insulin overdose, the half-time is prolonged as insulin overdose is increased. Therefore, we had to monitor and infuse glucose for 8 hours to stabilize the plasma glucose level.

Hypoglycemia is considered to be the most dangerous complication of DM treatment. Hypoglycemia induced by insulin is common in DM patients, but massive insulin overdose is infrequent in patients with DM or without DM.¹⁶⁾ Reports of massive insulin overdose are rare, but have been previously reported in a few cases of intentional suicide attempts by individuals with DM^{16,17)} and without DM.¹²⁾ Arem and Zoghbi¹⁷⁾ reported 8 patients who attempted suicide by self-administering insulin from 20 units to 3,200 units. The effect of an insulin overdose could last for several days if administered subcutaneously. This shows a relationship between the duration of hypoglycemia and the total dose or administration route of insulin. Serum insulin concentration linearly declines along a logarithmic scale.¹⁸⁾ Patients without DM were more likely to present hypoglycemia (plasma glucose < 50 mg/dl) and develop recurrent hypoglycemia despite intravenous glucose infusion

than patients with DM.¹⁵⁾

The mechanism of delayed recovery from hypoglycemia after insulin overdose is unclear. One possibility may be a reduced peripheral circulation caused by hypoglycemia, especially in diabetic patients with subcutaneous insulin overdose or decreased renal function. In addition, if patients were administered large amounts of fluid, the blood glucose level may quickly decrease.

A plasma glucose level has been maintained between 50 and 200 mg/dl in this patient. One reason that the plasma glucose level was not greatly decreased in this patient may be a limitation in the number of insulin binding receptors. The decreasing velocity of plasma glucose level cannot exceed 75-100 mg/dl/hr because of limited insulin binding receptors.¹⁹⁾

In conclusion, we recommend that insulin should be administered cautiously and that the blood glucose level be checked frequently and regularly in DM patients undergoing surgery. It is also recommended that the accurate generic name of the drug, dose and units of the drug be specified.

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