# Electrolyte Disorders Following Massive Insulin Overdose in a Patient with Type 2 Diabetes

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## Abstract

**We present a case of a 47-year-old man with Type 2 diabetes mellitus who attempted suicide with 2,100 U of insulin injected subcutaneously. Administration of dextrose intravenously was required to maintain the blood glucose concentration normally for 5 days. Moreover, hypokalemia, hypophosphatemia, and hypomagnesemia were also seen for 24 hours after insulin injection. The serum phosphorus and magnesium concentrations decreased to nadirs of 1.6 mg/dl and 1.6 mg/dl respectively 7 hours after insulin injection. Electrolyte disorders other than hypokalemia may be induced in hypoglycemic patients by massive insulin overdose.**
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*Key words:* suicide attempted with massive insulin, hypoglycemia, hypokalemia, hypophosphatemia, hypomagnesemia

## Introduction

Insulin self-injection therapy is practised by many patients with diabetes mellitus all over the world. Unfortunately, several cases of intentional insulin overdose have been reported (1–8). Systemic complications of cerebral damage, hypokalemia, pulmonary edema, hypertensive crisis, and respiratory insufficiency have been described (5). However, electrolyte disorders other than hypokalemia following massive insulin overdose have not been well documented.

We present in detail the case of a Type 2 diabetic patient who attempted suicide with 2,100 U of insulin injected subcutaneously. Several electrolyte disorders, such as hypokalemia, hypophosphatemia, and hypomagnesemia were observed for 24 hours after massive insulin injection.

## Case Report

A 47-year-old Japanese man with Type 2 diabetes mellitus was receiving 10 U of regular insulin (NovoLet®R, Novo Nordisk, Copenhagen, Denmark) 3 times and 10 U of NPH-insulin (NovoLet®N) once a day for 3 years. From the beginning of 1998, he seemed to be depressed because of the psychiatric disorder his wife had. On July 18, 1998, after quarreling with his wife he attempted suicide by ingesting 8 tablets of triazolam (Halcion®0.25 mg, Pharmacia & Upjohn, Bridgewater, NJ, USA), 10 tablets of zopiclone (Amoban®7.5 mg, Rhône-Poulenc Rorer, Paris, France), and one bottle of wine, and injecting 300 U regular insulin plus 1,800 U NPH-insulin subcutaneously into the abdomen which was the site he most frequently used. After injection, he telephoned our hospital and told us of his suicide attempt. While talking with a nurse, his voice gradually weakened and he stopped responding. Two hours later, he was discovered by police with farewell letters and he was carried to our emergency room.

On arrival, he was comatose. His vital signs were as follows: blood pressure 164/62 mmHg, temperature 36.8°C, and pulse 94/minutes. On physical examination, no external injuries were observed. No abnormal breath sounds were heard. Many injection sites were observed on the abdomen. Neurological examination did not show any focal signs. He was 1.75 m tall and weighed 94 kg.

The white-cell count was 12,800/mm$^3$ and Hb concentration was 15.9 g/dl. The blood glucose concentration was 28 mg/dl. Liver function was normal. The urea nitrogen was 10.5 mg/dl and creatinine was 1.1 mg/dl. The sodium, chloride, and calcium concentrations were normal. The potassium concentration was 2.4 mEq/*l*. The phosphorus concentration was 2.3 mg/dl and magnesium was 2.6 mg/dl. Serum immunoreactive insulin (RIA, Insulin RIA Bead II®, Dainabot, Tokyo) concentration was 710 μU/ml. There were no abnormal findings on the ECG.

First, the patient was administered a bolus of 80 ml 50% dextrose i.v. After administration of dextrose, the blood glucose concentration increased up to 148 mg/dl. He began to answer when his name was called. Second, gastrolavage was

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done. He was treated basically with 50% of dextrose solution and potassium chloride via a central-venous catheter. Glucagon was also injected intramuscularly twice during the 24 hours period after admission. A dose of 6.6 mg/kg/min of dextrose was required to maintain the blood glucose concentration between 100 and 200 mg/dl for 24 hours after admission (Fig. 1). The measurement of serum insulin concentrations showed two peaks. The first peak of serum insulin concentration was 1,180 μU/ml observed approximately 5 hours after insulin injection. The second peak was 490 μU/ml observed 11 hours after injection. The serum potassium concentrations increased to low-normal levels with potassium chloride supplementation. The serum calcium concentration remained normal. However, the serum phosphorus and magnesium concentrations decreased to nadirs of 1.6 mg/dl and 1.6 mg/dl respectively 7 hours after insulin injection (Fig. 1). The next day, the serum phosphorus and magnesium concentrations increased to low-normal levels without supplementation. The patient awoke completely and resumed intake of foods. However, dextrose infusion was required for 5 days to prevent hypoglycemia. After 7 days, NPH-insulin was reinstituted. No brain damage was evident on brain computed-tomography or neurological examination. The patient was referred to a psychiatry service.

## Discussion

The absorption rate of insulin depends on the physical state of insulin, injection volume, insulin concentration, blood flow, and presence or absence of degradation at the injection site (9). In our case, the serum insulin concentrations showed two peaks. Moreover, dextrose infusion was required to maintain the blood glucose concentration normally for 5 days. Injection of regular and NPH-insulin might make two peaks in serum insulin concentrations. Samuels and Eckel (6) reported a case of delayed absorption of subcutaneous insulin in a patient who self-administered 2,500 U of NPH-insulin. Their case also required dextrose infusion for 6 days. The injection dose may relate to the time of absorption. Stapczynski and Haskell (10) showed a significant relation between the amount of insulin taken as a single overdose and the total time of i.v. dextrose treatment needed until resolution of the hypoglycemic effects. Moreover, delayed absorption of subcutaneous insulin from

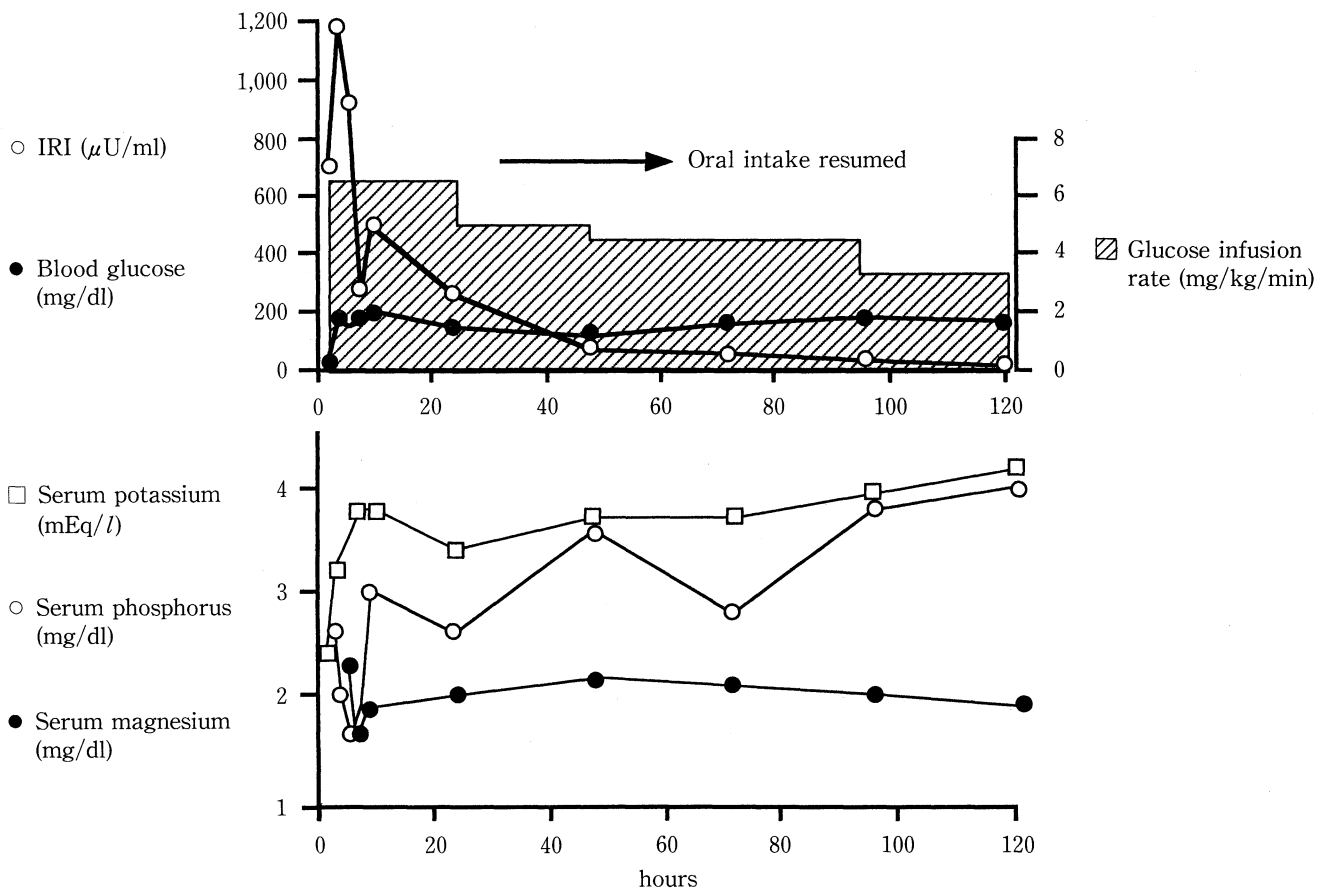


**Figure 1. Top: Serum concentration of immunoreactive insulin (IRI, μU/ml), blood glucose (mg/dl), and glucose infusion rate (mg/kg/min) required to maintain normal blood glucose during 120 hours after injection with suicidal intent of an insulin overdose of 2,100 U. Bottom: Serum potassium (mEq/*l*), phosphorus (mg/dl), and magnesium (mg/dl) concentrations within 120 hours after injection of insulin overdose of 2,100 U.**

repeatedly injected sites was reported (11). In the present case, the patient injected overdose of insulin into the site he most frequently used.

Fasching et al (8) stated that in the presence of high serum insulin concentrations following insulin overdose, glucose dynamics closely resemble that observed in healthy non-diabetic humans and patients with Type 1 diabetes mellitus during a hyperinsulinemic-euglycemic glucose clamp. They demonstrated that the glucose disposal rate was approximately 14.0 mg/kg/min in healthy subjects and Type 1 diabetic patients during 10 mU/kg/min clamp, which increases serum insulin concentrations to about 1,003 μU/ml (12). In the present case, the maximum peak of serum insulin concentration was 1,180 μU/ml similar to 10 mU/kg/min clamp data. However, the glucose disposal rate was low at 6.6 mg/kg/min. The patient might have relative insulin resistance because he was an obese Type 2 diabetic patient. Relative insulin resistance and glucagon administration in this case might reduce the glucose disposal rate compared with hyperinsulinemic-euglycemic glucose clamp data.

Insulin has been proposed as one of the regulatory hormones of phosphorus and magnesium balance. Phosphorus uptake by muscle is thought to be important in the hypophosphatemia associated with insulin infusion (13). Bohannon (14) reported two patients who showed severe and moderate hypophosphatemia during intravenous insulin therapy for diabetic ketoacidosis and hyperosmolar nonketotic state. Lostroh and Krahl (15) demonstrated that insulin added in vitro promptly promoted a net increase in the accumulation of magnesium and potassium in uterine smooth muscle cells. Several studies based on hyperinsulinemic-euglycemic glucose clamp indicated these effects (16–18). In the present case, hypophosphatemia and hypomagnesemia were observed for 24 hours after insulin injection. Hypophosphatemia and hypomagnesemia can cause neuromuscular, central nervous, and cardiovascular disorders (19, 20). In patients with hypophosphatemia, depletion of both ATP and 2, 3-diphosphoglycerate increases the affinity of Hb for oxygen, which results in decreased delivery of oxygen to tissues (19). This effect may potentiate cerebral damage by hypoglycemia. Hypomagnesemia is recognized to cause cardiac arrhythmias and potentiates the arrhythmic effect of hypokalemia (20). Moreover, hypophosphatemia can reduce the threshold for ventricular arrhythmias (21). Vogl and Youngwirth [1] reported a case of attempted suicide with 2,000 U of insulin injection complicated with sinus tachycardia, ventricular arrhythmias, and elevation of the ST segments on the ECG without hypokalemia. In the present case, electrolyte disorders did not cause any obvious manifestations. The reasons why clinical manifestations did not occur in this case might include the only modestly reduced serum electrolyte concentrations and the correction of the serum potassium level. Serum electrolytes including phosphorus and magnesium should be measured in cases of massive insulin overdose complicated with neuromuscular, central nervous, or cardiovascular disorders.

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