Case Report

Attempted Suicide by Massive Insulin Injection: A Case Report and Review of the Literature

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The authors present a case of an 80-year-old man, non-diabetic, who attempted suicide by injecting himself subcutaneously with 10,000 units of Humulin R and 6,000 units of Humulin N. Administration of dextrose intravenously was required for 13 days to maintain the capillary blood glucose within the range of 100-180 mg/dl. Hyponatremia, hypokalemia, hypophosphatemia, and elevated liver enzymes were also seen after massive insulin injection. Glucose requirement index was established to demonstrate the trend of glucose requirement during hospitalization. He recovered completely without any complication after monitoring blood glucose and titrating intravenous glucose carefully for two weeks. Current literature about how to manage insulin overdose was reviewed in the present article.

Keywords: *Insulin overdose, Complications, Glucose requirement index*

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Cases of intentional massive overdoses of insulin are infrequent, and even more uncommon for those who inject themselves with more than 3,000 units of insulin. The severity and final outcome of patients' condition does not seem to be related with the dose of insulin administered. Early detection of hypoglycemia and careful intravenous glucose administration are still the main treatment for this condition. The authors describe a case with massive insulin overdose who survived without complications.

Case Report

An 80-year-old previously healthy, non-diabetic man was transferred to Theptarin Hospital because of self-injected insulin administration. He had a history of depressive disorder probably from a diagnosis of possible end-staged prostate cancer a few months earlier. He was found unconscious by his driver and was taken to another hospital about 17 hrs after the injection of insulin.

He was taken to an emergency room where his plasma glucose was found to be 26 mg/dl. No focal neurologic signs were noted. After administration of 50 ml of 50% glucose, he regained full consciousness and his plasma glucose increased to 158 mg/dl. He experienced repeated episodes of hypoglycemia subsequently.

Careful history taking revealed that he attempted suicide by injecting himself subcutaneously with 10,000 units of Humulin R and 6,000 units of Humulin N, which he bought from a local drug store. He denied ingesting or injecting any other substances. One hour after injecting insulin, he was still fully conscious so he thought that this suicide method would not work. He changed his mind about ending his life and consumed many chocolate bars and high-carbohydrate drinks. The actual amounts of carbohydrate ingested by the patient at home could not be quantified. During the night, he reported several episodes of diaphoresis and tremulousness. In the morning, his driver found him to be unresponsive in his house so he was taken to the emergency room.

On admission, three fresh injection sites were noted in his lower abdomen. He was given intravenous glucose infusion of 10% dextrose in normal saline, intravenous boluses of 50% dextrose in water, and was orally administered carbohydrates for four days

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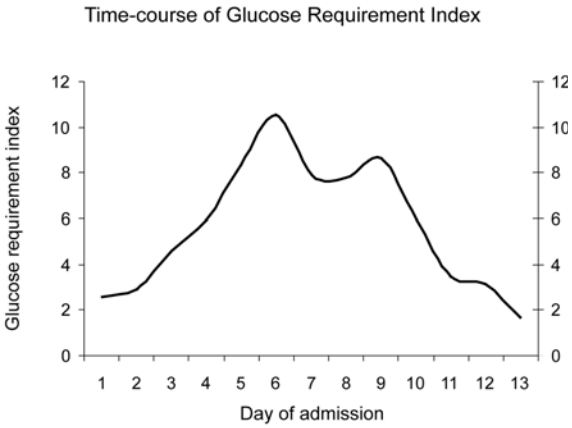
but he still had repeated episodes of hypoglycemia. The laboratory data revealed leukocytosis (WBC of 24,800/mm^3 with 91% of neutrophils) and serum potassium of 3.0 mEq/l. Other laboratory results were not remarkable. On day 2, he started to have a low-graded fever without a localized source of infection. Intravenous ceftriaxone was given as an empirical antibiotic. On day 3, his serum sodium decreased from 136 mEq/l to 119 mEq/l without any clinical manifestation of hyponatremia. Intravenous 3% NaCl was given at rate 10 cc/hr to correct his serum sodium level over 48 hrs. Serum fasting insulin level was measured on the third day of admission. The result revealed the insulin level was more than 1,000 μU/ml (normal fasting insulin level 2-24 μU/ml). On day 4 of admission (115 hrs after insulin administration), he was transferred to Theptarin Hospital at his wife's request. The patient received total glucose loads of 1,585 g in the first 96 hrs.

On arrival at Theptarin Hospital, the patient was lethargic without focal neurological deficit. His plasma glucose level was 28 mg/dl. After administration of an intravenous bolus of 50 ml of 50% glucose, he regained consciousness and his plasma glucose level rose to 91 mg/dl. On physical examination, his body temperature was 37.5°C, pulse rate was 94/min, respiration rate was 22/min, and blood pressure was 108/84 mmHg. Minimal fine crepitations were heard in the lower part of both lungs. Systolic ejection murmur grade II/VI were noted at left upper sternal border. No jugular venous distension was seen. Other physical exams were unremarkable. He was allowed liberal oral intake of food and was administered a 50% dextrose infusion at a rate of 50 g of glucose/hr via central line. The initial laboratory tests showed leukocytosis (WBC of 14,800/mm^3 with 78% of neutrophils), hyponatremia (serum sodium 125 mEq/l), hypokalemia (serum potassium 3.25 mEq/l) and elevated liver enzymes (SGOT 224 U/L and SGPT 239 U/L). Viral hepatitis profiles (Hepatitis A, B, and C) were negative. Intravenous KCl was added in his intravenous fluid to correct hypokalemia. The dextrose infusion was adjusted to maintain his capillary blood glucose in the range of 100 to180 mg/dl. He still had repeated episodes of hypoglycemia, which required intermittent intravenous boluses of 50% dextrose in water over the next 24 hrs after admission. Time-course of blood glucose and amount of glucose administration (as demonstrated by glucose requirement index) during his admission are shown in the Fig. 1.

The next day he still had a persistent fever. Although no source of infection was identified, intravenous antibiotic prophylaxis was given to cover the possibility of nosocomial infection. Intravenous furosemide was also given intermittently to balance his volume status. He still had a few episodes of hypoglycemia. His serum insulin level was measured at Theptarin Hospital with the value always more than 300 μU/ml. (The serum insulin that exceeds 300 μU/ml could not be measured quantitatively in Theptarin laboratory.) His potassium level fell from 3.25 to 2.9 mEq/l even though intravenous KCl was given. SGOT/SGPT levels decreased to 136/191 U/L. The serum phosphate was extremely low with the value less than 0.70 mg/dl (normal serum phosphate level 2.3-4.7 mg/dl). The serum magnesium was 1.7 mg/dl (normal serum magnesium level 1.6-2.6 mg/dl). Serum CPK revealed normal result. Intravenous phosphate supplements were given to correct severe hypophosphatemia.



Day	Index
1	2.57
2	2.92
3	4.60
4	5.96
5	8.33
6	10.57
7	7.90
8	7.81
9	8.63
10	6.00
11	3.47
12	3.16
13	1.67

Fig. 1 Time-course of glucose requirement index during admission. This index was established as the ratio of the amount of glucose given in 24 hrs over the mean of plasma glucose levels during the same 24-hr period

Over the next 96 hrs, the patient received a dextrose infusion at 10 g/hour to maintain his blood glucose. No hypoglycemic episode was observed during this period. Fever also subsided over this period. No source of infection was identified. His serum sodium was followed up and showed the persistent hyponatremia (serum sodium was in range 122-126 mEq/l). Serum osmolarity was recorded at 250 mOsmol/kg (Normal serum osmolarity 275-295 mOsmol/kg) and urine osmolarity was recorded at 79 mOsmol/kg. Urine sodium level was less than 20 mEq/l and urine potassium level was 10 mEq/l. Oral sodium supplement was given to maintain plasma sodium concentration.

The dextrose infusion requirement was reduced in the next 72 hrs (264 hrs after administration of insulin). His serum insulin level decreased as well. Multiple blood cultures came back with negative results. No fever was detected so the antibiotic was stopped. The patient's condition improved. All laboratory tests including liver enzymes improved except the persistence of hyponatremia (plasma sodium was 124 mEq/l on the last day of admission). He received a total of 9,005 g of intravenous dextrose during his two hospital stays for two weeks after his attempted insulin overdose. A psychiatrist was consulted to evaluate his psychiatric problem before he was discharged from Theptarin Hospital. The patient was followed up one week after discharge. His plasma sodium increased to the normal level without any further hypoglycemic symptom. Other laboratory tests were also unremarkable. No complication was detected during follow up.

Discussion

Attempted suicidal insulin overdose is uncommon when compared with the widespread use of insulin for more than 80 years. Most reported cases were diabetic patients who were prescribed insulin to control their diabetes[1-2]. However, insulin overdose might be more common than previously supposed, especially in health care professionals and individuals in close contact with diabetic patients[3]. Moreover, insulin had been used in the past to commit homicide because no method developed to measure insulin level at that time[4].

In the earlier literature, the dose of insulin used varied from 20 units to 3,200 units[3]. The presented patient who injected himself with the total dose 16,000 units of insulin is considered to be the first patient in the world who survived with such a massive dose of insulin. When compared with the other case reports, the total dose of insulin in the present case is the highest dose to use for attempted suicide. This case seems to confirm the conclusion from previous reports that there is no correlation between the dose of insulin administered and the final outcome[2,5]. Delay in treatment of hypoglycemia appears to be the major prognosis to determine the outcome instead. Although the duration of hypoglycemia correlated with the type and amount of insulin administered, slow absorption of insulin from the injected sites (Depot effect) and delayed clearance of the absorbed insulin are also the main factors to make it difficult to predict the duration of infused intravenous glucose[7,8].

To estimate glucose requirement in this condition, one might compare it with the experimental euglycemic clamp technique in which the amount of glucose infused during insulin infusion should be equal with the measure of insulin-stimulated peripheral glucose uptake. Reported glucose infusion rates in insulin overdose situations have ranged from 0.17-0.67 g/kg/hour (11.9-46.9 g/hour for a 70-kg adult)[8-10]. The duration of infusion lasted from 6 hrs to 96 hrs in previous case series. The presented patient received a glucose infusion, ranging from 32 -90 g/hr for 300 hrs. The authors represented the amount of infused glucose in term of a glucose requirement index. The present index was established as the ratio of the amount of glucose given in 24 hrs over the mean of plasma glucose levels during the same 24-hr period to compare the glucose requirement in each day during the treatment. The glucose requirement index was used in the previous report to depict the trend of glucose requirement[2]. Surprisingly, this ratio showed the maximum value in day 6 of admission, contrasted with the authors' prediction that the peak should be observed in the first day of admission. Unfortunately, the authors could not quantify the exact values of serum insulin during the first week of admission. Therefore, it was not known whether the serum insulin levels correlate with the amount of glucose requirement in the first week. However, the glucose requirement index was simply used as a surrogate marker of the severity of hypoglycemia. It did not help to predict the duration and amount of glucose infused in insulin overdose. From the presented patient's data as shown in fig. 1, the pattern of the glucose requirement index graph might reflect the depot effect of intermediate acting insulin from injected sites.

The pharmacokinetic profiles change of regular and intermediate acting insulin could not be predicted exactly in the setting of massive overdoses.

Dialysis could not be used in case of insulin overdose because of its large molecular weight (6,000 daltons). Insulin is not significantly removed by either peritoneal or hemodialysis. Although some previous reports advocated the local excision of subcutaneous fat in insulin injected sites in the management of insulin overdose[11], this procedure should be reserved in selected cases only because of difficulty in accurate identification of the injected site. The frequent monitoring of blood glucose and titrating intravenous glucose are still the cornerstone of management in these cases[12].

Apart from the concern of recurrent hypoglycemic episodes, other less-known side effects from the massive use of insulin should also be considered during the treatment including hypokalemia, hypophosphatemia, hypomagnesemia[13], acute hepatic steatosis[14], and acute pulmonary edema[15]. Electrolyte disturbances other than hypokalemia should be recognized when treating these patients. As seen in the presented patient, severe hypophosphatemia (serum phosphate < 1.5 mg/dl) was detected in the first week of admission. Symptoms of severe hypophosphatemia, including nausea, muscle weakness, irritability, convulsion, respiratory failure, rhabdomyolysis, and hemolytic anemia are non-specific so it may not be recognized in a critically ill patient. Hypophosphatemia following massive insulin overdose occurred in the same way as seen in treatment of patients with diabetic ketoacidosis[16]. Shift of phosphorus from extracellular to intracellular compartments is the primary mechanisms of hypophosphatemia in massive insulin injection. In severe hypophosphatemia, parenteral replacement should be given to maintain the serum phosphate level into the normal range.

Moreover, insulin itself can also enhance reabsorption of sodium, causing fluid retention[17], which might contribute to dilutional hyponatremia in the presented patient. The treatment in this condition should be aimed to get rid of free water by using furosemide rather than administering hypertonic saline solution.

Acute hepatic steatosis is another side effect seen in massive insulin overdose and excessive glucose administration. The cause of this side effect originated from triglyceride accumulation in hepatocytes as a consequence of the increase production of triglyceride. Over-correction of hypoglycemia results in the acute hepatic steatosis as reported by Jolliet et al[14]. The presented patient also developed hepatitis when he was transferred to Theptarin Hospital. His hepatitis resolved completely after he recovered from insulin overdose. Even though no histologic proof is available, the rapid improvement once glucose administration was tapered down, in the absence of other identifiable causes of hepatitis, favors the occurrence of acute hepatic steatosis in the presented patient.

Another possible side effect from massive insulin overdose which physicians should be aware of in these patients is acute pulmonary edema. This effect was postulated that the large doses of insulin might cause fluids and protein to leak from the intravascular to the alveolar space. Actually, the association between hypoglycemia and pulmonary edema had been established since the early use of insulin in clinical practice[15]. Intravenous fluid should be given carefully when treated the patients with massive insulin overdose.

In conclusion, the authors present a case with attempted suicidal massive insulin injection, which is considered to be a rare condition. The present report is the first report that describes the natural course of glucose requirement in such a massive dose of insulin. Dextrose infusion, with liberal oral intake when possible, and monitoring for electrolyte changes, making adjustments as needed, are recommended for the treatment of intentional insulin overdose. Some rare, but possible, complications should also be taken into consideration as potential complications of massive insulin administration.

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รายงานผู้ป่วยและทบทวนวรรณกรรมในผู้ป่วยที่พยายามฆ่าตัวตายโดยการใช้ยาอินซูลินปริมาณมากฉีดเข้าตัวเอง

ยศพล เตียวจิตต์เจริญ, น้ำเพชร เล็กพิทยา, เทพ หิมะทองคำ

รายงานผู้ป่วยชายอายุ 80 ปี ไม่มีโรคประจำตัว พยายามฆ่าตัวตายโดยการใช้ยาอินซูลินชนิดออกฤทธิ์สั้นจำนวน 10,000 ยูนิต และยาอินซูลินชนิดออกฤทธิ์ปานกลางจำนวน 6,000 ยูนิต ฉีดเข้าใต้ผิวหนังตัวเอง ผู้ป่วยได้รับการรักษาโดยให้น้ำตาลกลูโคสเข้าทางหลอดเลือดเป็นเวลา 13 วันเพื่อควบคุมระดับน้ำตาลในเลือดให้อยู่ระหว่าง 100 ถึง 180 mg/dl ระหว่างการรักษาผู้ป่วยรายนี้มีปัญหาโซเดียมต่ำ โปตัสเซียมต่ำ และฟอสเฟตต่ำ ร่วมกับการทำงานของตับผิดปกติร่วมด้วย เป็นเวลา 2 สัปดาห์ อาการผู้ป่วยดีขึ้นโดยไม่พบภาวะแทรกซ้อนใด ๆ ผู้นิพนธ์ได้ทบทวนวรรณกรรมที่เกี่ยวข้องกับการรักษาภาวะที่ใช้ยาอินซูลินเกินขนาด