Case Report

Insulin glargine overdose

Fatma Sarı Doğan, Özge Ecmel Onur[1], Arzu Denizbaşı Altınok[1], Özlem Güneysel[2]

Department of Emergency Medicine, Goztepe Training and Research Hospital, [1]Marmara University School of Medicine, Istanbul, Turkey, [2]Emergency Medicine Clinic, Dr. Lutfi Kirdar Kartal Education and Research Hospital, Emergency Medicine Clinic Istanbul, Turkey.

ABSTRACT

Insulin glargine is a long acting novel recombinant human insulin analogue indicated to improve glycemic control, in adults and children with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus. The time course of action of insulins including insulin glargine may vary between individuals and/or within the same individual. Insulin glargine is given as a 24-h dosing regimen and has no documented half-life or peak effect. Hypoglycemia is the most common adverse effect of insulin, including insulin glargine. As with all insulins, the timing of hypoglycemia may differ among various insulin formulations. We present a case of a 76-year-old male insulin-dependent diabetic patient with refractory hypoglycemia secondary to an intentional overdose of insulin glargine. We would like to highlight the necessity of prolonging IV glucose infusion, for a much longer period than expected from pharmacokinetic properties of these insulin analogues after intentional massive overdose.

Key words: Hypoglycemia, Insulin glargine, lantus, overdose, suicide attempted

INTRODUCTION

Insulin glargine injection (rDNA origin) is a novel recombinant human insulin analog indicated for once-daily subcutaneous administration in the treatment of patients over 17 years of age with Type 1 or Type 2 diabetes mellitus who require basal (long acting) insulin for the control of hyperglycemia. The longer duration of action (up to 24 h) of insulin glargine is directly related to its slower rate of absorption and supports subcutaneous administration of once-daily. The time course of action of insulins including insulin glargine may vary between individuals and/or within the same individual.[1]

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CASE REPORT

A 76-year-old male presented to our Emergency Department (ED) after an intentional overdose of insulin glargine (LANTUS®). He was found by his friend diaphoretic and anxious, but responsive. He reported that he attempted to suicide by injecting himself 500 units insulin glargine subcutaneously. There was no information about blood glucose level at the time of ambulance arrival.

On initial ED evaluation, he was conscious, Glasgow Coma Score was 15/15; and vital signs were as follows:

Address for correspondence:
Fatma Sarı Doğan, Goztepe Training and Research Hospital, Doktor Erkin Cad. Kadıköy/Istanbul, Turkey.
E-mail: fatmasdogan@gmail.com

Blood pressure 120/70 mmHg, pulse rate 98 bpm, body temperature 36 °C; and respiratory rate 18 pm. Diaphoresis was still continuing and physical examination revealed nothing pathological but tachycardia.

Finger-stick glucose was 30 mg/dl (Reference range: 70-106 mg/dl). Simultaneous chemistry revealed 41 mg/dl. He was started 50 cc 50 % dextrose IV and continued on 10 % dextrose at 50 cc/h. Over the next 96 h he received a 10 % dextrose infusion at 50 cc/h and he was needed to administer extra glucose boluses for several times because of hypoglycemia periods [Figure 1].

Serum potassium level was 3.11 meq/l (Reference range: 3.5 – 5.2 meq/l). Other parameters such as sodium, phosphate, calcium and liver function tests were in the normal range. Oral potassium chloride was started since serum level was found as low as 3.17 meq/l. Oral potassium chloride was arranged as needed during follow up period.

In his past medical history, he emphasized insulin-dependent diabetes for 25 years, hypertension, parkinson disease, panic disorder; and dementia. Current medications included insulin glargine 14 units twice daily, Losartan plus, levodopa+carbidopa+entacapone and piracetam.

After 96 h, he was transferred to Internal Medicine ward for close monitoring; then consulted to psychiatry and endocrinology.

At the fifth day of follow up, hypoglycemia periods were terminated and he was discharged on appointed outpatient clinic.

DISCUSSION

Insulin glargine is a long acting novel recombinant human insulin analog indicated to improve glycemic control in adults and children with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus. Hypoglycemia is the most common adverse effect of insulin, including insulin glargine.[1] Time course of action of insulins, including insulin glargine, may vary between individuals and/or within the same individual. The doses and timing of antidiabetic medications must be determined and adjusted individually to achieve the desired blood glucose levels.[1] Insulin glargine is given as a 24-h dosing regimen and has no documented half-life or peak effect.[2]

Reports of insulin overdose are rare. The major effects of insulin overdose are secondary to the insult to the CNS produced by hypoglycemia. The mainstay of insulin overdose management is glucose replacement therapy.[3]

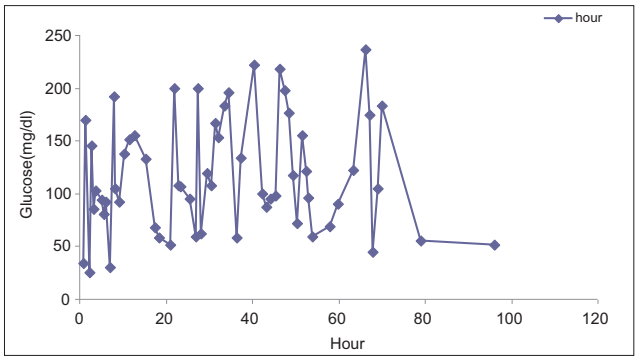

Figure 1: Serum glucose levels (mg/dl) during the hospitalization period.

Insulin overdose is potentially dangerous because some complications can occur such as hypokalemia, hypomagnesemia, hypophosphatemia, acute steatosis, pulmonary edema and permanent cognitive function impairment.[4,5] The treatment of such insulin overdose is based on the prevention of hypoglycemic episodes by continuous glucose infusion, liberal oral feeding, capillary glucose blood monitoring and monitoring for electrolyte changes and also glargine, protracted effect between 20 and 24 h.[2]

This case report confirms the existence of a more prolonged hypoglycemic effect of long acting insulin analogs such as glargine after massive injection. The last episode of hypoglycemia occurred 96 h after the overdose injection. The cause of the dissociation between large doses of insulin and the severity of subsequent hypoglycemia remains unclear. We reported side effect to Ministry of Health and also to the medical company which produces insulin glargine .

In the report of Tofade and Liles, a 33-year-old woman who intentionally injected herself high dose of insulin, and she recovered from the resulting hypoglycemia after 40 h of dextrose infusion and was transferred to a mental health facility. 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.[4] Fromont *et al* confirm the existence of a more prolonged hypoglycemic effect of long acting insulin analogues such as glargine after massive injection.[5] Lu and Inboriboon treated their patient, a 51-year-old women with insulin dependent diabetes and medication overdose, with continuous intravenous dextrose infusion with liberal oral intake, and continued to have recurrent hypoglycemic episodes 96 h into her hospital stay.[6]

Hypoglycemic reactions are evaluated routinely in the ED; Emergency physicians should maintain a high degree of suspicion regarding suicidal intent in diabetics with

hypoglycemia who respond minimally to the administration of concentrated glucose solutions or in hypoglycemic presentations by nondiabetics who have access to diabetic medications. Fingerstick glucose evaluations or serum glucose levels should be obtained routinely at 15 to 30 minutes after glucose administration in any hypoglycemic patient besides monitoring for electrolyte changes.

CONCLUSION

This clinical observation emphasizes that clinicians should be aware of the unusually prolonged action of long acting insulin analog glargine after massive injection in order to avoid a too early interruption of glucose infusion and a subsequent risk of relapse of severe hypoglycemic episodes and be conscious of the hypoglycemic status that lasts over 24 h.

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