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Prolonged hypoglycemia after an insulin glargine overdose in a patient with type 2 diabetes mellitus

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Abstract: A fifty-seven-year-old male patient self-administered maximum 300 units of glargine by subcutaneous injection. He was found after being in an unconscious state for approximately 15 hours, and was transferred to a nearby medical facility. He had been taking glargine for type 2 diabetes mellitus. He had been in a depressive state following his retirement. He was diagnosed with prolonged hypoglycemia induced by a suicide attempt and was transported to our hospital by a physician staffed helicopter. On arrival, He was alert and admitted to an intensive care unit where he received a continuous drip infusion with 10% glucose and intermittent 50% glucose injection (40ml) when his blood glucose level fell to <70mg/dl (his blood glucose level was measured every 30 minutes). The patient consumed a 1600 Kcal meal each day. At 36 hours after admission, he no longer showed hypoglycemia and did not require glucose injections. The total amount of glucose required from admission until he left the intensive care unit was 1244 g. He was discharged on the 15th day of hospitalization after treatment for transient delirium and a depressive state by psychologists. As we could not find any such cases in which the use of glargine in a suicide attempt resulted in death, glargine might be useful for preventing suicide attempts using insulin and might therefore be a useful hypoglycemic drug for treating psychiatric patients with diabetes mellitus.
Keywords: glargine; suicide; psychiatric disease; diabetes mellitus.

INTRODUCTION

Hypoglycemia can occur in patients who use hypoglycemic agents for diabetes or other drugs (such as beta-blockers), and patients with critical illnesses, malnutrition, or hormone deficiencies, especially adrenal insufficiency, bariatric surgery, hepatic failure, sepsis, paraneoplastic syndrome and insulinoma [1]. We report the case of a patient with type 2 diabetes mellitus who experienced prolonged hypoglycemia after an insulin glargine overdose.

CASE PRESENTATION

A fifty-seven-year-old male patient self-administered maximum 300 units of glargine by subcutaneous injection. He was found after being in an unconscious state for approximately 15 hours, and was transferred to a nearby medical facility. He had been taking pioglitazone, sitagliptin, miglitol, epalrestat and glargine for type 2 diabetes mellitus since he was 46 years of age. He had been in a depressive state following his retirement. He was diagnosed with prolonged hypoglycemia induced by a suicide attempt and was transported to our hospital by a physician staffed helicopter. On arrival, his Glasgow Coma Scale score was 15. His blood pressure was 180/80 mmHg and his heart rate was 80 beats per minute (BPM). His pulse oximetry was 99% under room air. A physiological examination, chest X-ray, electrocardiogram and head computed tomography revealed no remarkable findings. The patient's complete blood counts were as follows: white blood cells, 18,200/mm^3; hemoglobin, 12.3 g/dl and platelets, 22.3 x $10^4/mm^3$. Serum biochemical analyses revealed the following findings: total bilirubin, 0.8 mg/dl; aspartate aminotransferase, 28 IU/L; alanine aminotransferase, 17 IU/L; total protein, 7.0 g/dl; glucose, 87 mg/dl; blood urea nitrogen, 13.0 mg/dl; creatinine, 0.47 mg/dl; sodium, 133 mEq/L; potassium, 3.9 mEq/L; chloride, 95 mEq/L; HbA_1C 7.4%.; prothrombin time, 10.4 (12.1) s; activated partial thromboplastin time, 20.3 (25.0) s. He was admitted to an intensive care unit where he received a continuous drip infusion with 10% glucose and intermittent 50% glucose injection (40ml) when his blood glucose level fell to <70mg/dl (his blood glucose level was measured every 30 minutes). The patient consumed a 1600 Kcal meal each day. The frequency of 50% glucose injections and the level of blood glucose after admission are shown in Figure 1. The patient's blood insulin level on the 2nd day of hospitalization was 40 (0-17) μU/mL. At 36 hours after admission, he no longer showed hypoglycemia and did not require glucose injections. From 40 hours after admission, his glucose level was maintained at over 200mg/dl, which necessitated the restarting of hypoglycemic drugs. He was then transferred to a general ward. The total amount of

glucose required from admission until he left the intensive care unit was 1244 g. He was discharged on the 15th day of hospitalization after treatment for transient delirium and a depressive state by psychologists.

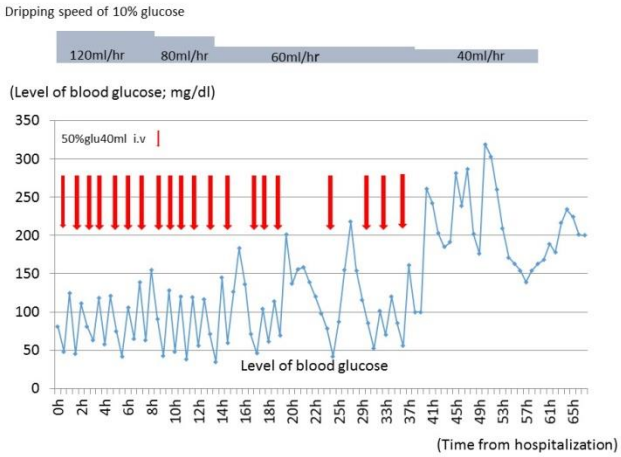

Fig-1: The frequency of 50% glucose injections and the level of blood glucose after admission At 36 hours after admission, he no longer shows hypoglycemia and does not require glucose injections.

Table-1: A list of cases involving patients who attempted suicide by injecting glargine

Author	**Age Sex**	**Underlying disease**	**Insulin** (Unit)	**Recovery** (hour)	**Total glucose** (g)	**Outcome**
Uesugi	38 F	Depression	300	46	?	No deficit
Tsujino	35 M	Depression	300	50	?	No deficit
Ohama	29 F	Psychosis	640	51	1025	No deficit
Tsujimoto	41 M	None	180	36	?	No deficit
Tsujimoto	41 M	None	180	36	?	No deficit
Dogan	76 M	Panic	500	96	?	No deficit
Kumar	12 F	Depression	2000	130	?	?
Mork	39 M	None	3800	109	?	No deficit
Lu	51 F	None	2700	96	?	No deficit
Ashawesh	31 F	Depression	1000	106	?	No deficit
Fuller	37 M	None	150	48	?	No deficit
Fromont	22 F	None	300	30	?	No deficit
Brvar	21 F	None	26	53	?	No deficit
Tofade	33 F	None	300	48	460	No deficit
Karatas	45 M	Depression	3600	120	?	No deficit
Present	57 M	Depression	300?	40	1244	No deficit

DISCUSSION

There are numerous reports concerning self-induced hypoglycemia in patients attempting suicide using insulin analogs; however, the literature (including the Japanese literature) only includes 14 case reports involving the use of glargine (Table 1) [2-15]. Generally, a massive dose of a long-acting hypoglycemic drug such as glargine results in a long hypoglycemic episode in comparison to short- or medium-acting insulin. The duration of hypoglycemia in cases involving the injection of a massive dose of glargine is also reported to be prolonged in comparison to a standard dose of glargine [13,16]. The average duration of hypoglycemic action after a standard dose of glargine is 24 hours. However, when a massive dose of glargine is injected, the duration of hypoglycemic action can be prolonged from 30–130 hours. Accordingly, when a massive dose of glargine is injected, the physician should take care as the hypoglycemic episode may last for as long as several days. It has been reported that the rate at which the blood glucose level is reduced is not affected by the dose of insulin [17]. The mechanisms underlying the independence of the rate of blood glucose reduction,

even after a massive dose of insulin, are reported to involve the insulin-induced degradation of the insulin receptor substrate or decreases in insulin-mediated glucose transport when the concentration of insulin in the blood remains high for extended periods of time [18-22]. Actually, even after the injection of a massive dose of insulin, the glucose volume required to correct hypoglycemia remained between 0.3 and 0.6 g/kg/hour; the present case required 0.6 g/kg/hour [17].

We only measured the insulin level once because the biochemical measurement of the blood insulin level does not necessarily reflect the true level of glargine due to cross-reactivity [3]. In addition, glargine is soon metabolized when it is injected, and the metabolite has hypoglycemic activity [23]. Accordingly, attention is required when interpreting the insulin levels of patients who use insulin analogs.

Suicide attempts involving the injection of insulin can result in death [24]. However, we could not find any such cases in which the use of glargine in a suicide attempt resulted in death. This might be because glargine slowly reduces the blood glucose level slowly in comparison to other insulin analogs. Glargine might be useful for preventing suicide attempts using insulin and might therefore be a useful hypoglycemic drug for treating psychiatric patients with diabetes mellitus.

Conflict of interest

We do not have conflict of interest to declare.

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