

Prolonged hyperinsulinemia after subcutaneous injection of 2400 U regular insulin in a suicide attempt: Time course of serum insulin with frequent measurements

Yoshihisa Hiromine, Yumiko Kawabata, Takaaki Yamauchi, Shinsuke Noso, Naru Babaya, Takeshi Harada, Hiroyuki Ito, Hiroshi Ikegami*

ABSTRACT

We studied the time course of serum insulin level in a patient who injected large amounts of regular insulin in an attempted suicide. A 58-year-old woman attempted suicide by subcutaneously injecting herself with 2400 U regular insulin. On arrival, the serum glucose level was 2.4 mmol/L (44 mg/dL) and the serum insulin level was 40,000 pmol/L (5700 μ IU/mL). The serum insulin level was high, with a maximum of 110,000 pmol/L (16,000 μ IU/mL) at 13 h after injection, followed by an initial rapid decrease and a subsequent slow decrease, with hyperinsulinemia lasting as long as 5 days after injection. (*J Diabetes Invest*, doi: 10.1111/j.2040-1124.2012.00211.x, 2012)

KEY WORDS: Hyperinsulinemia, Hypoglycemia, Insulin

INTRODUCTION

In contrast to the common occurrence of insulin-induced hypoglycemia in patients treated with insulin, hypoglycemia as a result of intentional overdose with insulin is uncommon. In particular, self-administration of a large amount of insulin in non-diabetic subjects is extremely rare. Furthermore, detailed reports on the plasma level of insulin after a massive overdose of insulin injection are limited.

We report a patient who injected a large amount of regular insulin in an attempted suicide. The plasma level of insulin was frequently measured to evaluate the time-course of insulin disappearance.

CASE REPORT

A 58-year-old woman with no significant medical history attempted suicide by injecting herself with 2400 U regular insulin subcutaneously in multiple sites of the anterior abdomen at approximately 05.00 h (1200 U) and 06.30 h (1200 U) on the day of presentation. She had not been diagnosed as having diabetes mellitus, but her brother was diagnosed with type 2 diabetes mellitus and was treated with insulin, which was used for her suicide attempt. After the overdose, she asked her brother to call emergency rescue services and arrived at the emergency department of Kinki University Hospital, Osaka-sayama, Osaka, Japan at 09.45 h.

On arrival, the plasma glucose level was 2.4 mmol/L. The patient was still conscious (Glasgow coma scale 10). Physical examination findings were normal, except for multiple needle injection sites across her anterior abdomen. Laboratory data on admission are shown in Table 1. Glycated hemoglobin (HbA_{1c}; %) was estimated as a National Glycohemoglobin Standardization Program equivalent value (%) calculated by the formula HbA_{1c} (%) = HbA_{1c} (Japan Diabetes Society) (%) + 0.4%¹.

Hypoglycemia was immediately diagnosed, and a bolus dose of 60 mL of 50% glucose was injected intravenously and continuous intravenous infusion was started. After injection of 50% glucose, the patient's consciousness became clear and oral food intake (1600 kcal/day, 32.3 kcal/kg standard bodyweight) was allowed at 18.00 hours, 13 h after insulin injection, and continued until hospital day 10. Intravenous glucose infusion was discontinued on hospital day 6, 124 h after insulin injection, with no further hypoglycemia. The total amount of glucose infused was 2791 g.

Serum insulin level was measured in samples frequently collected after arrival in the emergency department. The serum insulin level was 40,000 pmol/L (5700 μ IU/mL) on arrival, which was approximately 5 h after the first insulin injection, reached a maximum level of 110,000 pmol/L (16,000 μ IU/mL) approximately 13 h after injection, then gradually decreased to a normal level (Figure 1).

DISCUSSION

For regular insulin, the mean predicted time of onset of action occurs 0.75 h after administration, with peak activity at 2 h and a duration of 6 h². The detailed profile after massive injection of

Department of Endocrinology, Metabolism, and Diabetes, Kinki University School of Medicine, Osaka-sayama, Osaka, Japan

*Corresponding author. Hiroshi Ikegami Tel.: +81-72-366-0221 Fax: +81-72-366-2095 E-mail address: ikegami@med.kindai.ac.jp

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Table 1 | Laboratory tests on admission

Peripheral blood	
White blood cell count	12.9 × 10 ⁹ /L
Red blood cell count	4.36 × 10 ¹² /L
Hemoglobin	157 g/L
Hematocrit	44.6%
Platelet count	292 × 10 ⁹ /L
Blood chemistry	
Na	145 mmol/L
K	2.7 mmol/L
Cl	110 mmol/L
Total protein	74 g/L
Albumin	44 g/L
Urea nitrogen	3.57 mmol/L
Creatinine	34.5 μmol/L
Aspartate aminotransferase	36 U/L
Alanine aminotransferase	36 U/L
γ-Glutamyl transferase	51 U/L
Total cholesterol	5.17 mmol/L
Triacylglycerol	6.37 mmol/L
HDL-cholesterol	0.52 mmol/L
Glucose	2.4 mmol/L
s-CPR	0.07 nmol/L
IRI	40,000 pmol/L
HbA _{1c}	6.5%
Anti-GAD Ab	<0.3 U/mL

Anti-GAD Ab, antiglutamic acid decarboxylase antibody; HbA_{1c}, glycated hemoglobin; HDL, high-density lipoprotein; IRI, immunoreactive insulin; s-CPR, connecting peptide immunoreactivity serum.

insulin, however, is largely unknown. Frequent measurement of serum insulin after injection of 2400 U regular insulin in a subject never treated with insulin in the present study enabled us to investigate the time-course of serum insulin after injection of a massive dose. The data showed prolonged hyperinsulinemia with a peak at 13 h after injection, slow disappearance and hyperinsulinemia for as long as 5 days after injection.

The maximum plasma insulin level is reported to correlate well with the dose of insulin injected³. Some of the studies, however, did not show a clear peak of insulin, as a result of inappropriate timing and/or frequency of insulin measurements, resulting in the initial value being the maximum value, which was followed by a linear decrease⁴. Frequent measurement of serum insulin starting soon after admission made it possible to identify a clear peak, with an initial increase phase from 40,000 pmol/L on admission to the maximum plasma insulin level of 110,000 pmol/L at 13 h after injection, followed by a decrease phase lasting as long as 5 days (Figure 1). The detailed time-course from the peak towards the decrease phase suggested that the decrease in serum insulin consists of two phases, an initial rapid decrease from the peak at 13 h until 24 h after injection, followed by a slow and steady decrease phase from day 3 to day 7. The half-life for the rapid decrease and the slow decrease was approximately 5.3 and 26.2 h, respectively, using Winonlin[®] 5.2 software (Pharsight Corporation, Mountain

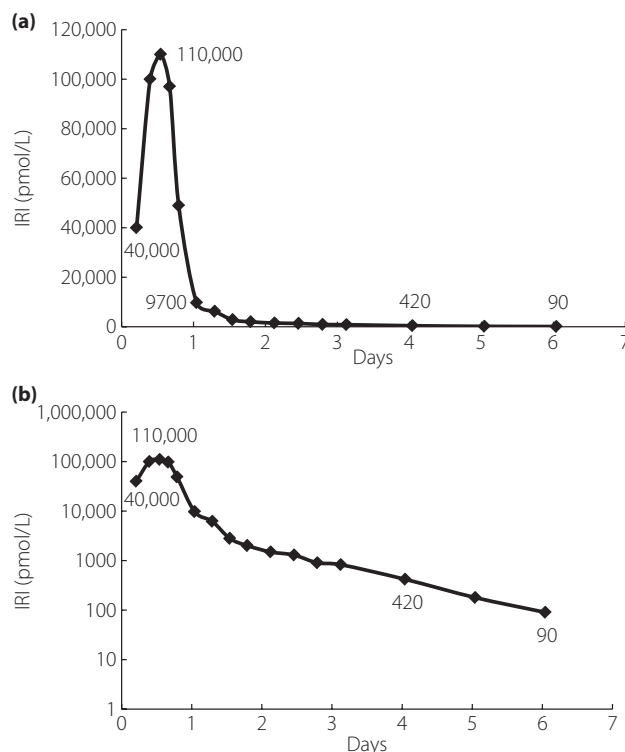


Figure 1 | Time course of serum insulin level after intentional overdose (2400 U) of regular insulin injected subcutaneously. Insulin level is shown on the y-axis on (a) a linear and (b) logarithmic scale. IRI, immunoreactive insulin.

View, CA, USA). A biphasic decline in insulin after injection has previously been suggested, with apparent half-lives of 4 and 10 h⁵.

In the present case, the maximum rate of glucose infusion to avoid hypoglycemia was 2.1 mmol/kg/h (0.37 g/kg/h), which was not in proportion to the extremely high insulin levels. As the maximal insulin effect on glucose uptake was reported to plateau at approximately 1400 pmol/L⁶, a further increase in insulin level does not lead to a parallel increase in glucose uptake⁷. In contrast to the relatively low glucose requirement, glucose infusion had to be maintained for as long as 120 h to prevent hypoglycemia, which reflects prolonged hyperinsulinemia, as shown in Figure 1. These data suggest that a massive overdose of insulin does not result in a proportional increase in the glucose infusion rate, but leads to prolongation of the duration of glucose infusion to avoid hypoglycemia⁸. Another possibility for relatively low glucose requirement is oral food intake in addition to intravenous infusion of glucose.

In the present case, the interval between insulin self-injection and initiation of therapy was within 5 h, which might be one of the reasons why neither relapse of hypoglycemia nor adverse sequelae resulting from hypoglycemia occurred⁹. Another possible reason for the mild hypoglycemia and complete recovery from hypoglycemia is the presence of insulin resistance in the patient. Insulin sensitivity as evaluated by homeostasis model

assessment for insulin resistance index was 5.2, indicating the presence of insulin resistance associated with obesity (body mass index 34.0 kg/m²). Although her fasting plasma glucose level was not in the diabetic range, she showed a mild diabetic pattern with a 2-h plasma glucose level of 14.1 mmol/L by 75 g oral glucose tolerance test. These data suggest that insulin resistance and glucose intolerance might be among the reasons for the mild hypoglycemia and benign clinical course, despite as much as 2400 U insulin being injected.

In conclusion, frequent measurement of serum insulin in a patient who was never treated with insulin and attempted suicide by subcutaneously injecting herself with 2400 U regular insulin showed a very high peak at 13 h after injection, and an initial rapid decrease followed by a slow decrease of serum insulin, resulting in hyperinsulinemia lasting as long as 5 days.

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The authors declare no conflict of interest.

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