Delayed hypoglycemic effect of insulin overdose in a diabetic child: a case report

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ABSTRACT

Background: Insulin overdose can result in fatal hypoglycemia. We report on a diabetic child who received an unintentional insulin overdose.

Case Presentation: A 13-year-old girl with type 1 diabetes, who was on insulin pump therapy, developed high blood glucose (BG) level due to pump malfunction. She gave herself 7 ml (700 units) instead of seven units by an error. She presented to hospital 2 hours later when this was recognized. The initial BG in the emergency room was 13.9 mmol/l. A dextrose infusion was started 6 hours after the insulin injections when her BG dropped significantly before it reached a lowest level of 3.3 mmol/l, 9 hours after the event. It was only possible to discontinue this infusion 15 hours after insulin injections when BG was stable.

Conclusion: Hypoglycemia could be delayed in insulin overdose in diabetic children. This may necessitate prolonged monitoring beyond the usual half-life of insulin.

Keywords: Insulin, overdose, delayed hypoglycemia, dextrose, glucagon, aspart, diabetes.

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Background

Insulin overdose can be a significant emergency condition due to risk of fatal hypoglycemia [1]. Mortality accounts for 2% of the cases of insulin overdoses [2]. There are few reports that discuss unintentional insulin overdose in teenagers as most of the reported cases were secondary to mental disorders or suicidal attempts [2,3]. Insulin aspart is rapid acting insulin with potential of short duration hypoglycemic episodes [4]. However, the hypoglycemic effect of insulin can be prolonged in case of insulin overdose with maximum effect at the first few hours after the injection(s) [5]. Different hypotheses were postulated to explain the pathophysiological process of this prolonged action of insulin; some were confirmed by the experiments [6]. We report on a teenager with type 1 diabetes mellitus (T1DM) who received an unintentional insulin aspart overdose, which resulted in a delayed onset of hypoglycemia.

Case Presentation

We report a 13-year-old Saudi girl, who is a known case of T1DM on insulin pump therapy. She developed blood glucose (BG) reading "HIGH" which is more than 33.3 mmol/l (600 mg/dl) due to pump malfunction. Mistakenly, instead of taking seven units of insulin aspart as a correction dose, she gave herself 7 ml (700 units) of insulin aspart by insulin syringes as been advised on the dose over the phone by her sister, who is a doctor, and usually counsel her younger sister in management. She received seven injections (1 ml/syringe) that were given in the patient abdomen and both thighs. The patient presented to our Emergency Department after 2 hours from the injection time when this error was recognized. She was fully conscious with normal vital signs. The injection site in her abdomen was lipodystrophic. The initial BG reading at the emergency room was 13.9 mmol/l (250 mg/dl), and that falsely reassured the emergency room (EM) staff. Therefore, the patient was not started on intravenous (IV) dextrose infusion, and her insulin pump was suspended. However, the patient continues on frequent BG monitoring every 30 minutes. Her oral intake was minimal due to poor appetite. Her BG was decreased gradually till it reached 3.8 mmol/l (70 mg/dl) after 6 hours from the received injections, hence, started on 10% dextrose IV infusion. After that, BG improved but started to decline again gradually during the dextrose infusion reaching the lowest level of 3.3 mmol/l (60 mg/dl), after 9 hours of the insulin injections. This was treated by bolus of 10% dextrose and 1 mg of intramuscular glucagon (Figure 1). Investigations, ordered later in the patient by endocrinology team, showed equivalent levels of BG in the lab, normal electrolytes, venous blood gas, and renal functions (Tables 1 and 2). Six hours later, i.e., 15 hours after the overdose by insulin injections, dextrose infusion was discontinued due to stabilization of BG

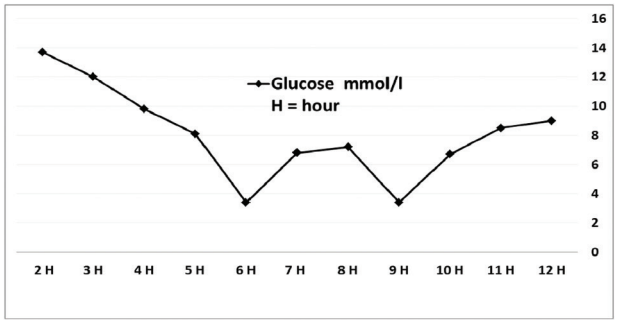


Figure 1. *Hospital BG levels over time from insulin injections.*

Table 1. Initial level of electrolytes at presentation.

ELECTROLYTES	LEVEL
Na (mmol/l)	132
K (mmol/l)	3.6
Cl (mmol/l)	103
BUN (mmol/l)	5
Creatinine (µmol/l)	79

Table 2. Level of C-peptide and insulin (at 12 hours post-injection).

Insulin (uIU/ml)	3.8
C-Peptide (ng/ml)	0.5

level. Nevertheless, the patient was kept on continuous monitoring till completed 12 hours, in which she did not develop hypoglycemia, after discontinuation of dextrose infusion.

Discussion

Insulin overdose can be a serious condition [1]. In a recent report, T1DM patients accounted for more than 50% of insulin overdose cases [2]. An unintentional insulin overdose accounts for 5% of the total cases. Approximately, 50% of the total cases had psychiatric illnesses [2]. The recovery from risk of hypoglycemia following insulin overdose occurs maximally in 1 week with a mean time of approximately 72 hours [2,5].

It is important to identify the maximum glucose clearance rate in cases of insulin overdose as this could anticipate the development of hypoglycemia and the duration needed for glucose infusion [7–9]. In our case, the initial BG reading at home in the glucometer was "HIGH" which means more than 33.3 mmol/l (600 mg/dl), but the exact high level is unknown. Therefore, the rate of decreasing of glucose during the initial 2 hours after the injections could not be accurately identified. Although some reported cases had a delayed onset of hypoglycemia, after a huge dose of insulin injection [9,10].

Teenager's behavior and problems related to insulin injection site are well known factors of diabetic mismanagement [11]. The other possibility that could explain the situation in our patient is that our patient might have not actually received the claimed insulin aspart dose due to either expired insulin, poor technique of injection, or a part of teenager's manipulation. Last, but not the least, the patient could have used lipohypertrophy site of injection that consequently leads to delayed of insulin absorption.

The prolonged effect of hypoglycemia in insulin overdose is more commonly dose rather than insulin type dependent [5]. Different mechanisms might explain the prolonged hypoglycemic effect in short acting insulin overdose. First, decrease absorption of insulin from the injection site due to the mechanical effect that leads to compression in the local microvascular circulation, which is supported by experimental studies [5,12]. In addition, surgical incisions of the injection site have been used as a modality of treatment [13]. Second, prolongation of half-life of insulin due to decreased insulin clearance when the maximum capacity of hepatic and renal receptors of insulin excretion is exceeded [6]. Moreover, insulin pharmacokinetics is suggested to be unique. For instance, the IV administration of glargine, long acting insulin, did not result in hypoglycemia in compared to similar dose given by subcutaneous route [14].

The severity and serious consequences are more common in non-diabetic patient who received the insulin overdose, because of the possible presence of insulin autoantibodies as well as absence of endogenous insulin in patient with T1DM [15]. Nonetheless, the most common electrolyte imbalance, other than hypoglycemia, is hypokalemia due to insulin-induced potassium shift from extracellular to intracellular compartment [2].

There are different modalities of treatments of insulin overdose, and the most common used is an IV glucose therapy, which includes boluses and infusions. Other modalities include glucagon, oral carbohydrates, surgical incision at the injection site, octreotide, and hydrocortisone [2,9,13]. In addition, other management should be include electrocardiogram (ECG) monitoring and optimization of serum potassium level that could be drop secondary to insulin overdose. Use of continues glucose monitoring device during the hospitalization may be helpful to guide the physician when to stop the treatment [16].

Understanding the possibilities of progress in different scenarios, as above, in term of immediate or slow development of hypoglycemia is a cornerstone in management of such cases. In our patient, the impression of stability of BG initially lead to the false opinion that possibly delayed the initiation of IV glucose infusion and the requesting insulin level and c-peptide in the list of investigations at presentation. Using of insulin pen instead of insulin syringe may decrease the risk of miscalculation of insulin correction dose.

Conclusion

Insulin overdose may lead to a delayed hypoglycemic effect. Hence, affected patients should be monitored for this risk even beyond the half-life of the overdosed insulin.

Acknowledgment

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List of Abbreviations

BG	Blood glucose
ECG	Electrocardiogram
ER	Emergency room
IV	Intravenous
T1DM	Type 1 diabetes mellitus

Consent for publication

Informed consent was obtained form the patient and her family.

Ethical approval

The manscript follows the rules and regulation of institution review board in the King Abdullah International Medical Research Center (KAIMRC) in publishing of patient information including confidentiality and consent for publication.

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Summary of the case

Patient (gender, age)	1	Female, 12 years
Final diagnosis	2	T1DM, insulin overdose
Symptoms	3	Hypoglycemia
Medications	4	IV 10% dextrose, IM glucagon
Clinical procedure	5	N/A
Specialty	6	Endocrinology