

A case of acute insulin poisoning

一個急性胰島素中毒個案

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A 32-year-old lady presented to the emergency department for suicidal attempt by self-injection of insulin (Protaphane 210 units). She developed repeated episodes of hypoglycaemia even with continuous intravenous infusion of 10% dextrose solution during observation. However, she did not develop serious complications of hypoglycaemia and was subsequently discharged after conservative treatment. Acute insulin poisoning is uncommon. The management of this uncommon poisoning is reviewed in this case report. (*Hong Kong j. emerg.med.* 2006;13:232-234)

一名 32 歲女士自己注射胰島素（諾和靈 210 單位）試圖自殺後，到急症室求診。即使在觀察期間不斷地以靜脈輸注 10% 葡萄糖溶液，她反覆地形成低血糖的時段。然而，她沒有發展至低血糖的嚴重併發症，經保守療法後出院。急性胰島素中毒是不常見的，本個案報告還評論這不尋常中毒的治理。

Keywords: C-peptide, insulin overdose, long acting insulin

關鍵詞：C-肽、胰島素中毒、長效胰島素

Case history

A 32-year-old lady presented to our emergency department in November 2005 after self-injection of 210 units Protaphane over her abdominal wall for suicidal attempt about 24 hours before arrival. The patient's father was the first person to discover the patient's act of suicide. Her father did not seek medical help at that time but treated her daughter with maltose at home. However, she developed marked hypoglycaemic symptoms including dizziness and cold sweating, but without loss of consciousness or convulsion. She was finally brought to the emergency

department by ambulance. On arrival at the emergency department, her blood pressure was 107/68 mmHg, pulse rate 92 beats per minute, respiratory rate 18 breaths per minute, tympanic temperature 36.5°C and SpO₂ 100% on room air. She was fully conscious with Glasgow coma score of 15/15. The physical examination revealed no focal neurological deficits. The initial haemostix level was 2.2 mmol/L. No formal blood test including renal function test was performed, as the patient was reluctant to have blood sampling except capillary glucose measurement. She was given continuous glucose infusion and also oral glucose water. She was subsequently transferred to the emergency observation ward for further management and close monitoring. During the initial two days of stay in the emergency observation ward, she developed repeated episodes of hypoglycaemia despite continuous infusion of 10% dextrose solution and frequent oral feeding (Figure 1). On the third day of observation, her condition improved and further glucose supplementation was not necessary. She was discharged

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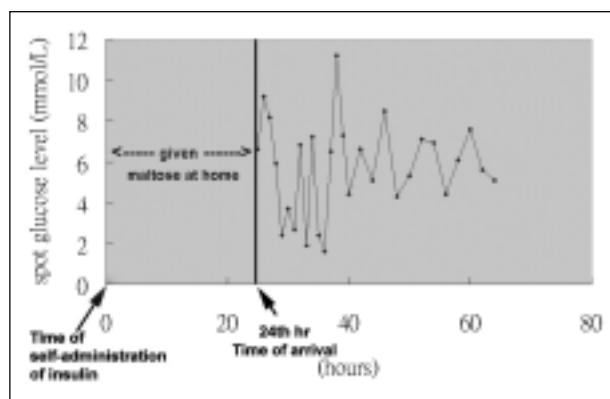


Figure 1. Time course of blood glucose levels of the patient.

subsequently after seventy-two hours of hospital stay. A detailed psychiatric assessment during the ward stay revealed a past history of depression and a long history of intentional drug overdose with repeated admissions into hospital in Singapore. She had been followed up by private psychiatrists after moving to Hong Kong. She lived with her father and felt distressed in taking care of him who was suffering from diabetes mellitus. She attempted suicide by self-injection of the insulin preparation from her father this time. Medical social service and psychiatric follow up were provided to the patient.

Discussion

Only a few case reports on suicidal insulin overdose could be found on literature search. The term, factitious hypoglycaemia, describes the situation of hypoglycaemia due to malicious or self-administration of insulin. This condition shares many clinical and laboratory features with insulinoma. It may be difficult to differentiate insulinoma from intentional insulin overdose as the history given by the patient who attempts suicide is often unreliable. Factitious hypoglycaemia is most commonly seen among medical personnel, pharmacists, relatives of diabetics and diabetic patients who have easy access to antidiabetic drugs. Unexplained hypoglycaemia in patients with psychiatric illness, such as depression, is an important clinical clue to intentional insulin overdose. Patients with hypoglycaemia unresponsive or minimally responsive to concentrated glucose infusions should

raise the suspicion of administration of exogenous insulin¹ and sulfonylurea overdose. In individuals taking exogenous insulin, factitious hypoglycaemia can be distinguished from insulinoma by the presence of high insulin levels without a concomitant increase in the C-peptide level, which is suppressed by the exogenous insulin. The triad of simultaneous hypoglycaemia, high insulin levels, and suppressed C-peptide is pathognomonic of exogenous insulin administration.² Hypoglycaemia with a high or normal C-peptide level is suggestive of insulinoma or overdose of sulfonylurea or non-sulfonylurea secretagogues. However, in our case, C-peptide assay needs to be sent to another hospital for analysis. Other toxicological causes of hypoglycaemia, such as overdose of salicylate, alcohol, β -blocker and other oral hypoglycaemic agents (OHA) should also be considered. Patients with hypoglycaemia may also present as trauma cases like injury after a fall or non-trauma cases like aspiration associated with loss of consciousness.³

Profound hypoglycaemia secondary to insulin overdose may cause serious morbidity and even mortality. Hypoglycaemia can cause convulsion and permanent neurological deficits. Acute myocardial infarction secondary to hypoglycaemia has been reported.⁴ An epidemiological study on insulin overdose in a regional poisons unit in Germany reported 2.7% death among 160 patients and 2.7% of the patients with insulin overdose survived with cerebral defects.⁵ Apart from the hypoglycaemic complications, insulin overdose can also cause electrolytes disturbance particularly hypokalaemia.

Protaphane, a long-acting insulin preparation, is commonly used in both patients with insulin-dependent diabetes mellitus and non-insulin-dependent diabetes mellitus. Its onset of action is within one hour and maximum effect occurs within 4 to 12 hours after injection. The entire duration of action is approximately 24 hours. The half-life of insulin in the blood stream is only a few minutes. However, the time-action profile of insulin is determined by the absorption characteristics of the insulin preparation. In overdose situation, absorption of insulin can be prolonged due to the depot effect.

Adequate glucose replacement with close glucose monitoring is essential in the management of factitious hypoglycaemia. The initial management of patient with hypoglycaemia is intravenous administration of glucose e.g. 10% dextrose solution in adults. Continuous and prolonged intravenous glucose administration is necessary due to the depot effect after a massive dose of insulin injection. The blood glucose-lowering effect is further prolonged when long-acting formulations are involved as in this case. Hypoglycaemia could occur one week after a relatively minor insulin overdose.⁴ Concomitant ingestion of drugs should always be considered. Glucagon is not effective in the treatment of factitious hypoglycaemia, as glycogen stores in the liver would have been depleted.¹ In contrast to the management of hypoglycaemia secondary to overdose of OHA, e.g. sulfonylurea, diazoxide is not useful as it is a direct inhibitor of insulin release from the pancreas.¹ Haemodialysis to enhance elimination will not shorten the duration of action of insulin, which depends on the rate of absorption rather than elimination. For those situations with massive injection of long-acting insulin preparations, surgical debulking of the subcutaneous tissue around the injection site could be considered. There were several case reports of successful outcome with this surgical procedure in the management of insulin overdose.^{6,7} Surgical excision was not considered in this case as the patient presented late (24 hours after the injection) and there was no swelling over the abdominal wall to help locating probable injection sites. Post-excision surgical scar and disfigurement should also be taken into serious account before decision. Also, surgical excision may not be feasible in those cases with multiple sites of injection. Cerebral damage can be a result of prolonged hypoglycaemia as well as repeated short episodes of hypoglycaemia with fluctuating glucose level. Theoretically, an artificial pancreas can automatically smooth out the effect of insulin and be able to deliver either glucose or glucagon in case of overshoot hypoglycaemia. Therefore it may help to prevent the development of post-hypoglycaemic encephalopathy secondary to fluctuating glucose levels.¹

Summary

Factitious hypoglycaemia secondary to acute insulin overdose is rarely encountered in the emergency department. Hypoglycaemia can result in neurological deficits and fatality. This case report illustrated the classical presentation of a patient with factitious hypoglycaemia. Patients with easy access to antidiabetic drugs and psychiatric illness presenting with unexplained hypoglycaemia should raise the suspicion of exogenous insulin administration. Adequate glucose replacement with close monitoring of blood glucose and potassium levels will be the mainstay of treatment. Prolonged observation and monitoring is expected due to the depot effect especially with long-acting insulin preparations. Surgical removal of subcutaneous tissue at the injection site or an artificial pancreas may be useful.

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