Case Report

Postmortem Vitreous Glucose Estimation in Suicidal Insulin Overdose: A Case Report and Review of Literature

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ABSTRACT

Suicidal attempts by self administration of insulin in non-diabetics are known to occur. Deaths too are sporadically reported. Various techniques like quantification of insulin and C-peptides by radioimmunoassay (RIA), postmortem blood glucose levels, vitreous humour glucose, combined values of glucose and lactate, molar ratio of insulin to C-peptide (I:C) are being used for documentation of hypoglycaemia in deaths due to insulin poisoning.

We report a case wherein a 25-year-old nurse committed suicide by injecting rapid acting insulin intravenously. Autopsy was conducted approximately 10 hours after the incident. Fatal hypoglycaemia was detected by vitreous humour glucose analysis.

This case report emphasizes the importance of using vitreous humour as a tool to detect fatal hypoglycaemia in a case of overdose with hypoglycaemic agents, along with a brief review of literature.

Key Words: Insulin; Hypoglycaemia; Vitreous humour

Introduction

Oral hypoglycaemic agents and insulins are increasingly being employed to end one's own life. Aside from suicide, insulin has also been reported as an agent of homicide.[1,2] In the 2005 annual report of the American Association of Poison Control Centers, 3934 of the 2,424,180 inquiries (0.16%) reported drug exposures involving insulin.[3] Suicidal insulin overdose is more common in diabetic patients; however non-diabetic individuals are increasingly adopting this method for suicides.

Insulins are ineffective orally because of their proteolytic digestion and must be injected. They are administered mainly by subcutaneous route for usual diabetic control, but may be infused intravenously in severe cases. An intravenous injection of insulin produces a maximum glucose decline in about 30 minutes, whereas a subcutaneous administration takes 2–3 hours.[4]

The onset of action of short acting insulins (Actrapid, Humulin S, etc) is 0.5–2 hours with peak action at around 1–5 hours.[5] Hypoglycaemia results when overdose is injected, manifesting as tachycardia, restlessness, cold sweat, hunger, nausea, trembling, tiredness, lack of concentration, slurred speech, impairment of vision and finally loss of consciousness. Furthermore apathy, drowsiness, state of confusion, loss of memory, asynergia and aggressiveness may be observed.[6]

The diagnosis of insulin toxicosis is difficult because insulin is present in normal human serum, and the concentration can be greatly elevated after a meal. The diagnosis of fatal hypoglycaemia caused by insulin is thought to be only established by a combination of postmortem biochemistry, patho-morphological alterations and anamnesis.[7]

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Case History: A 25-year-old female, nurse by profession, was found lying unconscious at 06:00 am in her bedroom, which was locked from inside. Two empty vials of human actrapid insulin (each vial containing 10 ml equivalent to 400 IU of human insulin, that is 800 IU of human insulin in two vials) and a 10 ml disposable injection syringe with needle *in situ* were found on the right side of her body. She was declared 'brought dead' on arrival at the emergency department of the hospital. On interviewing, it was found that she was last seen at around 10 pm the previous night. She had been living alone, and past history suggested that she was suffering from depression.

An autopsy was performed about 10 hours after the death. On external examination, the body was moderately built and nourished, with length 157 cm. Rigor mortis was present throughout the body. Postmortem staining was fixed over the back. Puncture mark (of IV injection) was seen on the dorsum of left hand with injection track in the underlying vein.

On internal examination, brain was congested and edematous with petechial haemorrhages in the white matter. All the other organs were apparently normal. Stomach was empty without any unusual smell, and the mucosa was normal. There was no significant pre-existing disease that could have caused or contributed to her death.

Viscera and blood were preserved and sent for chemical analysis at the Regional Forensic Science Laboratory (RFSL). Needle mark with surrounding skin, subcutaneous tissue and underlying muscles along with skin and tissue from non-injection site as a 'control sample' were sent unfixed to RFSL for detection of any injectable drug. The RFSL reported that no poison was detected in the viscera and blood. Due to unavailability of RIA kits at RFSL, insulin and C-peptides detection was not possible.

Vitreous humour that had been aspirated at the time of the autopsy was then subjected to biochemical analysis for glucose estimation. Vitreous humor glucose was estimated by glucose oxidase method and found to be 2.5 mg/dL, which indicates fatal hypoglycaemia.[8]

Empty insulin vials with syringe and needle were considered as corroborative evidence of injected exogenous insulin. The cause of death was recorded as hypoglycaemic encephalopathy due to insulin intoxication and the manner of death was determined to be suicide.

Discussion

An investigation of hyperinsulinaemia must be initiated when hypoglycaemia has been detected, particularly in non-diabetics with a psychiatric history. Critchley et al reported 3 non-diabetics among 15 patients who attempted self poisoning by insulin injections.[9] Rapid-acting insulin was reported to be involved in 14 out of 25 patients in a study by Mégarbane et al.[10] In previous reports of suicidal insulin overdose in non-diabetic individuals, the source of the insulin was a mother, an ex-wife, a cohabitant, a husband, and, presumably, a hospital pharmacy.[11] Doctors[12] and nurses[10] are known to end their lives by injecting insulin. Drugs like beta blockers[13] and glipizide[14] have been reported to be used with injectable insulin for suicides. A delay of more than 6 hours between the overdose and medical treatment is one of the factor for poor prognosis.[10]

Deaths due to insulin overdosage are rare and in such circumstances it is difficult to detect fatal hypoglycaemia due to fast and erratic postmortem diffusion of blood glucose in body fluids. Techniques like postmortem blood glucose levels, vitreous humour glucose, quantification of insulin and C-peptides by radioimmunoassay, combined values of glucose and lactate levels,[14] and molar ratio of insulin to C-peptide (I:C)[16] are being used for documentation of hypoglycaemia due to insulin overdose. Quantitation of C peptide, a cleavage product of endogenous pro-insulin, is essential for the accurate interpretation of insulin levels. C peptide is not present in exogenous insulin (human or animal); thus, a low C-peptide level and a high insulin level suggest an exogenous source of insulin.[4]

Low level of glucose in blood is clinically diagnostic of hypoglycaemia in cases of overdose by hypoglycaemic agents. However, postmortem blood glucose estimation is not considered to be helpful, as it often might remain either normal or elevated in insulin overdose cases. This is due to the postmortem release of glucose from the body reserves, which render postmortem blood glucose levels invalid in a diagnosis of hypoglycaemia.[17]

Both glucose and insulin are unstable in postmortem blood and so the longer the delay between death and the collection of postmortem samples the greater the uncertainty of the exact concentrations of these analytes at

the time of death.[18] Further, blood collected after a postmortem period of 6–8 hours, and vitreous humour collected after more than 12 hours may be rendered unsuitable for an accurate evaluation of the glycaemic status in the agonal period.[5]

Vitreous humour biochemical analysis is a useful tool when morphologic alterations of the lethal disease are missing, e.g., in diabetes mellitus, alcoholic ketoacidosis or in cases like insulin poisoning and when insulin detection assays are not available. Vitreous humour resists putrefaction longer than other body fluids as it is sterile and remains well protected inside the eye. After extraction it should be preserved with sodium fluoride (10 mg/ml).[19] Differences of the concentrations between the two eyes are not statistically significant.[20]

Coe reported that insulin and C-peptide rarely penetrate the blood-vitreous barrier.[21] Glucose levels in vitreous fluid correlate with glucose antemortem serum levels and they amount to 50% of antemortem serum concentrations and 85% of postmortem serum concentrations.[22] Glucose levels in vitreous humour will decrease as the postmortem interval increases. Normal parameters in vitreous humour for glucose has been determined to be within the range of 27–180 mg% with mean level of 66 mg% at postmortem interval of 3–10 hours (**Table 1**).[8]

The mode of death in such circumstances may vary from profound hypoglycaemia, aspiration of the gastric contents, cardiac arrhythmia associated with hypokalaemia and catecholamine release. Death may rarely be due to idiosyncratic acute anaphylaxis.[12]

In the present case, as a professional nurse, the deceased not only had access to a plethora of insulins that are available in the hospital ward, but also with the knowledge of different insulins, fatal dose and the art of giving injection, she was able to successfully execute a planned suicide. The type of insulin used (actrapid), lack of immediate medical assistance, fasting (empty stomach) and non-diabetic status accentuated the hypoglycaemia to fatal state.

Conclusion

A diagnosis of hypoglycaemia can primarily be achieved on the base of anamnesis, symptomatology, toxicological, pathomorphological and substantially by biochemical estimations. In spite of advances in postmortem biochemistry, investigations are highly underutilized, particularly in developing countries like India. In cases of fatal insulin self-injection, quantification of blood insulin and C-peptides form the cornerstone of detection of hyperinsulinaemia. However, kits that can detect these are available only in specialized laboratories. Due to transportation challenges at such centers and erratic nature of postmortem fluids, vitreous humour analysis could become a tool of choice for detection of hypoglycaemia. Postmortem 'diagnosis' of insulin injection death has to be made by detection of hypoglycaemia and circumstantial evidence.

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Table 1 Standard Deviations and Observed Ranges of Glucose (mg/100 ml) in Vitreous Humour Published as Normal Values in the Literature[8]

	n	x	Range	1 SD	2 SD
Naumann 1959	211	62	17–105		
Leahy/Faber 1967	43				28–89
*Coe 1969**	60	84	37-180	40	
	50	66	27-180	36	
	35	51	18-106	28	

*Mean postmortem interval for taking samples: 1.75 h (0.5–2.5); 5.75 h (3–10); 17.25 h (10.5–29)

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