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Short Communication

Acute Insulin Poisoning: A Tunisian Series of Cases

Sahar Habacha Mamlouk*, Bassem Chatbri, Nasreddine Foudhaili,

and Nozha Brahmi

Centre d'assistance médicale urgente, rue Abulkassem Al Chebbi, Tunisia

Abstract

Injecting insulin for a suicidal purpose is uncommon. Few series had reported insulin poisoning (IP). Our study aimed to describe IP in a series of cases. Our study was retrospectively conducted over four years between 2012 and 2015. It included all patients admitted for IP in a suicidal attempt and who's presented clinical signs of hypoglycemia (sweats, neurologic and digestive signs).

Forty-three patients aged of 31 ± 13 years were collected. Their sex-ratio was of 0.72. Only 32% of patients were diabetics. Rapid acting insulin (RI) was found in 30%, long acting insulin (LI) in 58% and mixed intoxication in 3 cases. Route of administration was subcutaneous in all cases with a median injected dose was 120 UI [50; 302]. The median delay of signs onset was 105 minutes [15; 120] for RI and 3 hours [1; 6] for LI with a median consultation delay of 4 hours [1; 48]. Dizziness (53.5%), sweats (42%), palpitations (23%), coma (21%), paresthesia (18%), nausea (14%), seizures (11%) were the most common signs. In patients who didn't receive carbohydrates before admission, the median blood glucose level was 0.33 g/L [0.12; 0.5]. The median required dose of injected carbohydrate was 175 g [90; 200] in addition to oral intake. Outcome was favorable in 93% with hospital discharge in 24 hours [24; 72]. Outcomes were fatal in two cases and one patient remained in chronic coma because of late care. Insulin intoxication may have had good prognosis if patients received early and adequate medical care.

ABBREVIATIONS

IP: Insulin Poisoning; GCS: Glasgow Coma Scale; LI: Long Acting Insulin; RI: Rapid Acting Insulin

INTRODUCTION

Insulin poisoning (IP) is rare. Clinical signs are various, ranging from discomfort sensation to severe neurological manifestations which may compromise vital and functional prognosis. Our study aimed to describe epidemiological profile, clinical manifestations and complications of IP.

MATERIALS AND METHODS

We carried out a three-year retrospective study since January 2012 to December 2015 in a Tunisian teaching toxicological Intensive Care Unit. All patients hospitalized for IP were included. Diagnosis of insulin intoxication was retained in patients who presented to our emergency room with clinical signs of hypoglycemia (sweat, neurological signs, digestive disorders), secondary to insulin self-injection without therapeutic indication. Hypoglycemia was defined as less than 0.5 g/L for non-diabetic patients.

We had also included patients who had history of insulin injection, clinical signs of hypoglycemia even they did not have hypoglycemia since they received carbohydrates before first

*Corresponding author

Sahar Habacha Mamlouk, Centre d'assistance médicale urgente, rue Abulkassem Al Chebbi, Tunis, Tunisia, Tel: 216 71 249 026; Email: sahar.habacha@ gmail.com

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medical exam. Coma was defined by a Glasgow Coma Scale (GCS) below 9. Data were collected and analyzed using SPSS program in its 23 versions.

RESULTS AND DISCUSSION

Forty-three patients were collected. They were 25 women and 18 men with a sex ratio of 0.72. The mean age was $31 \pm$ 13 years. Only 14 patients (32%) were diabetic. History of psychiatric disorders was present in 46% of cases. Forty-two patients injected insulin for suicidal attempt and one patient was addicted to this hormone and has been hospitalized six times for IP.

Rapid acting insulin (RI) was involved in 30% of cases and long acting insulin (LI) in 58%. IP was due to association of RI and LI in 3 patients. Route of administration was subcutaneous in all patients. The median injected dose was 120 UI [50; 302]. The median delay of signs onset was 105 minutes [15; 120] for RI and 3 hours [1; 6] for LI. The most frequent signs were: dizziness in 53.5% of cases, sweating in 42%, palpitations in 23%, loss of consciousness in 21% with coma in 10 patients, paresthesia in 18%, nausea in 14% and seizures in 11%. The median consultation delay was 4 hours [1; 48]. The median blood glucose level for patients who didn't receive carbohydrates before admission was 0.33 g/L [0.12; 0.5]. Hypokalemia was registered in 35% of cases with a mean level of 2.97 \pm 0.21 mmol/L. The

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median daily intake of carbohydrates was 175 g [90; 200] using parenteral route in addition to encouraged oral carbohydrates intake in conscious patients which represent 93% of cases. The average duration of intravenous intake was 23 ± 3.3 hours [16; 64]. Surviving and free of sequalae patients were discharged in 1 day [1; 3].

Poisoning was fatal in two cases (4.5%). Another patient remained in chronic coma. Common point between these three patients was late of medical management with a mean consultation delay of 30.7 ± 18 hours. Intentional insulin intoxication is rarely described. Most recent reported cases were isolated [1-5]. In a retrospective English study, conducted in 1994, including 56 admissions for insulin intoxication, 80% of them were long term treated with insulin [6]. The results of an old German study conducted between 1995 and 2004, showed that insulin was involved in 30.5% of intoxications with antidiabetics [7]. In 2006, the results of a French study carried out in an ICU showed that IP represent 0.01% of hospital admissions for intoxication [8]. Our series is among the fewer biggest ones which emphasize on insulin toxicodynetics by showing chronology between insulin injection and beginning of clinical signs of hypoglycemia. The median delay of appearance of clinical signs was 105 minutes [15; 120] for RI and 3 hours [1; 6] for LI. IP was moderate in the majority of cases and severe in 21% of cases with loss of consciousness. In his study, Baud showed that the capillary glycaemia in prehospital care was of $2.5 \pm 2.8 \text{ mmol/l}$ (ranging between 0 and 11), the GCS was of 10 ± 5 (ranging from 3 to 15). Initial presentation revealed agitation in 5 patients, sweating in 4 cases and seizures in 2 [8].

In the English study conducted in 1994, including 51 patients for IP, confusion, coma, or convulsions were present in 89% of cases. Generalized convulsions were described in 20% of episodes and 5% of patients suffered from transient focal neurological disturbances [6].

Hypoglycemia is the first consequence of insulin injection. Signs of hypoglycemia appear when blood glucose decreases below 0.3 g/L, including confusion, coma, "pseudo vascular" focal deficits and partial or generalized seizures [6,8]. We can also observe agitation, nervousness, anxiety, dizziness, feeling hungry, sweats, tremors, grasping, spasms, myoclonus, stiffness of decerebration [8], hemiplegia [9]. Symptoms related to sympathetic hyper-reactivity may be lacking for diabetic patients suffering from vegetative neuropathy [8]. Hypoglycemia below 0.1 g/L induced deep hypotonic coma and ample breathing [10-12]. Hypoglycemia can also be associated with tachycardia, palpitations, and even acute coronary syndrome for patients without cardiovascular risk factors and with a normal coronarography. A Coronary spasm has been involved [13,14]. Acute pulmonary oedema can be observed in IP [1,15]. Myocarditis caused by release of high doses of cathecolamines secondary to stress has been suggested as the main mechanism [15]. Deep hypoglycemia may also cause acute steatosis [16]. Prolonged or late corrected hypoglycemia can lead to irreversible neuropsychological sequelae such as alterations in cognitive functions, memory impairment, motor deficit syndromes, chronic coma or persistent vegetative states [10,11].

In our study, parenteral carbohydrates were required during

 23 ± 3.3 hours [16; 64]. Parenteral needs of carbohydrates were estimated at 175 g [90; 200], but this quantity doesn't give exact information about the total carbohydrates received dose since 93% of patients had favorably evolved in few time and were encouraged to intake carbohydrates by oral route. Unfortunately, oral intake was not quantified. After stopping parenteral intake, patients were kept under survey for 8 hours then they were discharged.

Gradwohl-Matis et al., reported life-threatening hypoglycemia for a 64-year- old woman who injected mixture of fast and longacting insulin and had been in coma for 6 days and needed continuous glucose infusion at the rate of 6–14 g/h for 3 days followed by full enteral nutrition [2]. Mork et al., reported a case of a 39-year-old male who attempted suicide, by injecting subcutaneously insulin. He had no clinical signs but he had hypoglycemia at 0.5 g/L, hypokalemia at 2.8 mmol/L. Continuous 10% dextrose infusion was needed for 58 hours [5].

Median hospital stay was of 48 to 72 hours in our study and of 2 days [1; 67] in Hart's studies [6]. Mortality was of 4.5% in our study, 7% in Hart's study [6], and 8% in Baud's study [8]. According to Behera pulmonary oedema and cardiac arythmia may be the main involved causes of death [1].

CONCLUSION

Insulin poisoning is not rare but it seems to be under estimated. It is potentially serious since it has neurological and cardiovascular consequences but its treatment is not complicated and needs only to be implemented early and appropriately with a vigilant monitoring to avoid complications threatening vital and functional prognosis.

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