

A fatal case of Metformin intoxication

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ABSTRACT

Metformin is an oral antidiabetic drug in the biguanide class. It is the first-line drug of choice for the treatment of type 2 diabetes. The most common symptoms following overdose appear to include vomiting, diarrhea, abdominal pain, tachycardia, drowsiness, and, rarely, hypoglycemia. The major potentially life-threatening complication of Metformin overdose is metabolic acidosis. We report a case of fatal Metformin toxicity following an acute intentional Metformin intoxication. Our patient 21-year-old girl who was asymptomatic when she came to Emergency department developed severe metabolic acidosis, cardiovascular compromise, hypoglycemia, and death following an acute intentional Metformin intoxication. Dysrhythmia developed later due to refractory metabolic acidosis. Severe metformin overdose could be lethal despite the patient being asymptomatic at the time of arrival. Thus the patient with severe metformin toxicity could be asymptomatic for a few hours and in the lack of any symptoms or signs of overdose he or she must be treated with early intensive sodium bicarbonate (alkalization) and hemodialysis.

KEY WORDS: Metformin, Drug Toxicity, Metabolic acidosis, Overdose.

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INTRODUCTION

Metformin is an oral antidiabetic drug in the biguanide class. It is the first-line drug of choice for the treatment of type 2 diabetes, in particular, in overweight and obese people and those with normal kidney function. Metformin can cause few adverse effects—the most common is gastrointesti-

nal upset—and is associated with a low risk of hypoglycemia. Metabolic acidosis can be a serious concern in overdose and when it is prescribed to people with contraindications. The most common symptoms following overdose appear to include vomiting, diarrhea, abdominal pain, tachycardia, drowsiness, and, rarely, hypoglycemia. The major potentially life-threatening complication of Metformin overdose is metabolic acidosis. Treatment of Metformin overdose is generally supportive, as there is no specific antidote. We report a case of fatal Metformin toxicity following an acute intentional Metformin intoxication.

CASE REPORT

Our patients was a 21-years-old female who presented to the emergency department (ED) three hours after ingestion of 100 grams of Metformin as a consequence of a family dispute. On admission, the patient was asymptomatic. In physical examination, vital signs were in normal range. First EKG, ABG, Serum electrolytes, and renal function test were at normal range. A bedside glucometer also showed a

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blood sugar level at normal range (84 mg/dl). Gastric decontamination (lavage) was done with preparation of nasogastric tube and followed by a single dose of activated charcoal (50 grams) with 70 grams of sorbitol. Five hours after ingestion she had nausea and vomiting and her blood sugar was 75 mg/dl. Seven hours after ingestion she progressively developed loss of consciousness associated with severe hemodynamic compromise, severe metabolic acidosis, and hypoglycemia (Blood sugar 30 mg/dl). At this time, she had blood pressure 65/50 mm Hg and pulse rate was 115 beats/min. Arterial blood gas (ABG) showed PH: 7.11, PaO₂: 44.3 mmHg, PCO₂: 34 mmHg, HCO₃: 12.3 mmol/l and base excess (BE): -17.4.

She was under mechanical ventilation at the intensive care unit. Initial treatment included: administration of large dose of intravenous Sodium bicarbonate (2meq/kg initial dose & repeated every 15 minutes to maximum 528 meq), 2 vials of Hypertonic dextrose 50%, 100 ml/h Dextrose water 10%, Crystalloid fluid, and Infusion of norepinephrine but she remained in hypovolemic shock state and her clinical condition deteriorated abruptly with following recurrent seizure and worsening of metabolic acidosis (ABG; PH: 6.7, PaO₂: 45 mmHg, PCO₂: 28 mmHg). Despite intensive alkalization, severe metabolic acidosis did not correct. Ultimately, she underwent emergent hemodialysis. Acidosis because of refractory hemodialysis was performed. However, her condition deteriorated promptly with ventricular bradyarrhythmias and she died 14 hours after ingestion during hemodialysis.

DISCUSSION

Metformin is an antihyperglycemic drug which has been used for treatment of NIDDM. The increasing availability of Metformin increases the risk of intentional overdose.¹ Profound and prolonged hypoglycemia could happen in metformin overdose that require iv dextrose and the use of octreotide as an antidote.² Hypoglycemia in our case was successfully treated simply by intravenous hypertonic dextrose. The onset of symptomatic hypoglycemia and acidosis after metformin intoxication may occur at variable time interval depending on amount of the ingestion.³ In our case, despite ingestion of 100 grams of metformin, she became symptomatic five hours after ingestion and her condition became critical seven hours after ingestion.

Metformin intoxication also can cause fatal metabolic acidosis especially when accompanied by coingestion or medical conditions like a renal disease that alter metformin elimination.⁴ It is not known what dose is necessary to precipitate lactic acidosis in individual with normal renal function.³

Galea et al also reported severe acidosis and rhabdomyolysis following metformin intoxication that was successfully treated with hemofiltration.⁵ Some studies have^{1,6} also showed that high-volume hemofiltration or veno-venous hemodialysis could result a good outcome in severe cases of metformin toxicity.

In our case, despite ingestion of large amount of drug and lack of any underlying disease the patient was asymptomatic and all laboratory data were at normal range for five hours after swallowing and the patient's clinical condition deteriorated promptly followed by severe refractory metabolic acidosis, hemodynamic instability that was worsening hour to hour, and finally death. This case shows that the patient with severe metformin toxicity could be asymptomatic for a few hours and lack of any symptoms or signs of overdose he or she must be treated with early intensive sodium bicarbonate (alkalization) and hemodialysis.

Abbreviations:

ED – Emergency department.

NIDDM – Non insulin dependent diabetes mellitus.

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