Kidney International (2009) **75,** 757–758; doi:10.1038/ki.2008.682

The Case | A suicidal woman with delayed high anion gap metabolic acidosis

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Table 1 | Laboratory findings on admission and 7 h later

Variable	Admission	7 h later	Normal value
BUN (mg/100 ml)	—	12.7	6–20
Creatinine (mg/100 ml)	1.01	1.87	0.5–1.5
Sodium (mmol/l)	132	151	135–145
Potassium (mmol/l)	4	2.7	3.5–5.5
Lactate (mmol/l)	—	28.8	0.5–2.2
Chloride (mmol/l)	—	105.2	98–107
pH	7.256	7.082	7.35–7.45
PaO_2 (mm Hg)	233.3	239.7	75–100
$PaCO_2$ (mm Hg)	44.9	18.2	32–42
Bicarbonate (mmol/l)	19.5	5.3	20–24
Base excess (mmol/l)	−7.6	−24.7	−3.3–2.3
SaO_2 (%)	99.7	99.4	—
Osmolarity (mOsm/kg)	321	—	280–295
Ketone bodies (mmol/l)	0.2	—	<0.6
Glucose (mg/100 ml)	391	—	70–115
Body temperature (°C)	36.5	35.7	—
Blood pressure (mm Hg)[a]	140/79	91/37	

BUN, blood urea nitrogen; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen; SaO_2, oxygen saturation.
[a]Systolic/diastolic.

A 56-year-old woman with type 2 diabetes was brought to the emergency department after having ingested an unknown number of zolpidem tablets and another unknown medication. She had been semiconscious at home for at least 1 h. On admission, her Glasgow Coma Scale was 7/15 and blood pressure was 140/79 mm Hg; her laboratory results are shown in Table 1. She was intubated because of tachypnea and agitation. Arterial blood gas analysis indicated mild metabolic acidosis (Table 1).

Severe metabolic acidosis (pH 7.0) with high anion gap (40.5) subsequently developed 7 h later, accompanied by hypotension to 91/37 mm Hg, and hypothermia to 35.7 °C.

What are the acid–base diagnoses?
What is the etiology of these disorders?

SEE NEXT PAGE FOR ANSWERS

The Diagnosis | Lactic acidosis caused by metformin overdose– and zolpidem overdose–induced acute respiratory acidosis

An intravenous inotropic agent (dopamine) was administered, and emergent hemodialysis was initiated. The patient regained consciousness and was extubated the following day. After recovering completely, our patient admitted to have ingested sixty 500-mg metformin tablets and three hundred 10-mg zolpidem tablets in a suicide attempt. We suspected an overdose of metformin because the patient presented with high anion gap metabolic acidosis and a high blood lactate concentration. An overdose of zolpidem aggravated the patient's condition by inducing respiratory failure; zolpidem is not dialyzable.[1] Signs of acute zolpidem intoxication include drowsiness, coma, and respiratory failure. No electrocardiographic or biological abnormalities can be specifically attributed to zolpidem.[1]

Lactic acidosis is known to be associated with high serum levels of metformin. The mechanism by which metformin causes lactic acidosis is not clear, but by inhibiting pyruvate carboxylase and decreasing glucose utilization, lactate production is increased in the liver. Metformin is not metabolized in the body and is largely excreted unchanged in the urine.[2] Plasma protein binding is negligible and metformin is dialyzable. Risk factors for metformin-induced lactic acidosis include renal failure, congestive heart failure, acute or chronic metabolic acidosis, intravascular iodinated contrast material use, age $\geqslant$ 80 years, hepatic disease, hypoxia, dehydration, sepsis, and excessive alcohol intake.[3]

In most reported cases of metformin overdose,[2,4–6] severe type B lactic acidosis developed within 4–9 h of metformin overdose because of the continuous tissue production of lactate resulting from the prolonged action of metformin.[5] Mortality secondary to lactic acidosis in intensive care patients is reported to be as high as 80%.[4] There is no consensus about the best treatment for metformin overdose. In some cases,[2,4–6] bicarbonate hemodialysis was more effective at clearing metformin from the body than was intravenous administration of bicarbonate. Delayed initiation of bicarbonate hemodialysis can lead to severe cardiovascular collapse and consequent type A lactic acidosis.[2,5,6] Our patient was intubated and received cardiovascular support and bicarbonate hemodialysis immediately after lactic acidosis was suspected. The patient's condition improved soon after treatment began. Thirteen hours after admission, blood pH was 7.39, $PaCO_2$ was 25 mm Hg, serum bicarbonate was 15.1 mmol/l, base deficit was 9.9 mmol/l, blood lactate was 1 mmol/l, and creatinine was 0.66 mg/100 ml. The patient was discharged uneventfully after 6 days of hospitalization.

Metformin intoxication should be suspected in patients with unexplained high anion gap metabolic acidosis and serum lactate levels should be checked. Early initiation of bicarbonate hemodialysis or hemofiltration can reduce the mortality rate in these patients.

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