Case Report

The fatal booze!—triple acid–base disorder in a patient with alcohol intoxication

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Received August 12, 2015. Accepted August 25, 2015

Abstract

Patients of chronic alcohol abuse can present with a variety of acid-base disorders and electrolyte disturbances. Lactic acidosis (LA) along with alcoholic ketoacidosis is an infrequent and underappreciated cause of wide anion-gap metabolic acidosis in alcoholic patients. The likelihood of misdiagnosing the condition is high because of the lack of awareness and presence of nonspecific clinical signs and symptoms shared with other clinical abnormalities such as acute pancreatitis, methanol or ethylene glycol poisoning, and diabetic ketoacidosis, which exist in these patients. As this condition is reversible with early intervention, promptly recognizing the condition and initiating proper treatment by the physicians would go a long way in preventing the morbidity and mortality in these patients. The outcome for such patients is excellent with early intervention. We report a patient with history of chronic alcoholism and alcohol binge admitted to the emergency department with triple acid–base disorder, which included life-threatening high anion-gap metabolic acidosis owing to concomitant LA and alcohol-related ketoacidosis in which the primary element was LA along with metabolic and respiratory alkalosis.

KEY WORDS: Anion-gap metabolic acidosis, lactic acidosis, alcohol-related ketoacidosis, alkalosis

Introduction

Alcoholism is a major issue globally. Its prevalence in India has been calculated at 30% (Benegal et al., 2000). Individuals with history of chronic alcoholism frequently have a constellation of acid–base, fluid, and electrolyte abnormalities, which play a significant role in their morbidity and mortality. In chronic alcoholism, an abrupt cessation or reduction of alcohol consumption leads to the development of alcoholic ketoacidosis (AKA), which is a poorly diagnosed medical emergency and a common cause for admission to the emergency departments. In an autopsy study of alcoholic persons, it was the cause of death in 7% of cases.[1] AKA is characterized by increased anion-gap metabolic acidosis. Less commonly described cause of high anion-gap metabolic acidosis in alcoholics is lactic acidosis. Severe lactic acidosis following only ethanol intoxication is rarely described in literature. We report a case of a chronic alcoholic patient who had primary wide anion-gap metabolic acidosis (concomitant severe lactic acidosis and ketoacidosis) caused by alcohol intoxication coupled with thiamine deficiency and concurrent respiratory and metabolic alkalosis, thus highlighting the complexity of metabolic derangements in persons with chronic alcohol abuse.

Case Report

A 30-year-old male patient, driver by occupation, unmarried was admitted in the intensive care unit (ICU) with complaints of breathing difficulty and several episodes of vomiting of 1 day duration. There was no abdominal pain, loose stools, or fever. Patient was a chronic alcoholic person for the past several years and would consume more than 100 g of indigenously made alcohol (locally called hadia) every day. He admitted to drinking large amount of alcohol during the previous 2 days but denied to ingesting any other toxic substance. During the last 48 h before admission, he had not taken food...
at all. There was no history of significant medical ailment except alcohol abuse.

On admission, he was thin built, oriented to person but not to time and place, and showed mild pallor, and his breath revealed a strong smell of alcohol. There was dehydration, no jaundice, pedal edema, clubbing, and lymphadenopathy. He was afebrile, respiratory rate was 36/min, pulse was 110/min, and regular and blood pressure in supine position was 128/84 mm Hg. Examinations of cardiovascular, respiratory system, abdomen showed normal findings. Examination of central nervous system revealed slightly confused state with normal sized pupils, reacting to light, no nystagmus, no ophthalmoplegia, no focal neurological deficit, and soft neck. His random blood sugar on admission was 54 mg/dL. His complete blood picture revealed hemoglobin 12.6 g/dL, MCV 98 fl, total leukocyte count of 11,300/mm³ with 78% neutrophils, 20% lymphocytes, and 2% monocytes, and platelet count of 1.78 lakhs/mm³. His blood urea nitrogen (BUN) and serum creatinine were 76 and 0.8 mg/dL, respectively, while liver function tests showed total serum bilirubin 12.6 g/dL, ALT 152 U/L, AST 859 U/L, ALP 92 U/L, GGT 168 U/L, serum albumin 3.2 g/dL, serum globulin 3.8 g/dL and PT (INR) 1.4. His serum sodium, potassium, and ionized calcium were 128 mmol/L, 4.3 mmol/L, and 0.6 mg/dL, respectively. His serum osmolality measured on admission was 318 mOsm/kg of H₂O. The osmolal gap in our patient was 32 mOsm/kg of H₂O. The osmolal gap is 10–15 mOsm/kg of H₂O, and serum ketones was nil, and blood alcohol level was estimated to be approximately 1% of all the hospitalized nonsurgical patients.[5] Our patient was admitted to ICU with very severe, life-threatening wide anion-gap metabolic acidosis following an alcohol binge. However, acidosis of this degree is distinctly uncommon following ethanol ingestion alone. In a study by Halperin et al.[6] of 10 alcohol-dependent patients with 13 episodes of metabolic acidosis, the average arterial pH was 7.29 and serum lactate level was 7.3 mmol/L.[6] Four other case reports of lactic acidosis in nondiabetic alcoholic patients are documented where serum lactate levels were 7, 1, 6, and 3 mmol/L, respectively.[4–7]

Thus, on the basis of the severity of patient’s metabolic acidosis, the possibility of ingestion of toxic alcohols such as methanol, ethylene glycol, isopropanol was considered. This was supported by the evidence of a high plasma osmolal gap, which is the difference between the measured plasma osmolality in the laboratory and calculated plasma osmolality. The osmolal gap is often used as a screen for toxic alcohol ingestion. The calculated plasma osmolality was 286 mOsm/kg of H₂O. The osmolal gap in our patient was 32 mOsm/kg of H₂O. The normal osmolal gap is 10–15 mOsm/kg of H₂O and increases in the presence of low molecular weight substances. An osmolal gap of >25 mOsm/kg of H₂O suggests the presence of toxic alcohol but cannot identify the type of alcohol.[9]

Review of literature has suggested that the osmolal gap can be increased in patients with ethanol-induced acidosis without the presence of other alcohols,[10] presumably owing to the presence of acetone, which is produced by ethanol metabolism and by starvation.[11–13] The contribution of ethanol to the serum osmolality can be obtained by the formula “ethanol (mg/dL)/3.7”[14] which, in the present case, was 78/3.7 = 21.08 mOsm/kg of H₂O. The recalculated serum osmolality

Discussion

Lactic acidosis is defined as large anion-gap metabolic acidosis with arterial pH less than 7.35 and lactate level greater than 5 mmol/L. In critically ill patients, it is associated with serious underlying pathologic conditions. The prevalence is estimated to be approximately 1% of all the hospitalized nonsurgical patients.[2] Our patient was admitted to ICU with very severe, life-threatening wide anion-gap metabolic acidosis following an alcohol binge. However, acidosis of this degree is distinctly uncommon following ethanol ingestion alone. In a study by Halperin et al.[5] of 10 alcohol-dependent patients with 13 episodes of metabolic acidosis, the average arterial pH was 7.29 and serum lactate level was 7.3 mmol/L.[5] Four other case reports of lactic acidosis in nondiabetic alcoholic patients are documented where serum lactate levels were 7, 1, 6, and 3 mmol/L, respectively.[4–7]

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would then be $286 + 21.1 = 307.1$ mOsm/kg of H$_2$O. Thus, the osmolal gap now would be 11.1 mOsm/kg, which is within the normal range and can be explained by ethanol consumption alone. Our patient vehemently denied intake of toxic alcohols, and, hence, his blood toxicology screen was not sent as these tests are not routinely available in our hospital.

### Table 1: Serial arterial blood gas analysis (ABG) till discharge

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0 h</th>
<th>1 h</th>
<th>2 h</th>
<th>4 h</th>
<th>8 h</th>
<th>24 h</th>
<th>48 h</th>
<th>96 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCO$_2$ (mm Hg)</td>
<td>7.0</td>
<td>10.1</td>
<td>10.4</td>
<td>13.1</td>
<td>17.7</td>
<td>29.5</td>
<td>39.8</td>
<td>42.2</td>
</tr>
<tr>
<td>PO$_2$ (mm Hg)</td>
<td>131</td>
<td>135</td>
<td>139</td>
<td>75.8</td>
<td>106</td>
<td>80.4</td>
<td>80.2</td>
<td>78.4</td>
</tr>
<tr>
<td>HCO$_3^-$ (mmol/L)</td>
<td>4.1</td>
<td>5.7</td>
<td>6.7</td>
<td>8.2</td>
<td>10.6</td>
<td>18.6</td>
<td>21.5</td>
<td>22.4</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>21</td>
<td>21</td>
<td>21</td>
<td>18</td>
<td>17</td>
<td>9.7</td>
<td>6.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Na$^+$ (mmol/L)</td>
<td>128</td>
<td>124</td>
<td>121</td>
<td>122</td>
<td>122</td>
<td>130</td>
<td>133</td>
<td>134</td>
</tr>
<tr>
<td>K$^+$ (mmol/L)</td>
<td>4.3</td>
<td>4.5</td>
<td>4.7</td>
<td>3.9</td>
<td>4.0</td>
<td>3.2</td>
<td>2.9</td>
<td>3.4</td>
</tr>
<tr>
<td>Anion gap</td>
<td>44.2</td>
<td>29.8</td>
<td>25</td>
<td>26.7</td>
<td>23.4</td>
<td>22.6</td>
<td>18.4</td>
<td>17.5</td>
</tr>
</tbody>
</table>
Our patient did not show hypotension and hypoxia (SaO₂ on ambient air was 98%), factors responsible for type A lactic acidosis. In a case reported by Hulme ad Sherwood, severe lactic acidosis of 31 mmol/L was seen in a patient with alcohol-related generalized seizures. Our patient did not experience seizures before admission. The question then arouse as to why this patient developed such severe lactic acidosis.

Ethanol is oxidized to acetaldehyde and then to acetate with the generation of two molecules of NADH: “Pyruvate, which is produced from metabolism of glucose and aminoacids, is metabolized to lactate, driven by the ratio of NADH to NAD⁺. This path is the primary mechanism of alcohol metabolism in acute alcoholic intoxication, and drives the formation of large quantities of lactate. Lactate can only be metabolized in the presence of the enzyme pyruvate dehydrogenase (PDH).” Figure 3 back to pyruvate, which then enters the gluconeogenic pathway or enters the mitochondria to be metabolized to acetyl CoA by the enzyme pyruvate dehydrogenase (PDH). Acetyl CoA then enters the Kreb’s cycle to produce CO₂, water and 38 molecules of ATP. The enzyme PDH requires cofactor thiamine pyrophosphate. Thus, in case of thiamine deficiency, lactate cannot be metabolized to pyruvate and accumulates in large amounts resulting in severe lactic acidosis. Thus, lactate production is function of both pyruvate and NADH levels. The presence of ethanol show an additive effect on lactate formation, over and above that caused owing to thiamine deficiency alone.

It is not clear why certain individuals with alcohol dependency develop severe lactic acidosis, whereas others, such as those reported by Halperin et al., develop only mild acidosis. A review of the literature of alcohol-related lactic acidosis revealed only a few case reports in which arterial pH was <7.0. The answer probably lies in thiamine deficiency, importance of which was first emphasized by Campbell. Thiamine deficiency, when present, makes a patient prone to life-threatening lactic acidosis. Our patient stayed alone and most of the times took alcohol, neglecting his diet and, therefore, was more likely to be in poor nutritional state and experience thiamine deficiency than an individual supported by family. Individuals with alcohol dependency have been found to experience multiple vitamin deficiencies, especially B vitamins. We, however, did not document his thiamine deficiency owing to the lack of this facility.

Approximately about 1,400 mmol of lactate is produced daily in the body of a 70-kg man, which is buffered by 1,400 mmol of HCO₃⁻ to sodium lactate. Under normal circumstances, liver takes up more than 60% of the lactate and converts it back to pyruvate in presence of the enzyme lactate dehydrogenase. About 10% to 20% of the lactate is removed by the kidney. Our patient showed alcohol-related liver injury as evidenced by AST>ALT ratio of >1.5 and abnormal PT (INR), which too would have contributed to lactic acidosis owing to defective lactate metabolism in the liver.

In our patient, lactate levels alone could not account for the entirety of the anion gap. His initial serum glucose level was low excluding diabetic ketoacidosis as a cause of the anion-gap metabolic acidosis. As his blood lactate level (21 mmol/L) was less than Δ anion gap (30.2 mmol/L) and there was no history of toxic alcohol intake, in the presence of high urinary ketones, following a binge alcohol drinking, the only explanation was that this patient experienced associated AKA. Thus, our patient showed combined lactic and ketoacidosis, in which the primary element was lactic acidosis.

![Figure 3: The metabolic pathways of ethanol and its role in lactate production.](image-url)
In 1940, Dillion and his colleagues first described alcoholic ketoacidosis as a distinct entity.[10] It is characterized by an increased anion-gap metabolic acidosis with high serum ketone levels. It is typically found in patients after abrupt decrease in food and alcohol intake. Patients typically present with gastrointestinal symptoms such as abdominal pain, nausea and intractable vomiting and altered mental status.

Our patient had not eaten for 48 h before admission, had been drinking heavily, and was volume depleted initially, which set an ideal milieu for the development of alcoholic ketoacidosis.

Starvation causes the hepatic glycogen stores to deplete and ketogenesis to take place in the liver, decreased insulin sensitivity and increased production of counterregulatory hormones such as glucagon, cortisol, and epinephrine. They cause enhanced lipolysis, causing the release of free fatty acids to the liver, where they are preferentially converted into keto bodies. Furthermore, prolonged vomiting causes dehydration, which in turn decreases renal perfusion and limits urinary excretion of ketoacids. In addition, volume depletion suppresses insulin release and increases concentration of counterregulatory hormones leading to viscous cycle.

In addition, there is inhibition of gluconeogenesis by alcohol, resulting in hypoglycemia. Other acid-base disorders are also commonly found in this population.

Diagnosis may pose a problem owing to difficulty in detecting the ketone body. The usual method for detection of serum ketone is the nitroprusside test. This method is very sensitive for detection of acetoacetate but not sensitive for detection of beta hydroxy butyric acid, which is the main ketone body in AKA. The increased NADH:NAD ratio resulting from ethanol metabolism accentuates the enzymatic reaction from acetoacetate to hydroxybutyrate, explaining the acidosis seen with a negative serum nitroprusside reaction and strong urinary ketone positive reaction. We, however, could not measure beta hydroxybutyrate levels as this facility was not available in our hospital.

During the first 24 h of his hospital admission, his serum bicarbonate level rose to 18 mmol/L, accompanied by a rise in the serum pH. During this period, the urine ketone level remained high but the test for serum ketones, which was initially negative, became positive. There was an apparent worsening of the serum ketone level, while other measurements suggested that the patient’s condition was improving. This could be explained by the conversion of beta hydroxybutyrate back to acetoacetate, as a predominance of NADH drove the reaction in the opposite direction during treatment. Because acetoacetate is the substance primarily measured in the nitroprusside reaction, the increasingly higher serum ketone levels do not reflect worsening of the metabolic condition but rather the conversion of the ketones to a form that is now measured by the laboratory test.

Seven episodes of severe alcoholic ketoacidosis following an alcohol binge in chronic alcohol abusers are described in literature in six nondiabetic female patients, including one pregnant lady who developed two episodes.[16] Their mean pH was 7.25 and mean anion gap 18. All were treated with dextrose normal saline and small amount of bicarbonate and they improved with treatment.

Using Winter’s formula for calculating CO₂ compensation in metabolic acidosis (PCO₂ = 1.5 × HCO₃⁻ + 8 ± 2), predicted PCO₂ ranged between 12.2 and 16.2, which is higher than CO₂ level of 7 mm Hg observed in our patient. This suggested the presence of respiratory alkalosis. At the same time, the ratio of Δ anion gap to Δ HCO₃⁻ was > 1, which suggested the presence of metabolic alkalosis caused by repeated vomiting. Thus, our patient showed “triple” acid-base disorder. It is present in about 10% of cases of AKA.[17]

**Management**

Treatment of lactic acidosis involves identification and treatment of the underlying cause. Treatment includes restoration of intravenous fluid volume, supplemental oxygen, improving cardiac output with fluids and inotropes, and management of sepsis. The use of sodium bicarbonate for the treatment of lactic acidosis is recommended but is also widely criticized. The arguments against its use are that such a therapy causes hypercapnia and exerts negative effect on intracellular pH (causing it to become more acidic paradoxically), it does not improve cardiovascular parameters, it may decrease the ionized calcium levels, and there is no improvement in the outcome of the patients treated with bicarbonate. However, such therapy may possibly “buy time” while the underlying cause of acidosis is determined and treated. Dichloroacetate, although decreased the lactate concentration, showed no beneficial effects on the outcome.

In case of severe lactic acidosis in alcohol-dependent patients, such as in this case, it is important to consider the possibility of underlying thiamine deficiency. In this situation, intravenous thiamine must be supplemented as early as possible, as it helps in the reversal of acidosis. Hemodialysis should be considered in life-threatening cases.[10] Alcohol-related ketoacidosis responds rapidly to intravenous fluids with glucose and normal saline and are indicated except in patients with cardiac failure where fluid administration requires careful monitoring and in patients with hyperglycemia where close monitoring of glucose levels is required.[10] The outcome of such patients with alcohol-related lactic acidosis is excellent with early intervention.

**Conclusion**

To conclude, our patient presented with severe, life-threatening anion-gap metabolic acidosis, probably as a result of severe lactic acidosis caused by acute alcohol binge coupled with thiamine deficiency. The anion gap was also partly contributed by AKA. Patient responded well to intravenous fluids, thiamine administration, and one bicarbonate hemodialysis and was discharged in stable condition. Prompt recognition of the abnormalities and stepwise assessment of the laboratory parameters by physician are crucial for developing an appropriate management plan for reversal of this condition.
References


How to cite this article: Kamath S, Pathak S, Yadav P. The fatal booze!—triple acid–base disorder in a patient with alcohol intoxication. Int J Med Sci Public Health 2016;5:823-828

Source of Support: Nil, Conflict of Interest: None declared.