BRIEF COMMUNICATION

Hypokalaemia in alcoholic patients

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Abstract
Hypokalaemia is commonly found among the electrolyte abnormalities observed in chronic alcoholics. However, the underlying mechanisms of the decreased potassium levels are not well known. We undertook the present study to analyse the possible pathogenetic mechanisms of hypokalaemia in a large group of alcoholic patients (n = 127) admitted to our hospital for causes related to alcohol abuse. Serum potassium levels were significantly lower in alcoholic patients compared to the control population (3.8 ± 1.1 mmol/l vs. 4.6 ± 0.9 mmol/l). In 12 of these patients inappropriate kaliuresis was observed due mainly to the co-existent hypomagnesaemia. Two of the remaining four patients had a history of diarrhoea, while the other two had alcohol withdrawal syndrome with considerable respiratory alkalosis. Patients with hypokalaemia had hypomagnesaemia and respiratory alkalosis more commonly compared to the normokalaemic ones. We conclude that hypokalaemia is a relatively common electrolyte abnormality observed in alcoholic patients owing to various pathophysiological mechanisms. Among them, inappropriate kaliuresis due to the co-existent hypomagnesaemia predominates. [Elisaf M, Liberopoulos E, Bairaktari E, Siamopoulos K. Hypokalaemia in alcoholic patients. Drug Alcohol Rev 2002;21:73–76]

Key words: alcoholism, hypokalaemia, hypomagnesaemia, inappropriate kaliuresis.

Introduction
Electrolyte abnormalities are usually observed in chronic alcoholics [1,2]. Even though magnesium and phosphorus homeostasis disturbances are encountered more commonly in these patients, hypokalaemia is also found frequently, especially in hospitalized withdrawing alcoholics and in patients with alcoholic ketoacidosis [1–4]. However, raised plasma ethanol concentrations have been reported to exert negligible effects on potassium homeostasis [5]. It is noteworthy that the underlying mechanisms of hypokalaemia in these patients are not well clarified. In the current study we attempt to analyse the possible pathophysiological mechanisms of hypokalaemia in a large group of alcoholic patients admitted to our hospital for causes related to alcohol abuse.

Material and methods
One hundred twenty-seven consecutive patients (120 male, seven female) aged 29–72 years were studied. For inclusion in the study the patients had to have had a large intake of alcohol for at least 5 years and a weekly alcohol consumption of 600 g or more for the previous 3 months. The main reasons for admission are shown in Table 1. Excluded from the study were patients with diabetes mellitus (fasting serum glucose >140 mg/dl), renal disease (defined by previous exposure to recognized nephrotoxic drugs, abnormal urine analysis, pathological proteinuria or creatinine clearance <80 ml/min), ascites, acute pancreatitis, chronic obstructive lung disease, recent bleeding from the gastrointestinal tract, septic shock, convulsions occurring 1 hour before blood sampling and patients

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taking drugs that affect acid-base status and electrolyte parameters such as diuretics and antacids, and potassium, phosphate and magnesium supplements. We also studied 150 normal individuals age- and sex-matched with the patients who abstained from alcohol or consumed only small amounts (15–90 g of ethanol per week). They derived from a pool of subjects who visited our out-patient clinic for a check-up.

On admission, physical examination was performed and venous blood was obtained for the determination of serum osmolality (Posm), glucose, urea, creatinine, total proteins, albumin, lipid parameters (total cholesterol, triglycerides), sodium, chloride, potassium, magnesium, calcium and phosphorus before any therapeutic intervention. Arterial blood was also obtained for blood gas measurements. At the same time a fresh urine specimen was tested for osmolality (Uosm), creatinine, sodium, chloride, potassium, magnesium, calcium and phosphorus.

A standard formula was used to calculate the fractional excretion of potassium (FEK\(^+\)). Transtubular potassium gradient (TTKG) was calculated from the equation:

\[
\text{TTKG} = \frac{\text{Urine potassium} \times \text{Posm}}{\text{Serum potassium} \times \text{Uosm}}
\]

TTKG has been proposed recently as a semi-quantitative index of the activity of the potassium secretory process. A value more than 2 in hypokalaemic patients is highly suggestive of inappropriate kaliuresis [6,7].

**Results**

Sixty-nine of the 127 patients (54.3\%) had at least one acid-base or electrolyte abnormality. Serum potassium levels were significantly lower in alcoholic patients compared to 150 age- and sex-matched controls (3.8 ± 1.1 mmol/l vs. 4.6 ± 0.9 mmol/l, \(p < 0.0001\)). Hypokalaemia (serum potassium < 3.5 mmol/l) was found in 16 patients (12.6\%) with a range of serum potassium between 2.2 and 3.4 mmol/l. The causes of admission of hypokalaemic patients were alcohol withdrawal syndrome in six patients, acute intoxication in two, diarrhoea in two, upper gastrointestinal symptoms in two, chronic pancreatitis in two, anaemia in one and increased liver enzymes and/or hepatomegaly in one patient. Hypokalaemia was somewhat more common in patients with alcohol withdrawal syndrome compared to the remaining alcoholic patients (\(\chi^2 = 3.67, p<0.05\)).

No patient with hypokalaemia had already completed detoxification. All hypokalaemic patients had fasting serum glucose levels within normal limits (< 126 mg/dl) and normal muscle enzymes. Furthermore, even though these patients had evidence indicative of hypokalaemia electrocardiographic changes, they did not develop cardiac arrhythmias. In 12 of these 16 patients inappropriate kaliuresis evidenced by increased FEK\(^+\) > 6.4\% and TTKG > 2 was observed [7,8]. All but one of these patients had significant hypomagnesaemia (serum magnesium < 0.6 mmol/l), while one patient had profound vomiting-induced metabolic alkalosis with an arterial pH of 7.55 and serum bicarbonate concentration of 38 mmol/l. Two of the four remaining patients had a history of diarrhoea, while the other two had alcohol withdrawal syndrome with considerable respiratory alkalosis (arterial pH 7.52 and 7.54, respectively) and symptoms/signs of increased sympathetic activity. Besides these two patients, it should be mentioned that respiratory alkalosis was also present in six more hypokalaemic patients.

Patients with hypokalaemia had more commonly hypomagnesaemia and respiratory alkalosis compared to the normokalaemic ones. Furthermore, compared with the normokalaemic patients, hypokalaemic patients had lower serum concentrations of magnesium

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<tr>
<th>Reason</th>
<th>No.</th>
<th>%</th>
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<tbody>
<tr>
<td>Alcohol withdrawal syndrome</td>
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<td>19.7</td>
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<tr>
<td>Increased serum liver enzymes and/or hepatomegaly</td>
<td>27</td>
<td>21.2</td>
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<td>Acute intoxication</td>
<td>26</td>
<td>20.5</td>
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<tr>
<td>Anaemia</td>
<td>11</td>
<td>8.7</td>
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<tr>
<td>Diarrhoea</td>
<td>7</td>
<td>5.5</td>
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<tr>
<td>Chronic alcoholic pancreatitis</td>
<td>7</td>
<td>5.5</td>
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<td>Gastrointestinal symptoms (nausea, vomiting, gastritis, dyspepsia, epigastralgia)</td>
<td>6</td>
<td>4.7</td>
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<tr>
<td>Chronic myopathy</td>
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<td>6</td>
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<td>2.4</td>
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<tr>
<td>Ataxia</td>
<td>5</td>
<td>3.9</td>
</tr>
</tbody>
</table>

**Table 1. Main reasons for admission to hospital**
and bicarbonate but higher values of blood pH, as well as of FEK$^+$ and TTKG. A very good correlation between serum magnesium and potassium levels was evident in hypokalaemic patients ($r = 0.42, p < 0.01$), unlike the absence of such a correlation in the whole group of patients. Moreover, in hypokalaemic patients an inverse correlation was found between serum magnesium levels and the indices of potassium excretion [i.e. FEK$^+$ ($r = -0.49, p < 0.001$) and TTKG ($r = -0.29, p < 0.01$)]. In these patients a weak inverse correlation was also observed between arterial pH and serum potassium levels ($r = -0.21, p = 0.056$).

**Discussion**

The most common cause of hypokalaemia in our patients was the inappropriate kaliuria mainly due to the co-existent hypomagnesaemia, which was the predominant electrolyte abnormality observed in 29.9% of the patients studied [9]. Hypomagnesaemia of any cause can lead to potassium depletion due both to urinary and faecal losses. So far, the exact tubular defects accounting for the inappropriate kaliuresis have not been determined, although enhanced secretion of aldosterone may play a contributory role. In addition, decreased cell magnesium may open potassium channels in the luminal membrane of the loop of Henle. This increase in membrane permeability may lead to potassium leakage out of the cells and increase potassium excretion [10,11].

The importance of hypomagnesaemia in the development of hypokalaemia is strengthened by the observed correlation between serum potassium and magnesium levels, as well as between serum magnesium levels and indices of potassium excretion in hypokalaemic patients. In one patient inappropriate kaliuresis was the result of metabolic alkalosis, while in two patients increased potassium losses from the gastrointestinal tract because of diarrhoea was probably the main cause of hypokalaemia.

Increased cellular uptake of potassium ions as a result of the co-existent respiratory alkalosis and of β-adrenergic stimulation in cases of alcoholic withdrawal syndrome must have led to the development of hypokalaemia in two patients and contributed to the development of the decreased potassium levels in many other patients [12,13]. It has been reported that the serum potassium concentration falls less than 0.4 mmol/l per 0.1 unit increase in extracellular pH [13]. Therefore, the degree of hypokalaemia induced by the alkalasia is relatively mild. However, stress-induced adrenaline release could promote potassium entry into cells, a response that is mediated by the β$_2$ adrenergic receptors [14]. The contribution of respiratory alkalosis in the pathogenesis of hypokalaemia is reinforced by the inverse correlation between arterial pH and serum potassium levels observed in hypokalaemic patients. Hyperinsulinaemia may have also played a role in the development of hypokalaemia in some patients, since it is known that insulin promotes the movement of potassium into cells [15] and the concentration of circulating immunoreactive insulin was found to be elevated in hospitalized alcoholics [16]. Patients with hypokalaemia more commonly had hypomagnesaemia and respiratory alkalosis compared with the normokalaemic patients, a finding which is not unexpected considering that both these disturbances, as already stated, could have played a significant role in the pathogenesis of hypokalaemia.

Hypokalaemia may be responsible for some electrocardiographic derangements in alcoholic patients and may also produce life-threatening arrhythmias, which were not noted in our cohort [17,18]. Furthermore, hypokalaemia may cause muscle weakness or frank paralysis. Thus, the deranged potassium metabolism can play a role in alcohol myopathy [19]. In fact, several cases of proximal myopathy due to hypokalaemia associated with alcoholism have been described [20,21]. The importance of early recognition of low potassium states in alcohol-dependent patients with muscle weakness has been emphasized. However, no evidence of muscle damage was found in our alcoholic patients with hypokalaemia. Hypokalaemia may lead to impaired glucose tolerance, resulting mainly from a decrease in insulin secretion [22]. Even though the fasting glucose levels of our hypokalaemic patients were within normal limits we cannot excluded this possibility completely, since we did not perform glucose loading tests or determine insulin sensitivity.

In conclusion, hypokalaemia is a relatively common electrolyte abnormality observed in alcoholic patients owing to various pathophysiological mechanisms. Among them, inappropriate kaliuresis predominates due to the co-existent hypomagnesaemia.

**References**


