Harmful effect of saline infusion in a patient with glycyrrhizic acid poisoning

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ABSTRACT

Alcohol-free licorice beverages contain glycyrrhizic acid. Excess glycyrrhizic acid is a well-known cause of excess mineralocorticoid syndrome. We report a case of glycyrrhizic acid poisoning in an abstinent alcoholic complicated by severe pulmonary edema following excessive hydration with intravenous normal saline.

Keywords: alcohol-free drink, hypokalemia, glycyrrhizic acid, licorice, potassium, saline infusion, pulmonary edema

RÉSUMÉ

Les boissons non alcoolisées à base de réglisse contiennent de l'acide glycyrrhizique. L'ingestion excessive de ce composé est une cause bien connue du syndrome d'excès apparent en minéralocorticoïde. Nous présentons un cas d'intoxication à l'acide glycyrrhizique chez un alcoolique abstinent compliqué par un œdème pulmonaire grave consécutif à une hydratation excessive par sérum physiologique administré par voie intraveineuse.

INTRODUCTION

Alcohol-free licorice beverages, which may be abused by abstinent alcoholics, contain glycyrrhizic acid.[1] Excess glycyrrhizic acid is a recognized cause of excess mineralocorticoid syndrome.[2] Herein, we report a case of glycyrrhizic acid poisoning that was complicated by severe pulmonary edema following excessive hydration with intravenous normal saline.

CASE REPORT

A 66-year-old man was admitted to the emergency department for generalized muscular weakness, myalgia and difficulty walking. His medical history included chronic alcoholism and tobacco use, and was otherwise unremarkable. He was not taking any medications. For the 2 months before his admission, he had replaced alcohol with an alcohol-free licorice beverage (Cantanis, Leclerc; glycyrrhizic acid content 0.4 g/L). He reported consuming 4 L of this beverage each day (i.e., 1.6 g/d of glycyrrhizic acid).

At admission, his blood pressure was 160/90 mm Hg. Physical examination revealed the presence of neuromuscular weakness of both arms and legs, and his reflexes were absent. Pulmonary auscultation and a pulmonary radiograph were unremarkable. There was no leg edema or hepatojugular reflux. Serum laboratory testing was remarkable for the following: sodium 145 mmol/L, potassium 1.8 mmol/L, bicarbonate 40 mmol/L, creatinine 68 µmol/L and creatine kinase 156.3 µkat/L (9361 IU/L) (normal < 2.8 µkat/L [< 170 IU/L]). An electrocardiogram demonstrated flattened T waves with U waves. The diagnosis was hypokalemic myopathy due to overconsumption of an alcohol-free drink containing a high amount of glycyrrhizic acid.

Intravenous normal saline with 4 g/L of KCl (i.e., 54 mmol/L K+) was administered at 1 L every 8 hours. Twenty hours later, the patient's blood pressure had increased to 200/100 mm Hg and he developed acute pulmonary edema, which required mechanical ventilation for 48 hours, intravenous isosorbide dinitrate and diuretics. The patient's serum electrolytes during the first 24 hours are shown in Table 1. His plasma renin was eventually reported as 16.6 pmol/L (normal 66.4–945.6 pmol/L) and aldosterone 1581 pmol/L (normal 555–4438 pmol/L).

Five days later, the patient had completely recovered.

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His neurologic symptoms had resolved and a neurologic examination was unremarkable. His blood pressure had also returned to normal. The serum creatinine levels, which had peaked at 170 µmol/L, decreased to 80 µmol/L by day 10. Echocardiography performed a few days after the acute phase revealed the presence of mild dilated myocardiopathy with an ejection fraction of 50%.

At 1-month follow-up, spironolactone and furosemide were replaced with amlodipine at 5 mg daily. Doppler ultrasonography ruled out renal arterial stenosis. An adrenal computed tomography scan and coronary angiogram were both normal.

DISCUSSION

Several licorice drinks, with and without alcohol, are sold in many countries including Canada. Brands such as Pastis and Ricard contain considerable amounts of glycyrrhizic acid. Herein, we describe a case of pseudohyperaldosteronism secondary to excessive daily ingestion of an alcohol-free licorice drink. The decreased plasma renin and normal plasma aldosterone ruled out primary aldosteronism.

Aldosterone is the most important mineralocorticoid. It regulates electrolyte excretion and intravascular volume mainly through its effects on renal distal tubules and cortical-collecting ducts, where it acts to increase sodium resorption from, and potassium excretion into, the urine. Glycyrrhizic acid inhibits 11β-hydroxysteroid dehydrogenase, which converts cortisol to its inactive metabolite, cortisone. As mineralocorticoid receptors have similar affinities for cortisol and aldosterone, this results in hypokalemia, suppressed plasma renin activity, and hypertension.[3]

Glycyrrhizic acid poisoning does not usually cause pulmonary edema. Kuwatsuru and colleagues[4] previously reported a case of acute pulmonary edema following intravenous administration of Stronger Neo-Minophagen C (glycyrrhizin) and Chlor-Trimeton (chlorpheniramine maleate) to prevent an adverse reaction to radiographic contrast. Although the patient's symptoms disappeared within a few minutes, the abnormal densities initially observed on computed tomography took a week to disappear. More severe complications have also been observed (i.e., hypertension encephalopathy,[5] rhabdomyolysis[6] and hypokalemia-induced tetraparesis[7]). Glycyrrhizic acid poisoning may also lead to cardiac complications and death.[8]

Table 1. Serum biochemistry of the patient within the first 24 hours after admission

Test	Admission	2 h	12 h	18 h	24 h
Sodium, mmol/L	145	144	147	145	146
Potassium, mmol/L	1.8	1.8	1.8	2.2	2.4
Bicarbonate, mmol/L	40	40	43	40	38
BUN, mmol/L	1.9	1.9	1.4	2.0	1.9
Creatinine, µmol/L	68	64	60	58	56

BUN = blood urea nitrogen.

In the case described here, glycyrrhizic acid may have induced sodium retention and worsened pre-existing hypertension. The excessive saline infusion, which was given as a vehicle for intravenous potassium, combined with mild dilated myocardiopathy, led to severe acute pulmonary edema.

In cases where excessive glycyrrhizic acid ingestion induces severe hypokalemia, we suggest administrating a concentrated potassium solution via a central venous catheter accompanied by very close clinical and biological monitoring ideally in an intensive care unit.

Competing interests: None declared.

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