

Three cases of paralysis secondary to hypokalemia and rhabdomyolysis caused by licorice root consumption

Meyan kökü tüketiminin neden olduğu hipokalemi ve rabdomiyolize sekonder olarak gelişen üç paralizi olgusu

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Abstract

Licorice root is a widely consumed drink in warm seasons, especially in the East of Turkey. This drink is consumed plentifully especially in the month of Ramadan. We hereby presented 3 cases with muscle weakness, hypokalemia, rhabdomyolysis and hypertension developed secondary to excessive consumption of licorice root, which resolved with potassium replacement.

Keywords: Hypokalemia, licorice root, paralysis, rhabdomyolysis.

Öz

Meyan kökü, özellikle Türkiye'nin doğusunda sıcak mevsimlerde yaygın tüketilen bir içecektir. Bu içecek özellikle ramazan aylarında bol miktarda tüketilmektedir. Bu yazıda, aşırı meyan kökü tüketimi sınırı kas güçsüzlüğü, hipokalemi, rabdomiyoliz ve hipertansiyon gelişen ve potasyum replasmanı ile klinikleri düzelen 3 olgu sunduk.

Anahtar Sözcükler: Hipokalemi, meyan kökü, paralizi, rabdomiyoliz.

Introduction

Licorice root is a widely consumed drink in warm seasons, especially in the East of Turkey. In general, the adverse effects of this drink sold by vendors with the slogan of "cure-all" are not sufficiently known by the public. The consumption of this drink is much higher, especially in the month of Ramadan, after breaking the fast for quenching the thirst. It is uncontrollably sold next to the markets on every street. We presented 3 cases with muscle weakness, hypokalemia, rhabdomyolysis and hypertension developed secondary to excessive consumption of licorice root, which resolved with potassium replacement.

Case Report

Case 1

A 61-year-old male patient presented with weakness in the extremities, more pronounced in the lower extremities. He had a history of drinking 2 liters of licorice root extract 24 hours prior to his admission.

His past medical history revealed that he had hypertension; however, he was not receiving regular treatment. On neurological examination, he had quadriparesis (the muscle power was 3/5). The physical and neurological examination findings were normal. The blood pressure was 180/100 mm/Hg. In the laboratory analysis, he had hyperglycemia (glucose: 320 mg/dL), hypopotassemia (1.8 mmol/L), and elevated creatine phosphokinase (CK) (4320 U/L) levels. Electrocardiographic changes were consistent with hypopotassemia. Electroneuromyography (ENMG) findings were within normal limits. A nephrology consultation was requested and potassium chloride (KCl) infusion, at 10 mmol/h, was started. Following the complete amelioration of quadriparesis and hypokalemia in 3 days, KCl infusion was stopped and the patient was switched to oral treatment. Potassium citrate tablet once daily was started. After one week of oral treatment, serum potassium levels returned to normal and, the oral treatment was stopped.

Case 2

A 48-year-old male patient was admitted to our clinic with muscle weakness in the extremities, more pronounced in the lower extremities. He had a history of drinking 1.5-2 L/day of licorice root extract for 10 days.

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The patient had a history of hyperthyroidism, in which he had not received treatment for over a year.

On neurological examination, he had quadriparesis (muscle power was 1/5 in the lower and 3/5 in upper extremities). The physical and the other neurological examination findings were within normal limits. The blood pressure was 170/95 mmHg. On blood analysis, he had hypopotassemia (2.06 mmol/L) and elevated CK (1296 U/L) levels. Thyroid hormone analysis revealed the following results: TSH: 0.006 IU/L (0.34-5.60 IU/L), FreeT3: 5.32 pg/mL (2.5-4.10), and FreeT4: 2.24 ng/dL (0.61-1.24). His electrocardiogram showed T wave changes consistent with hypopotassemia.

On ENMG, sensorimotor polyneuropathy with axonal degeneration was determined. Upon consultation with the physicians in the department of endocrinology and metabolism, 2 tablets of propylthiouracil twice daily was started. A nephrology consultation was requested and potassium chloride (KCl) infusion at 10 mmol/h was initiated. The patient's quadriparesis and hypokalemia were completely ameliorated in 5 days. KCl infusion was stopped and he was switched to oral treatment (potassium citrate tablet, once daily). Serum potassium levels returned to normal after one week of oral treatment and the treatment was stopped.

Case 3

A 64-year-old male patient presented with sudden onset of extremity weakness. The patient had a history of drinking 1 L/day of licorice root extract for a period of one month. The patient's medical history was significant for hypertension, however he was not on anti-hypertensive treatment. He had quadriparesis (muscle power was 4/5 in the upper and 3/5 in the lower extremities). Deep tendon reflexes were hypoactive. Other systemic and neurological examination findings were within normal limits. His blood pressure was 200/120 mm/Hg. He had hyperglycemia (glucose: 177 mg/dL), hypopotassemia (K: 2.1 mmol/L) and elevated CK (2526 U/L) levels. There were changes in the ECG, which were consistent with hypopotassemia. On ENMG, sensorimotor polyneuropathy with axonal degeneration was determined. KCl infusion (10mmol/h) was initiated. The patient's quadriparesis completely resolved in 3 days. KCL infusion was stopped and oral potassium citrate tablet (once daily) was initiated. After one week of treatment, serum potassium levels returned to normal and, the treatment was stopped.

Discussion

In the east of Turkey, licorice syrup is made by the addition of water and ice to licorice roots, and is sold in special containers carried on the back or in pouches. Furthermore, licorice roots are used as additives in pharmaceutical industry, in the production of beer, and in

herbal teas consumed in order to lose weight and cessation of smoking. Licorice-containing products are used in confectioneries, health products, chewing tobacco, chewing gums and in some alcoholic drinks (1). Licorice, the root of *Glycyrrhiza* spp., has been used since ancient Egyptian, Greek, and Roman times in the West and since the Former Han era (the 2nd-3rd century BC.) in ancient China in the East. In traditional Chinese medicine, licorice is one of the most frequently used drugs. In Japan, the oldest specimen of licorice introduced from China in the middle of the 8th century still exists in Shosoin, the Imperial Storehouse, in Nara. Extracts of licorice were recommended as a remedy for gastric ulcer by Revers of the Netherlands in 1946, which was soon withdrawn owing to its side effects. Carbenoxolon sodium, glycyrrhetic acid, hemisuccinate Na was prepared from licorice to treat peptic ulcer in the UK. In Japan for the past 60 years, a glycyrrhizin preparation under the name of Stronger Neo-Minophagen C has been used clinically as an antiallergic and antihepatitis agent (2).

Some of the causes include muscle diseases, diseases of the neuromuscular junction, and polyneuropathies. Moreover, endocrine disorders and water and electrolyte balance disorders such as hypokalemia lead to acute and subacute muscle weakness. All the three patients had hypertension, hypokalemia and elevated levels of CK. The active compound of licorice, glycyrrhizic acid, inhibits the 11-beta-hydroxysteroid dehydrogenase enzyme, which facilitates the conversion of cortisol to cortisone, hence increasing the levels of cortisol (3,4). The increased cortisol levels in turn activate the mineralocorticoid receptors, and enhance the production of mineralocorticoids. This clinical picture, which resembles primary hyperaldosteronism, leads to hypertension by causing Na retention in the body, and to hypokalemia by an increase in potassium excretion. It has been reported that hypokalemia associated with low plasma level renin activity, may lead to death as a result of metabolic alkalosis and ventricular fibrillation (4).

Licorice has been reported to lead to myonecrosis, resulting in an increase in serum CK in the studies examining the muscle biopsy samples of similar cases. It has been emphasized that myonecrosis in addition to low serum potassium levels are important in the etiology of muscle weakness associated with the use of licorice (5). Similar symptoms and findings can also be observed in genetic abnormalities such as Cushing's syndrome including ectopic ACTH secretion, congenital adrenal hyperplasia, mineralocorticoid receptor anomalies, Liddle syndrome and excessive mineralocorticoid secretion (1,6).

Other causes leading to hypopotassemia such as excessive vomiting, diuretic use, alcohol consumption or

laxative use were not present in our patients. One of our patients had hyperthyroidism. Two of our cases had high fasting blood sugar levels in their follow-up; however, their HbA1c levels were normal, and the fasting blood glucose levels returned to normal in follow-up. Axonal polyneuropathy was present in 2 of our cases, however, this did not explain acute paralysis, which resolved following potassium replacement. The presence of hyperthyroidism in one of our cases brought to mind the possibility of thyrotoxic periodic paralysis, however, the patient did not have a previous history of similar attacks of paralysis, nor was there a family history. It has been reported that the onset and severity of symptoms may be related to individual susceptibility as well as to the licorice dose and length of use (1,3). Acute and subacute muscle weakness, more pronounced in the lower extremities was observed in all our patients. Two of our cases had consumed 1-2 liters of licorice syrup daily in a time span of 2-4 weeks, whereas one of our cases had drunk 2 liters of licorice in just one evening. This suggests that the development of paralysis related to the consumption of licorice root extract may be independent of the dose and duration of consumption. In the literature, a few cases of adverse effects have been reported following a one-time ingestion of an amount ranging between 50 grams to 2

liters (7). In the treatment, first, licorice intake should be discontinued and potassium should be replaced. Spironolactone, which is a potassium-sparing diuretic, and dexamethasone, which suppresses endogenous cortisol production, must be used in the treatment (1,8). Due to the long half-life of glycyrrhizic acid, the active compound of licorice, even with potassium replacement for a sufficient time and at a sufficient dose, amelioration of the clinical picture may be prolonged from a few days to a few weeks (6). For this reason, serum potassium, CK levels and blood pressure should be monitored for a few weeks.

In the treatment of our cases, we stopped the intake of licorice, provided intravenous KCL replacement at a dose of 10 mmol/L for 3 days, and administered potassium citrate tablets for a week. In the four-week follow-up examination, we observed that neurological examination findings, blood pressures, serum potassium and CK levels of the patients returned to normal.

Although licorice consumption is widespread, little is known about the adverse effects of muscle weakness, hypertension and rhabdomyolysis. Increasing the awareness of the public on this subject, especially in the month of Ramadan will reduce the development of similar clinical pictures.

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