REVIEW ARTICLE

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Cola-induced hypokalaemia: pathophysiological mechanisms and clinical implications

Editor's Choice

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Disclosure
None.

SUMMARY

Background/Aims: The consumption of soft drinks has increased considerably during the last decades. Among them, the cola-based preparations are possibly the refreshments with the largest sales worldwide. In addition to the possible detrimental effects of moderate, chronic cola consumption, it has been proposed that the consumption of large amounts of cola-based soft drinks may result in severe hypokalaemia. **Methods:** In this review, we discuss the clinical significance of these disturbances and summarise the pathophysiological mechanism that may underlie the development of this rare, but potentially severe, side effect. **Results/Conclusion:** Several lines of evidence suggest that the chronic consumption of large amounts of cola soft drinks may adversely affect potassium homeostasis and result in potentially severe conditions such as hypokalaemic myopathy.

Review Criteria
The information we consider in this review was gathered by an extensive research of PubMed using the terms 'cola', 'hypokalaemia', 'potassium' and 'caffeine' as keywords.

Message for the Clinic
The take-home message is that the chronic consumption of large amounts of cola soft drinks may adversely affect potassium homeostasis and result in potentially severe conditions such as hypokalaemic myopathy.

Introduction

The consumption of soft drinks has increased considerably during the last decades (1,2). Among them, the cola-based preparations are possibly the refreshments with the largest sales worldwide. During the previous years, important concerns have been raised about the effects of colas on human health. In addition to the possible detrimental effects of chronic cola consumption [enamel softening (3), bone demineralisation (4), development of metabolic syndrome and diabetes mellitus (5)], several lines of evidence suggest that the chronic consumption of large amounts of cola-based soft drinks may result in severe symptomatic hypokalaemia. These observations may have important public health implications as, recently, trends of increasing the portion size of these preparations have been noticed.

Clinical aspects of cola-induced hypokalaemia

To the best of our knowledge, the first report of cola-induced hypokalaemia was on 1993 by Matsunami et al. (6). The author and his colleagues described the case of a 21-year-old pregnant woman who was admitted to the hospital because of fatigue, appetite loss and a 1-week history of recurrent vomiting. The patient had consumed more than 3 l of cola per day for the previous 6 years and she had experienced similar symptoms during her first pregnancy, 2 years previously. The laboratory evaluation revealed severe hypokalaemia (potassium levels of 1.9 mEq/l), whereas the electrocardiogram showed complete atrioventricular block. The avoidance of cola intake along with potassium replacement resulted in an uneventful recovery (6). Several years later, Appel and Myles (7) reported on another pregnant woman who presented with ascending muscular weakness and very low serum potassium levels (2 mEq/l). The patient had a 10-month history of heavy cola consumption (6–7 l per day), and a thorough laboratory investigation excluded other common causes of hypokalaemia. Again, the avoidance of cola consumption led to a rapid and uneventful recovery (7). The aforementioned reports suggest that pregnant women may be more sensitive to the hypokalaemic effects of cola. Although the pathophysiological basis of this observation is not clear, it has been proposed that the pregnancy-induced decreases in plasma protein concentrations may reduce the serum concentrations of potassium and may potentiate the toxic effects of caffeine (an ingredient of cola soft drinks) on potassium homeostasis (7).

In addition to the pregnancy-related cases of cola-induced hypokalaemia, several other reports on non-pregnant individuals emphasise the adverse effects of cola overconsumption on potassium metabolism (Table 1). The quantities of cola consumed in these

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Table 1 Main points of the cola-induced hypokalaemia case reports

References	Duration of cola consumption	Amount per day	Potassium levels on admission (mEq/l)	Suggested cause*	Outcome†
Matsunami et al. (6)	6 years	3 l	1.9	Caffeine intoxication	Uneventful recovery
Appel and Myles (7)	10 months	6–7 l	2	Caffeine intoxication	Uneventful recovery
Rice and Faunt (8)	1–2 years	8 l	1.8	Caffeine intoxication	Uneventful recovery
Mudge and Johnson (9)	3 years	4–10 l	1.4	Caffeine intoxication-osmotic diuresis	Uneventful recovery
Lee et al. (10)	1.5 month	4–9 l	2.3	Caffeine intoxication	Uneventful recovery
Packer (11)	Several years	4 l	3	Fructose-induced osmotic diarrhoea	Uneventful recovery

*Main pathophysiological mechanism of cola-induced hypokalaemia according to the authors. †Upon cola discontinuation and potassium supplementation.

case studies varied from 2 to 9 l per day, whereas the most common complaints were muscular in origin and ranged from mild weakness to profound paralysis (8–11). All studied individuals had abnormally low serum potassium concentrations that could not be attributed to other more common causes of hypokalaemia. Fortunately, all patients had a rapid and complete recovery after the discontinuation of cola ingestion and the oral or intravenous supplementation of potassium (8–11, Table 1).

Mechanisms of cola-induced hypokalaemia

• Glucose-induced hypokalaemia: cola soft drinks may contain large amounts of glucose (up to 11 g of sugar per dl in regular colas) (11). Thus, the excessive consumption of these preparations may lead to osmotic diuresis and inappropriate urinary potassium loses. In addition, the large glycaemic load may result in hyperinsulinaemia which, in turn, may lead to potassium redistribution into cells.

• Fructose-induced hypokalaemia: high-fructose corn syrup (HFCS) comprises any of a group of corn syrups that has undergone enzymatic processing to increase its fructose content, and is then mixed with pure corn syrup, becoming a HFCS (12). HFCS is used in various types of food, from soft drinks and yogurt to cookies, salad dressing and tomato soup (12). When fructose is ingested in the form of sucrose or in equimolar concentrations with glucose, a disaccharide-related transporter facilitates its absorption in the intestine. However, when fructose in ingested alone or in excess (as in the case of HFCS consumption), it is absorbed in limited quantities by a mechanism of facilitated transport (13). Therefore, large amounts of unabsorbed fructose pass into the colon where they may result in the development of osmotic diarrhoea. Indeed, previously published reports have underscored the role of HFCS in the development of chronic osmotic diarrhoea and potassium depletion (13,14).

• Caffeine-induced hypokalaemia: cola soft drinks contain sufficient amounts of caffeine ranging from 95 to 160 mg/l (15). It is well known that the consumption of moderate quantities of caffeine (180–360 mg) may result in severe hypokalaemia because of potassium redistribution into cells, increased renal excretion of potassium or a combination of these mechanisms (16). The inhibition of phosphodiesterase and the resulting elevation in the levels of intracellular cyclic adenosine monophosphate (17), along with the caffeine-induced respiratory alkalosis and β-adrenergic stimulation possibly represent the main mechanisms that underlie the shift of potassium into the cells (18). On the other hand, the caffeine-mediated increase in diuresis may underlie the renal wasting of potassium, whereas the caffeine-induced increase in renin release may also play a contributory role (17).

The individual contribution of each of the aforementioned mechanisms in the pathophysiology of cola-induced hypokalaemia has not been determined and may vary in different patients. However, as it is outlined in the table, in most of the cases described in this review, caffeine intoxication was thought to play the most important role. In support to this assumption, several other cases of hypokalaemia have

been described in individuals consuming large amounts of caffeine-containing preparations (such as tea or coffee) (19,20) that do not contain glucose of fructose. On the other hand, hypokalaemia has been described after the ingestion of excessive quantities of non-caffeinated HFCS-containing soft drinks such as 'big red' (14). In these cases, the fructose-induced osmotic diarrhoea was the predominant mechanism of hypokalaemia. Finally, patients who habitually consume large amounts of cola may also exhibit several other causes that predispose to the development of hypokalaemia such as malnutrition, recurrent vomiting and consumption of medications such as diuretics of beta adrenergic agonists.

Conclusions

Several lines of evidence suggest that the chronic consumption of large amounts of cola soft drinks may adversely affect potassium homeostasis and result in potentially severe conditions such as hypokalaemic myopathy. In an era where the food industry presses towards an increase in portion sizes of these preparations, the aforementioned observations may have important public health implications. Although cola discontinuation and potassium supplementation usually lead to an uneventful recovery in the most of the cases, the cola-induced chronic hypokalaemia clearly predisposes to the development of potentially fatal complications such as cardiac arrhythmias (21,22). In addition, chronic hypokalaemia may be a cause of increased morbidity because of fatigue, loss of productivity and muscular symptoms that vary from mild weakness to profound paralysis. Further studies are needed to justify the use of limitations in the maximum recommended daily dose of these soft drinks.

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