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CASE REPORT

Coffee-induced Hypokalaemia

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Abstract: Taking an excess amount of caffeine (e.g. overdrinking caffeinated beverages) sometimes causes hypokalaemia. Although the detailed mechanism has not been clarified yet, an increased loss of potassium via the urine stream caused by the diuretic action of caffeine is proposed as one of the possibilities. We report the case of a 50-year-old female outpatient who rapidly developed severe generalized muscle weakness and fatigue. Her symptoms were considered to be principally due to hypokalaemia. Since her blood urea nitrogen concentration decreased greatly, it was suggested that she had massive polyuria due to overhydration (i.e. dilution of her body fluids). Initially, we considered that a urinary tract infection might have caused her illness. However, we found that she was a heavy coffee drinker and had constantly experienced massive diuresis. After a course of oral antibiotics, potassium replacement and stopping coffee (caffeine) ingestion, her symptoms resolved quickly. In conclusion, it was considered that overdrinking coffee (caffeine) induced her hypokalaemia. Probably, loss of potassium via the urine stream with secondary aldosteronism was the main cause of the hypokalaemia.

Keywords: caffeine, hypokalaemia

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Introduction

It has been reported that overdrinking caffeinated beverages (e.g. Coca-Cola, tea or coffee) sometimes causes medical complications.[1–11] For instance, it is empirically known that ingestion of caffeine (especially in large amounts) can induce hypokalaemia.[1,2,4–6,11] Although the detailed mechanism has not been clarified yet, losing potassium (K^+) via the urine stream due to the diuretic action of caffeine is proposed as one of the possibilities.[1,9,11]

Here the author reports a clinical case where heavy coffee drinking induced polyuria, secondary aldosteronism and then hypokalaemia.

Case Presentation

A 50-year-old female outpatient (height 150 cm, weight 44 kg) without significant past history was admitted in our hospital due to severe generalized muscle weakness and fatigue with high fever (38.7 °C). She could not walk by herself, and both her grips were less than 10 kg. Her blood pressure was normal (133/78 mmHg; pulse 70 beats/min, regular) and no other apparent abnormality was found on her physical examination. She took no medications (including herbal medicines such as liquorice or laxatives) and no abnormality had been noted during her annual health checks: i.e. her renal and endocrinal functions were normal, and she was not diabetic. In addition, she had no liver disease and she was not a strict vegetarian. Her daily food was well-balanced and its intake was normal.

Her clinical onset was relatively rapid: i.e. she was quite normal around three days prior to presentation. Firstly, she suffered progressive generalized muscle weakness and fatigue, and then her body temperature elevated. At last, her muscle weakness became intolerable, and nausea with slight vomiting occurred (but no diarrhoea). Table 1 shows her laboratory examination data demonstrating (1) considerable hypokalaemia with increased serum aldosterone, (2) low blood urea nitrogen (BUN), (3) increased serum C-reactive protein (CRP) and white blood cell (WBC) count, and (4) positive bacteria and WBC with low specific gravity in the urinalysis. However, we could not comprehensively interpret these data at that time.

Soon afterwards, careful checking of her anamnesis alerted us that she is a heavy coffee drinker and had already experienced massive diuresis with nocturia. She said that she usually takes >10 cups/day of strong coffee (without sugar) and haunts the lavatory day and night. Using the analytical contents of coffee,[3] her caffeine ingestion was estimated to be around >1200 mg/day, and her daily urine excretion volume was >3000 ml/day. After the onset of her symptoms, she seemed to take coffee more than usual as a "remedy" for her illness (but this made the matter rather worse). Her blood caffeine concentration was 12.3 mg/l (around 10–12 h after truncation of coffee ingestion), suggesting that she had surely overtaken coffee. Since her serum aldosterone level was relatively high (Table 1), it was possible that she had suffered a mild aldosteronism.

From these findings, the author considered that caffeine ingestion caused massive diuresis, the secondary aldosteronism and finally hypokalaemia. After administration of an oral antibiotic (levofloxacin 200 mg/day *bid* for one week), K^+ replacement (KCl 1.8 g/day *tid* for one week) and stopping caffeine ingestion, her symptoms resolved quickly (within three days).

Discussion

Initially, the author considered that bacterial infection had occurred within her urinary tract (cystitis and/or pyelonephritis). However, the lowered BUN level (<5 mg/dl) and hypokalaemia (2.9 mEq/l) were quite unexplainable at that time. Since K^+ replacement very quickly resolved her illness, hypokalaemia was very probably the main cause of her muscle weakness and fatigue, but the origin of this abnormality in the serum electrolyte was unknown. One clue was the low specific gravity of her urine, suggesting that her body fluids may have become diluted (i.e. urea was washed out from her body). Generally, a decreased BUN is caused by (1) a low protein diet, (2) severe liver damage, (3) increased anabolism or (4) massive diuresis (washing out from the body).[12] In this case, (4) was considered to be most likely, since other possibilities did not correspond with her clinical situation.

It is well known that urea is the final metabolite of protein and amino acids. However, this is not a simple waste, since the kidneys actively use urea for maintaining the concentration of urine.[13] For example, the kidneys cannot excrete concentrated urine if urea is washed out from the kidney medulla. Polyuria due to overhydration sometimes causes this kind of disorder, and the resultant loss of concentrative power of the

Table 1. Laboratory data of the patient.

Item (Biochemistry)	Reference	Patient	Item (Haematology)	Reference	Patient
Total protein	6.7–8.3 g/dl	7.7	White blood cell	4000–8000/10^{-6} l	13900
Serum albumin	4–5 g/dl	4.3	Red blood cell	350–500/10^{-10} l	398
Blood urea nitrogen	6–20 mg/dl	<5	Haematocrit	35–45%	34.9
Creatinine	0.47–0.79 mg/dl	0.5	Haemoglobin	12–15 g/d l	12.1
Total bilirubin	0.2–1 mg/dl	0.7	Platelet	13–37/10^{-10} l	20.2
Aspartate-aminotransferase	10–40 IU/l	44			
Alanine-aminotransferase	5–40 IU/l	38	**Item (Urology)**	**Reference**	**Patient**
Alkaline phosphatase	115–359 IU/l	235	Specific gravity	1.008–1.030	1.010
Lactate dehydrogenase	115–245 IU/l	217	pH	5–7.4	5.5
γ-glutamyl transpeptidase	0–30 IU/l	43	Protein	–	+
Choline esterase	200–459 IU/l	217	Sugar	–	–
Sodium (Na^+)	136–147 mEq/l	137	Ketones	–	–
Potassium (K^+)	3.6–5 mEq/l	2.9	Haematuria	–	+
Chloride (Cl^-)	98–109 mEq/l	101	Urobilinogen	±	±
Calcium (Ca^{2+})	8.7–10.1 mg/dl	8.6	Segments		
Inorganic phosphate	2.4–4.3 mg/dl	2.5	White blood cell	1–4/LPF[c]	1–4/HPF[d]
C-reactive protein	0–0.3 mg/dl	27.5	Red blood cell	1–4/LPF[c]	1–4/HPF[d]
Glucose	70–109 mg/dl	105	Epitherium	–	5–9/HPF[d]
Serum lactate	3–17 mg/dl	11.6	Bacteria	–	2+
Serum aldosterone	39–109 pg/ml[a]	163[a]	Crystals	–	–
Serum caffeine[b]	8–20 mg/l[b]	12.3			

[a]Measured at supine resting posture; the reference value shown here is determined by measuring serum aldosterone in healthy adults at the same posture.
[b]The reference value shown here is for the therapeutic range of caffeine.
[c]LPF: low power field (100x).
[d]HPF: high power field (400x).

kidneys will result in further diuresis (i.e. a vicious cycle will begin).

Before we noticed that she ingested a relatively large amount of caffeine, the author considered that a urinary tract infection might have caused such massive diuresis. Considering the result of her urinalysis, it was possible that she might have had pyelonephritis, which is well known to cause increased urine volume due to loss of the concentrative power of the kidneys. However, her clinical response to oral antibiotics was relatively quick, and therefore, it was difficult to consider that she had very serious pyelonephritis. In addition, her polyuria was obvious before her symptoms became evident. Therefore, we needed to find another cause for her polyuria, but there was still a possibility that the urinary tract infection was related to her illness in some way (as described below). Later, it was found that overdrinking of coffee induced diuresis, and therefore, the author came to think that her symptoms were a side effect of caffeine. Probably, massive diuresis caused by a large amount of caffeine ingestion (in coffee) induced the secondary aldosteronism and hypokalaemia.

When caffeine is used as therapeutically, the optimal blood concentration is suggested to be around 8–20 mg/l, and the maximal concentration in blood is <10 mg/l (typically 5–6 mg/l) after taking a single cup of coffee (containing *c.a.* 100 mg caffeine) in healthy adults (personal communication from coffee/caffeine manufacturers). Our patient's serum caffeine concentration of 12.3 mg/l indicates that she is certainly a heavy coffee drinker, but this level was still

within a therapeutic range (it had not reached a toxic level). However, she seemed to take coffee more than usual after the onset of her symptoms. In addition, she stopped drinking coffee at least 10–12 h before admittance to our hospital with her illness. Therefore, her real caffeine level at the onset of her symptoms was probably much higher than measured. Since the typical half life of plasma caffeine concentration is reported to be around 5–10 h,[9,10] her maximal plasma caffeine concentration was roughly estimated to be 20–40 mg/l. This seems to be enough to provoke the adverse effects of caffeine. Another possibility was that a urinary tract infection simultaneously occurring by chance might have potentiated the pharmacological activities of caffeine: i.e. the adverse effects of caffeine related to the diuretic action were induced at a lower plasma concentration than usual. In conclusion, we considered that caffeine ingestion in an excess amount was the principal cause of her symptoms.

A huge amount of caffeine is consumed worldwide, and this is the one of the chemical compounds that we most commonly ingest orally. However, in spite of its great popularity, few are aware of its toxicity, i.e. overdrinking caffeinated beverages (such as Coca-Cola, tea and coffee) sometimes causes medical complications. In the literature, 500–600 mg/day of caffeine ingestion was reported to be enough to provoke clinical symptoms (e.g. anxiety, mental stress, headaches and appetite loss).[3]

It is empirically known that taking an excess amount of caffeine sometimes causes hypokalaemia.[1,2,4–6,11] Although the detailed mechanism has not been clarified yet, the following mechanisms have been proposed as one of the possibilities:

a. Caffeine induces release of catecholamine, and thus increased plasma catecholamines activate membrane Na-K ATPase activity (via the adrenergic β_2 receptor). This will cause a transient shift of K^+ from plasma to the intracellular fluid (ICF), resulting in hypokalaemia.[7]
b. Caffeine inhibits the activity of phosphodiesterase. Intracellular cAMP level is then increased enough to activate Na-K ATPase. This will also cause a transient shift of K^+ into ICF.[7,8]
c. Caffeine induces diuresis[9] and thus causes increased excretion of K^+ into urine.[1,11] This is a net loss of K^+ from the body.[14] The mechanism of caffeine-induced diuresis is unknown, but an increased glomerular filtration ratio due to elevated cardiac output is likely.[9] Some investigators reported a direct action to renal tubules was possible as a mechanism of action.[15]
d. Caffeine activates the respiratory centre of the brain. This causes hyperventilation, and the resultant respiratory alkalosis induces hypokalaemia.[10]
e. Sugar contained in a beverage may stimulate insulin release, which will cause a transient shift of K^+ into ICF.[7,8] However, sugar-free beverage can induce hypokalaemia as well as sugar-containing one.[2]
f. Sugar in a large amount may induce massive diarrhoea, which will cause a net loss of K^+ from body fluids.[16]

Since our patient's urinary pH was slightly acidic and she had not consumed sugar-containing beverages, (d), (e), and (f) are unsuitable to explain her illness. In the literature, mechanisms (a) and (b) are considered most likely, but they cause only a transient shift of K^+ in the body fluid, i.e. such apparent hypokalaemia will be resolved as time passes. Although (a) and (b) were still possible causes of our patient's illness and we had no evidence to rule out these mechanisms, her laboratory data indicated that:

i. Her plasma sodium (Na^+) and calcium (Ca^{2+}) levels were at the lowest normal range, and her BUN was much decreased. These findings indicated that her body fluids had become diluted (solvents had been washed from the body into the urine).[12]
ii. The low specific gravity of her urine also suggested that her body fluids were diluted.[12]
iii. The increased plasma aldosterone level was probably due to the body's attempt to compensate possible hyponatremia (caused by the plasma dilution as mentioned in (i)). Therefore, K^+ loss into urine was further facilitated to cause symptomatic hypokalaemia by the secondary aldosteronism.
iv. It is known that hypokalaemia itself is a cause of reduced concentrative power of the kidneys (known as hypokalaemic nephropathy).[17] Therefore, a vicious circle will begin when once polyuria induces significant loss of K^+ into the urine (i.e. further diuresis occurs).
v. Renal tubular acidosis and its related diseases (e.g. Sjögren's syndrome) were ruled out by her annual

health checks. Her normal glucose and lactate levels suggest that she did not suffer from metabolic acidosis/disturbance.

From these findings, the author considered (c) as the most likely cause of her hypokalaemia. However, many investigators have suggested different mechanisms, as mentioned above, and therefore, caffeine-induced hypokalaemia may be probably a syndrome of multifactorial disorders.

Conclusion

Caffeine sometimes induces hypokalaemia. The mechanism has not been clarified yet, but aldosteronism due to diuresis was considered as one of the possible mechanisms. Physicians should pay attention to patients' drinking habits when their symptoms are unexplainable.

Disclosures

This manuscript has been read and approved by the author. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The author reports no conflicts of interest.

References

1. Rice JE, Faunt JD. Excessive cola consumption as a cause of hypokalaemic myopathy. *Intern Med J*. 2001;31:317–8.
2. Aizaki T, Osaka M, Hara H, et al. Hypokalemia with syncope caused by habitual drinking of oolong tea. *Intern Med*. 1999;38:252–6.
3. Abbott PJ. Caffeine: a toxicological overview. *Med J Aust*. 1986; 145:518–21.
4. Appel CC, Myles TD. Caffeine-induced hypokalemic paralysis in pregnancy. *Obstet Gynecol*. 2001;97:805–7.
5. Trewby PN, Rutter MD, Earl UM, Sattar MA. Teapot myositis. *Lancet*. 1998;351:1248.
6. Matsunami K, Imai A, Tamaya T. Hypokalemia in a pregnant woman with long-term heavy cola consumption. *Int J Gynecol Obstet*. 1994;44:283–4.
7. Bradberry SM, Vale JA. Disturbances of potassium homeostasis in poisoning. *J Toxicol Clin Toxicol*. 1995;33:295–310.
8. Gennari FJ. Hypokalemia. *N Engl J Med*. 1998;339:451–8.
9. Arnaud MJ. The pharmacology of caffeine. *Prog Drug Res*. 1987; 31:273–313.
10. Benowitz NL. Clinical pharmacology of caffeine. *Ann Rev Med*. 1990; 41:277–88.
11. Lee HJ, Kim DW, Cho HS, et al. Hypokalaemic paralysis induced by large amounts of cola consumption. *Nephrol Dial Transplant*. 2007;22:2729.
12. Wallach J. Interpretation of Diagnostic Tests. 6th ed., Little Brown, Boston, 1996.
13. Kurbel S, Dodig K, Radic R. The osmotic gradient in kidney medulla: a retold story. *Adv Physiol Educ*. 2002;26:278–81.
14. Neuhäuser-Berthold M, Beine S, Verwied SC, Lührmann PM. Coffee consumption and total body water homeostasis as measured by fluid balance and bioelectrical impedance analysis. *Ann Nutr Metab*. 1997;41:29–36.
15. Rieg T, Steigele H, Schnermann J, Richter K, Osswald H, Vallon V. Requirement of intact adenosine A_1 receptors for the diuretic and natriuretic action of the methylxanthines theophylline and caffeine. *J Parmacol Exp Ther*. 2005;313:403–9.
16. Packer CD. Chronic hypokalemia due to excessive cola consumption: a case report. *Cases J*. 2008;1:32(1–3).
17. Bock KD, Cremer W, Werner U. Chronic hypokalemic nephropathy: a clinical study. *Klin Wochenschr*. 1978;56(Suppl 1):91–6.