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Case Report

Use of Over-the-Counter Calcium Carbonate: Excess can be Harmful

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Abstract

Calcium carbonate, available over the counter, is commonly used by patients. Its excessive use has led to resurgence of milk-alkali syndrome (MAS). Clinical features of MAS are non-specific and can easily be missed. Undetected MAS can result in progressive renal impairment, which can even be permanent. Therefore, it is important to obtain detailed information about the use of medications including over-the-counter medications. Here, we present a case of a 61-year-old man who developed acute renal failure on top of chronic kidney disease as a result of the delayed diagnosis of MAS.

Keywords: Milk alkali syndrome; Calcium carbonate; Renal failure

Introduction

Calcium carbonate, available over the counter (OTC), is commonly used by patients for heartburn and dyspepsia. Furthermore, it is also prescribed for other conditions including prophylaxis and treatment of osteoporosis and phosphate binding in chronic kidney disease (CKD). Excessive use of calcium carbonate has led to an increase in the incidence of milk-alkali syndrome (MAS) and its associated complications [1,2]. Here, we report a case of milk alkali syndrome related to the excessive use of OTC calcium carbonate. The diagnosis was not made until after two months of symptoms when the patient had already developed significant renal impairment.

Case Presentation

A 61-year-old man presented with a 2-month history of increased thirst and urination and 1-week history of worsening weakness and lethargy. His past medical history was significant for hypertension, emphysema, CKD stage III secondary to focal segmental glomerulosclerosis, dyslipidemia, benign prostatic hyperplasia, anxiety, hiatal hernia and gastroesophageal reflux disease. His medications included amlodipine, telmisartan, fenofibrate, dutasteride, doxazosin, clonidine, alprazolam, and famotidine. However, he confessed non-compliance to all his medications. He denied smoking, drinking alcohol and use of illicit drugs.

On physical examination, he had heart rate of 58 beats per minute, blood pressure of 207/119 mmHg, respiratory rate of 17 per minute and temperature of 37^{O}C. Oral mucosa was dry and tongue was coated. The patient did not have any pallor, icterus, cyanosis or edema. Cardiac examination did not reveal any murmur, rubs or gallops. Chest auscultation was clear bilaterally. The remainder of the physical examination was unremarkable.

Laboratory tests revealed sodium of 137 mmol/l, potassium of 4 mmol/l, blood urea nitrogen (BUN) of 25 mg/dl, creatinine of 4.47 mg/dl, chloride of 99 mmol/l, bicarbonate of 40 mmol/l, corrected serum calcium of 12.4 mg/dl, inorganic phosphorus of 4.6 mg/dL and intact parathyroid hormone level of 4.0 pg/ml. His baseline renal function tests included: creatinine of 1.65 mg/dl, BUN of 19 mg/dl and corrected serum calcium of 9.6 mg/dl. His complete blood count, glucose, and liver function tests were within normal limits. Urine analysis was unremarkable except for protein of 30 mg/dl. Renal ultrasound was unremarkable. EKG showed sinus bradycardia with heart rate of 58 beats per minute and left ventricular hypertrophy. Serum protein electrophoresis was normal.

At this point, patient was interviewed again; direct questioning revealed excessive use of over-the-counter calcium carbonate since several months for heartburn. The patient was admitted with the diagnosis of milk-alkali syndrome secondary to calcium carbonate ingestion with acute renal failure on top of CKD and hypertensive urgency. The patient was started on intravenous saline infusion. Telmisartan and calcium carbonate were held. Clonidine was administered and the remainder of his medications was continued.

A few hours after the initiation of the above therapy, his blood pressure decreased to 180/90 mmHg. The patient started having a urine output of about 100 ml/hr. Next day, his laboratory tests showed corrected serum calcium of 11.3 mg/dl, BUN of 32 mg/dl, creatinine of 4.46 mg/dl, and bicarbonate of 31mmol/l. The patient was continued on intravenous saline infusion, and subsequently, telmisartan was restarted. On the sixth day of admission, bicarbonate and calcium normalized, whereas BUN and creatinine improved to 28 mg/dl, and 3.2 mg/dl respectively. His clinical symptoms improved and he was discharged home and was instructed to avoid excess use of calcium carbonate. A follow-up at 2 months showed further improvement of renal function tests with BUN of 23 mg/dl, and creatinine of 1.88 mg/dl.

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Discussion

MAS, previously commonly seen with consumption of milk and antacid, almost disappeared after the development of non-absorbable alkali, proton pump inhibitors and histamine-2 blockers [3]. However, excessive use of calcium carbonate has revived the problem making it the third leading cause of hypocalcaemia only after primary hyperparathyroidism and malignancy [1,2]. This has been referred to as calcium alkali syndrome by some of the authors [4]. Studies have shown that the incidence of MAS varies between 8 to 38% [1,2]. Use of less than 2 gram calcium carbonate in a day is generally considered safe but there are reports of MAS occurring with ingestion of 1 to 1.5 grams/day [2,5].

MAS encompass the triad of hypocalcaemia, metabolic alkalosis, and renal insufficiency. It can also cause metastatic calcification, pancreatitis and cardiac arrhythmia [6-8]. Classically, MAS is described to have 3 spectrums, which differ primarily in terms of duration of antacid use and resolution of renal failure with treatment. Acute syndrome can occur as early as one week of use but also resolves quickly with therapy. Sub acute syndrome, seen after prolonged but intermittent use, can lead to permanent renal function impairment [9]. Chronic syndrome is described with long and excessive use and consists of chronic hypocalcaemia, metastatic calcifications, band keratopathy and nephrocalcinosis. Hypocalcaemia improves slowly but there is usually minimal or no improvement in renal function [10].

Increased gastrointestinal absorption of calcium is the likely mechanism leading to hypocalcaemia in patients with MAS [11,12]. Hypocalcaemia causes dehydration and renal vasoconstriction leading to renal impairment. It also causes reduction in PTH production, which results in increased reabsorption of bicarbonate from proximal tubules. Alkalosis, in turn, enhances calcium reabsorption in the distal tubules [11]. CKD patients are at increased risk because of increased use of calcium in this patient population [1,2]. Additionally, a decline in glomerular filtration rate in CKD patients may increase the risk of MAS through a reduction of calcium filtration [13]. Development of MAS in CKD patients can lead to further decline in their renal function, as illustrated by this case.

Symptoms of MAS are non-specific and include nausea, vomiting, constipation, increased urinary frequency, fatigue, confusion, depression and palpitation. Furthermore, patients may be asymptomatic, thus delaying the presentation, as in this patient. The history of ingestion of calcium compounds provides useful clue to the diagnosis of MAS. Therefore, it is important to obtain detailed information about the use of medications including OTC medications as well as betel nut chewing; the later has also been shown to cause the syndrome [14,15]. Measurement of parathyroid hormone level helps to exclude hyperparathyroidism.

Prompt diagnosis and treatment determines outcome; delay can result in permanent renal impairment [9]. The use of calcium carbonate should be discontinued immediately. Volume repletion with intravenous fluids (e.g. 2 to 4 liter of normal saline daily) enhances filtration and excretion of calcium and is a crucial step in management. Once patient is adequately rehydrated, furosemide may be added, which further inhibit calcium reabsorption [2,16]. However, high volume diuresis, as a result of the use of normal saline and furosemide, can cause hypokalemia and Hypomagnesemia and requires monitoring. Bisphosphonates or calcitonin can also be used in certain cases. However, bisphosphonates have been shown to predispose to hypocalcaemia, which at times can be severe. Therefore, the use of bisphosphonates should be limited to refractory cases. Severe cases of MAS may need hemodialysis [2,12,16].

Conclusion

Excessive use of calcium carbonate can cause milk-alkali syndrome with its associated complications. This mandates careful use of calcium carbonate and public education regarding strict adherence to use as directed only. CKD patients are at increased risk because of increased use of calcium in this patient population. Delay in diagnosis can lead to renal impairment, which can be irreversible. High index of suspicion and careful history of prescribed as well as over-the-counter medication use can help establish the diagnosis.

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