Bowel Cleansing with Oral Sodium Phosphate is a Risk Factor for Nephropathy in Acromegaly

Akromegalide Oral Sodyum Fosfatla Bağırsak Temizliği, Nefropati İçin Risk Faktörüdür

Serpil Salman, Rıza Ataş, Refik Tanakol, Harika Boztepe, Sema Yarman, Faruk Alagöl

Istanbul University Istanbul Faculty of Medicine, Department of Endocrinology and Metabolic Diseases, Istanbul, Turkey

Abstract

Because of increased risk of colorectal carcinoma, screening by colonoscopy is recommended in patients with acromegaly. Cleansing should be vigorous in these patients due to increased bowel length and delayed colonic transit time. Recently, cases of phosphate nephropathy associated with a widely preferred purgative oral sodium phosphate (OSP) have been reported. Although main risk factors for phosphate nephropathy have been described, acromegaly has not been included as a risk factor. The present case is a 63-year old male patient, who developed transient renal failure after using three doses of OSP, which increased the serum phosphate level by 8.1 mg/dL. An acromegalic patient may have many risk factors for phosphate nephropathy after OSP administration, including having high basal serum phosphate levels, increased bowel transit time, need for high purgative dosages, increased tubular phosphate reabsorption, advanced age, and concurrent administration of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and nonsteroidal anti-inflammatory drugs (NSAIDs). Physicians should be warned against the risks of using OSP in acromegalic patients, and intensive follow-up is necessary in the hospital setting soon after OSP administration. Therefore, we suggest that acromegaly should be included as a risk factor for nephropathy due to OSP in the current guidelines. *Turk Jem 2008; 12: 104-6*

Key words: Acromegaly, bowel cleansing, renal failure,hyperphosphatemia

Özet

Akromegalisi olan hastalarda artmış kolorektal karsinom riskinden ötürü kolonoskopi ile tarama yapılması önerilmektedir. Bu hastalarda bağırsak uzunluğunun artması ve kolon transit zamanının uzaması nedeni ile barsak temizliğinin etkin olması gereklidir. Son yıllarda, oldukça sık kullanılan bir purgatif olan oral sodyum fosfat (OSP) kullanımına bağlı olarak fosfat nefropatisi gelişen vakalar bildirilmektedir. Fosfat nefropatisi için genel risk faktörleri tanımlanmış olmakla birlikte, akromegali bu risk faktörleri arasında bulunmamaktadır. Sunduğumuz 63 yaşındaki erkek hastada üç doz OSP kullanımından sonra serum fosfat düzeyinin bazale göre 8.1 mg/dl yükselmesinin ardından gelip geçici böbrek yetersizliği gelişmiştir. Akromegalik bir hastada OSP alımından sonra fosfat nefropatisi gelişmesi için yüksek bazal serum fosfor düzeyleri, uzamış barsak transit zamanı, yüksek doz purgatif ihtiyacı, artmış tubuler fosfat reabsorbsiyonu, ileri yaş, ve anjiyotensin konverting enzim (ACE) inhibitörü, anjiyotensin reseptör blokeri (ARB) ve nonsteroid antineflamatuvar (NSAI) ilaç kullanımı gibi çok sayıda risk faktörü bulunabilir. Hekimler, akromegalisi olan hastalarda OSP kullanımı konusunda dikkatli olmalı ve OSP kullanılması durumunda hastayı yatırarak yakın izlem yapmalıdırlar. Biz, klavuzlarda OSP kullanımına bağlı fosfat nefropatisi için risk faktörleri arasına akromegalinin alınmasını önermekteyiz. *Turk Jem 2008; 12:104-6*

Anahtar kelimeler: Akromegali, bağırsak temizliği, böbrek yetmezliği, hiperfosfatemi

Introduction

Screening by colonoscopy is strongly recommended in patients with acromegaly, because of their high risk for developing colorectal carcinoma due to elevated growth hormone levels (1). Because of increased bowel length and colonic transit time, preparing for a colonoscopy can be more difficult in acromegalic patients than in non-acromegalic patients. Beyond personal experience, there are no data regarding how these patients should be prepared for colonoscopy. The ideal agent for colonoscopy preparation should

Address for Correspondence: Serpil Salman, MD, Istanbul Universitesi, Istanbul Tıp Fakultesi, İç Hastalıkları Anabilim Dalı, Endokrinoloji ve Metabolizma Hastalıkları Bilim Dalı, Millet Cad. 34390, İstanbul-Turkey Phone.: +90 212 533 53 06 Fax: +90 212 635 88 76 E-mail: salmanserpil@yahoo.com **Recevied:** 24.04.2008 **Accepted:**

be effective, safe, easily-administered, inexpensive and well tolerated by the patient. Polyethylene glycol (PEG) and oral sodium phosphate (OSP) solutions are the two most widely-used purgative agents. Although PEG provides safe and effective bowel cleansing, poor compliance often results due to the salty taste, smell from the sulfates and large volume (3-4 L) of fluids to be ingested. OSP is another powerful osmotic laxative, requiring ingestion of relatively small volumes of fluids and thus providing an attractive alternative for colonic cleansing. Recent publications have pointed out that OSP should be used with caution in certain patients because of the risk of phosphate retention and nephrotoxicity (2).
This report presents a patient with acromegaly, who suffered from transient renal failure following OSP administration.

Case Report

A 63-year old male was admitted to the hospital with clinical features of acromegaly, gradually developing within the last six years. His past history was uneventful in terms of other chronic diseases, including diabetes mellitus and chronic kidney disease except mild hypertension controlled with amlodipine (5 mg daily). Blood pressure (130/80 mmHg) and pulse rate (80/min) were normal. Results from routine biochemical tests upon admission were as follows: fasting glucose 105 mg/dL, blood urea nitrogen (BUN) 14 mg/dL, creatinine 1.0 mg/dL, sodium 144 mEq/L, potassium 4.0 mEq/L, chloride 103 mEq/L, calcium 9.2 mg/dL, phosphate 4.5 mg/dL, and parathyroid hormone (PTH) 29 pg/mL. The levels of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) were 35.6 ng/mL and 931 ng/mL, respectively (IGF-1 reference range for 61-65 years: 75-212 ng/mL).
The patient was hospitalized for further investigation of acromegaly. GH failed to suppress below 40 ng/mL during an oral glucose tolerance test. Magnetic resonance imaging (MRI) of the pituitary showed a macroadenoma. The patient underwent a colonoscopy after bowel preparation with OSP solution. A relatively high dose of OSP was used (3 doses each of 45 mL compared to the standard 2 doses of 45 mL). Specifically, liquid OSP was administered at 12:00 P.M. and 6:00 P.M on the day before the procedure and at 5:00 A.M on procedure day. The patient did not have any episodes of nausea or vomiting.
The colonoscopic evaluation showed dolicocolon, and a polypoid lesion in the caecal area which actually proved to be a hyperplastic polyp after histopathological examination was performed on the excised lesion. Results of routine laboratory tests on the day following the colonoscopy were as follows: BUN 22 mg/dL, creatinine 1.2 mg/dL, sodium 144 mEq/L, potassium 3.6 mEq/L, chloride 101 mEq/L, calcium 8.7 mg/dL, phosphate 12.6 mg/dL. Because of increasing phosphate and creatinine concentrations, hydration was maintained by saline infusions of 3 L/day. Serum phosphate levels rapidly decreased to 4.6 mg/dL within 48 hours after the procedure. Subsequent investigations revealed that serum creatinine levels gradually increased up to 1.6 mg/dL until the ninth day after the OSP administration, while serum phosphate and calcium levels remained within the normal range. No pathological findings were detected in renal and abdominal evaluations by ultrasonography. Glomerular filtration rate (GFR) was measured and found to be 160 mL/min. Urinalysis was normal without proteinuria. On the third month of the follow-up, serum creatinine regressed to 1.3 mg/dL.

Discussion

There are some reports in the literature about clinical cases with severe morbidity, or even mortality, related to renal complications after use of OSP. Patients who have renal disease, impaired renal function, dehydration and uncorrected electrolyte abnormalities should not be allowed to use these purgatives (2). It is suggested to give OSP with caution to older individuals (>57 years) and/or to those taking medications affecting renal perfusion or function, such as diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and nonsteroidal anti-inflammatory drugs (NSAIDs) (2). Presently, there is no warning against the risks of this grave situation in acromegalic patients in current applied guidelines.
Clinical and histopathological data suggest that the main mechanisms of phosphate nephropathy are direct tubulotoxic effects of marked hyperphosphatemia and depositions of calcium phosphate crystals in the distal tubule and the collecting ducts (3). Increased intestinal phosphate absorption and subsequent renal calcium/phosphate excretion may be contributing factors for the development of renal damage after OSP ingestion in certain situations.
The recommended dosing regimen for OSP is to ingest 45 mL twice, with 10-12 hours between dosing, i.e, the night before and the morning of the colonoscopy procedure (2). After standard dosages of OSP are administered, the expected changes are an asymptomatic increase in serum phosphate by 4.6 mg/dL and a minimal decrease in serum calcium by 0.3 mg/dL (4). In our case, the serum phosphate level raised as much as 8.1 mg/dL, and the decline in calcium was 0.5 mg/dL. Both the prolonged bowel transit time due to dolicocolon and the relatively high dosage of OSP consumption for vigorous cleansing were supposedly the causes of the observed increase in serum phosphate levels and the consequent renal failure.
In acromegalic patients, hyperphosphatemia can occur as a result of direct stimulation of renal tubular phosphate reabsorption due to increased levels of IGF-1 (1). Calcium-phosphate product (CPP) is an important indicator of calcium phosphate precipitation in the kidney (normal range of CPP: 21-45.9). In our patient, the CPP level was 41.4 initially, and then reached 109.62 on the day after the colonoscopy.
One 45 mL bottle of OSP will result in an average fluid loss of 1.0-1.8 L since it osmotically draws plasma water into the bowel lumen (2). If defecation does not take place after phosphate containing purgative ingestion, pooling of the fluid in the gut lumen can potentially increase phosphate absorption, leading to sudden and severe hypernatremia and hyperphosphatemia (5). In addition to increased tubular phosphate load, phosphate driven natriuresis and osmotic diuresis may exacerbate dehydration and volume contraction caused by diarrhea (4). It is suggested that the water supplementation should be 4 L to overcome volume loss by diarrhea (4). The volume replaced in

our patient may have been insufficient. On the other hand, increased GFR and renal plasma flow (RPF) are some compensatory renal mechanisms in acromegaly (1), which may have served to protect the patient from more serious renal damage.

Acromegaly is a condition predisposing patients to OSP-induced nephropathy. Risk factors for phosphate nephropathy in these patients are high basal serum phosphate levels, increased bowel transit time, need for high purgative dosages, increased tubular phosphate re-absorption, advanced age and the concurrent administration of some drugs. In daily practice, endocrinology and gastroenterology physicians should be aware about the risk of using OSP in patients with acromegaly and should opt to follow these patients in the hospital in order to ensure effective hydration. We suggest that acromegaly should be included as a risk factor for nephropathy due to sodium phosphate enema in current guidelines.

References

1. Melmed S. Acromegaly. Endocrinology 5th edition (Ed: DeGroot JL, Jameson JL) Philadelphia, Elsevier & Saunders, 2006, 411-28.
2. Wexner SD, Beck DE, Baron TH, Fanelli RD, Hyman N, Shen B, Wasco KE. A consensus document on bowel preparation before colonoscopy: prepared by a task force from the American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). Gastrointest Endosc 2006; 63: 894-909.
3. Markowitz GS, Stokes MB, Radhakrishnan J, D'Agati VD. Acute phosphate nephropathy following oral sodium phosphate bowel purgative: an underrecognized cause of chronic renal failure. J Am Soc Nephrol 2005; 16: 3389-96.
4. Patel V, Emmett M, Santa Ana CA, Fordtran JS: Pathogenesis of nephrocalcinosis after sodium phosphate catharsis to prepare for colonoscopy: Intestinal phosphate absorption and its effect on urine mineral and electrolyte excretion. Hum Pathol 2004; 35: 675-84.
5. Bowers B. Evaluating the evidence for administering phosphate enemas. Br J Nurs 2006; 15: 378-81.