

COLONIC PSEUDO-OBSTRUCTION AND SEVERE HYPOKALEMIA IN AN ANURIC DIABETIC PATIENT ON HEMODIALYSIS: CASE REPORT AND REVIEW OF THE LITERATURE

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SUMMARY – Hypokalemia is a rare condition in the end-stage renal disease patients on hemodialysis, and especially in those with no residual diuresis. If hypokalemia occurs, it is usually transient and mostly associated with gastrointestinal loss of potassium (massive diarrheal stools), or appears immediately after hemodialysis with the use of dialysis solutions with potassium concentrations lower than 2 mmol/L. The aim of this report is to present a case of a female diabetic patient on hemodialysis with permanent severe hypokalemia associated with chronic colonic pseudo-obstruction and secretory diarrhea, and to point to the possible rare causes of permanent hypokalemia in anuric patients with end-stage renal disease as well as to the causal relations of persistent hypokalemia with changes in different organ systems.

Key words: *Intestinal pseudo-obstruction – etiology; Intestinal pseudo-obstruction – diagnosis; Intestinal pseudo-obstruction – therapy; Hypokalemia – etiology; Chronic diseases – therapy; Risk factors; Case report*

Introduction

Potassium (K⁺) is the main intracellular cation which participates in numerous intracellular and extracellular biochemical and electrophysiological processes. Homeostasis of potassium in the body depends on numerous factors, most important being regular kidney function, regular function of the intestine, and dietary intake of K⁺. The renal transport of K⁺ has been extensively reviewed and analyzed but there are no similar in-depth studies of intestinal potassium absorption and secretion, especially in patients with end-stage renal disease (ESRD). A vast majority of intestinal K⁺ absorption occurs in the small intestine; the contribution of the normal colon to net K⁺ absorption and secretion is trivial. K⁺ is absorbed or secreted mainly by passive mecha-

nisms; the rectum and perhaps the sigmoid colon have the capacity to actively secrete K⁺, but the quantitative and physiological significance of this active secretion is uncertain. The absorptive mechanisms of K⁺ are not disturbed by diarrhea *per se*, but fecal K⁺ losses are increased in diarrheal diseases by unabsorbed anions (which obligate K⁺), by electrochemical gradients secondary to active chloride secretion¹. The paradoxical negative K⁺ balance induced by chronic colonic pseudo-obstruction (CCPO) has been described. CCPO is a rare disease in which a severe colonic motility disorder impairs transit of chyme, so that patients suffer from symptoms of mechanical ileus without mechanical obstruction². CCPO may be a primary or secondary disorder due to muscular³, neurological, autoimmune⁴, metabolic⁵ or endocrine disorders⁶⁻⁹, inflammatory bowel diseases¹⁰, but may also occur following abdominal radiation or be caused by drugs¹¹. Intestinal pseudo-obstruction syndromes are increasingly recognized in clinical practice¹². In severe cases, the typical history of repeated symptoms of mechanical obstruction leading to un-

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successful laparotomies will give key clues for diagnosis. If CCPO is suspected, mechanical obstruction must be searched for carefully by radiological and endoscopic examinations^{13,14}. In our review, we have attempted to elucidate the possible causes and mechanisms of chronic severe hypokalemia in an anuric diabetic patient on HD with CCPO.

Case Report

Our patient was a 73-year-old woman with a history of diabetes mellitus type 2 for 16 years, well-controlled arterial hypertension, persistent hypokalemia recorded for 16 years at a range of 2.3-3.4 mmol/L on all repeat measurements despite daily supplementation of 1-2 g potassium chloride, and mild metabolic alkalosis with pH 7.45-7.50. The patient was treated with an ACE inhibitor, furosemide, oral hypoglycemic drug and calcium channel inhibitors. Ultrasonographic examination before starting HD revealed involutive changes of both kidneys. The kidneys were of normal size and no evidence of adrenal gland enlargement. The renal function impairment induced by diabetic nephropathy progressed to ESRD some 3 years before HD. Diabetic polyneuropathy and retinopathy were established. One year after the initiation of HD the patient became anuric and immobile. The electromyoneurographic analysis revealed changes suggestive of advanced polyneuropathy. The patient developed muscular atrophy of the lower extremities and signs of malnutrition with hypoalbuminemia. During medical treatment, no signs of heart failure were observed and electrocardiography recorded no cardiac arrhythmia; the patient's mental status was normal. Arterial pressure was regulated by an ACE inhibitor and calcium channel blockers. Glycemia was properly regulated. However, hypokalemia persisted on all repeat measurements. Upon the onset of anuria, diarrhea was more frequent, once daily in a quantity of 2-4 L, with marked abdominal distension before defecation, without abdominal pain or vomiting. Microbiological tests for bacterial or protozoan causes of diarrhea were negative. Stool tests for malabsorption syndrome were negative. The upper gastrointestinal tract endoscopy was normal. Gastrografin x-ray studies revealed no abnormalities of the stomach and small intestine, with normal gastric emptying and small bowel transit time. Two years after starting HD, abdominal distension was permanently present with daily massive diarrhea. X-ray revealed a large dilatation (of 11-13 cm in diameter) of the colon,

with no dilatation of the small intestine (Fig. 1). Flexible rectosigmoidoscopy excluded distal obstruction of the colon, with no evidence of malignancy, ischemic or inflammatory bowel disease. After repeat digital dilatation of the anal sphincter, the patient had massive diarrhea and colonic distension was less pronounced after this procedure. Despite drainage flatus and stool with daily repeat digital dilatation of the anal sphincter and through a flexible rectal tube, colonic distension progressed with time and diarrhea continued. Serum levels of K^+ were <3 mmol/L despite regular oral and parenteral K^+ supplementation. Serum aldosterone, renin, sodium, magnesium, and thyroid hormones were normal. There was no severe metabolic acidosis or alkalosis between HD sessions. Repeat ultrasonography and CT scan revealed no enlargement of suprarenal glands. Despite anuria but with normal food and liquid intake because of massive diarrhea, there was no need for liquid removal by ultrafiltration throughout HD. HD was only used for removal of uremic toxins.

The dialysis solution contained 2.0 mmol/L of K^+ ; on each HD session the patient received 30 mEq of potassium chloride (KCl) intravenously. Serum concentration of K^+ was 3.5-4 mmol/L immediately after HD and <3 mmol/L 24 h after HD in spite of regular daily oral intake of 3 g KCl and food rich in K^+ . Despite the use of a rectal tube for drainage of stool and flatus, and intravenous neostigmine, colonic distension and diarrhea persisted, and the only therapeutic measure was digital dilatation of the anal sphincter for stool provocation.



Fig. 1. X-ray of the abdomen with Gastrografin demonstrating massive distension of the colon with a rectosigmoid diameter of at least 13 cm.

During the 2-year follow up while continuing the above measures, the patient's condition did not worsen essentially. Because of the high risk of surgery we decided against colonostomy which some authors mention as the possible solution of CCPO.

Discussion

Under normal conditions, healthy persons absorb most of the K^+ they ingest in their diet and excrete an equal amount in the urine. Total body exchangeable K^+ averages 40 mEq/kg body weight and only 1.5%-2% of total body K^+ is extracellular. The usual daily intake of K^+ with food is 81-96 mEq, daily urinary loss of K^+ in an individual with regular kidney function is 66-102 mEq, and daily fecal loss is 4-14 mEq. In fact, serum K^+ of healthy individuals does not change regardless of the input of K^+ with food. If daily intake of K^+ is small, fecal K^+ excretion is <3.5 mEq. If food is rich in K^+ , fecal excretion of K^+ will grow mildly and more significantly with urine. Therefore, it is understandable that the increased intake of K^+ in ESRD patients can lead to an increase of serum K^+ concentrations to toxic values. Surprisingly, severe hyperkalemia often does not develop. In part, this is because surviving functional nephrons develop an increased capacity to excrete K^+ in urine. Numerous metabolic balance studies in ESRD patients (many of them treated by HD) found that fecal K^+ excretion was abnormally high. For example, in one such patient ingesting 100 mEq/day of K^+ , fecal K^+ excretion was 73 mEq/day. Several other patients excreted more than 50 mEq/day in stool, which is twice as high as fecal K^+ excretion in phenolphthalein-induced diarrhea, higher than K^+ excretion after treatment with cation exchange resin, and higher than in the vast majority of patients with chronic diarrhea. Cation exchange resin by mouth can increase fecal K^+ excretion to 40 mEq/day. The investigators suggest that increased fecal K^+ begins to contribute to the maintenance of K^+ balance when creatinine clearance decreases below 5 mL/min; this is the same point at which residual nephrons develop their maximal capacity to secrete K^+ into the urine¹⁵. The mechanism by which K^+ hypersecretion is triggered has not yet been elucidated; the pattern of ion transport and electrical events seems inconsistent with the response to aldosterone, and plasma aldosterone concentrations are not elevated in most patients with uremia, including those on hemodialysis¹⁶. If the K^+ hypersecretion is triggered by high mucosal K^+ content as

suggested by Malahan *et al.*, it would seem to be a response to K^+ overload rather than a response unique to the uremic process¹⁷. Another possible trigger mechanism involves urea (NH_4). In chronic renal failure, where blood urea concentration is very high, urea would presumably equilibrate across the permeable upper small intestine. When this urea-rich fluid is moved into the colon, the urea would be metabolized to NH_4^+ . NH_4^+ might then block K^+ absorption or stimulate K^+ secretion.

Considering severe hypokalemia in spite of regular oral and parenteral restitution of K^+ with impossibility of K^+ loss with urine in anuric patient and with normal serum sodium concentration, our patient developed secretory diarrhea caused by increased secretion of K^+ in the colon in physiologic conditions as reported to occur in patients with ESRD¹⁸. The retrograde analysis of laboratory results in our patient for 16 years back when hypokalemia had been first recorded, pointed to suspicion of some rare, then unrecognized causes of persistent hypokalemia (Bartter syndrome, Liddle syndrome¹⁹, Gitelman syndrome²⁰⁻²¹, or primary hyperaldosteronism²²) which *sui generis* lead with time to renal function impairment (kaliopenic nephropathy²³), paresthesias, and muscular weakness with resultant muscular atrophy²⁴. In all these disorders, a disorder of distal renal tubular function with hyperkaliuria and consequential hypokalemia with normal serum sodium concentration is present and may be accompanied by arterial hypertension and mild metabolic alkalosis, as in our patient.

The probability that unrecognized primary hyperaldosteronism at the beginning of the disease had caused hypokalemia was small, although normal plasma renin activities and serum aldosterone in our patient had no diagnostic value considering the need of complex patient preparation for these endocrinological tests, practically impossible in patients on HD²⁵. Repeat CT analysis of adrenal glands revealed no enlargement, so the probability of primary hyperaldosteronism was reduced. Aside from this, some authors report that hyperaldosteronism has no significant influence on the increased secretion of K^+ in colon. Hyperaldosteronism increases fecal K^+ excretion by only 3 mEq/day²⁶. Diabetic nephropathy was the main factor that contributed to the progression of chronic renal failure to terminal stage, which demanded the initiation of HD treatment. With the occurrence of anuria in our patient, the possible disorder of distal renal tubules in the urinary secretion of K^+

lost importance. Diabetic autonomic neuropathies alone can lead to CCPO, and it is known that intestinal paralysis occurs resulting in severe hypokalemia. Damage to the colonic autonomic innervation in combination with long-term hypokalemia in our patient permanently favored colonic pseudo-obstruction with large, additional losses of K^+ through massive secretory diarrhea. Patients with high fecal K^+ excretion also had abnormally high fecal weight, up to 500 g/day. In fact, there was an excellent correlation between fecal weight and fecal K^+ excretion, with fecal K^+ concentration averaging 117 mEq/kg. In patients whose stool weight exceeded 300 g/day, fecal water content was 83% (normal 75%), indicating that most of the increase in fecal weight was caused by increased water rather than increased solid parts of stool. Even though stool weights were abnormally high and the percentage of water content was elevated, these patients did not have increased stool frequency¹⁸.

The method and successful medical treatment of CCPO depend on the cause. In case of advanced diabetic autonomic neuropathy, neostigmine usually fails^{27,28}. Regular supplementation of K^+ with regular controls of serum K^+ is necessary. Because of massive diarrhea dehydration is possible, and adequate oral or parenteral hydration is necessary. In some patients rectal tubes may be a good way for removal of gases and stool from the colon because of decreased distension; however, long-term presence of tube in the rectum can cause mechanical damage (rectal ulcerations), therefore daily digital dilatation of anal sphincter to provoke emptying of stool and gases is preferred²⁹. Because of the high risk of surgery in our patient, we decided against colonostomy, which some authors mention as the possible solution of CCPO^{30,31}.

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Sažetak

PSEUDOOPSTRUKCIJA DEBELOG CRIJEVA I TEŠKA HIPOKALEMIJA U ANURIČNE DIJABETIČNE BOLESNICE LIJEČENE HEMODIJALIZOM: PRIKAZ BOLESNICE I LITERATURE

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Hipokalemija je vrlo rijetka u bolesnika s kroničnim bubrežnim zatajenjem koji se liječe hemodijalizom, a pogotovo u onih koji nemaju ostatnu diurezu. Ako se hipokalemija pojavi, obično je prolazna i najčešće povezana s gubitkom kalija putem probavnog sustava (obilne proljevaste stolice) ili se javlja neposredno nakon hemodijalize uz primjenu otopine za dijalizu u kojoj je koncentracija kalija manja od 2 mmol/L. Cilj ovoga rada je prikazati slučaj dijabetične bolesnice liječene hemodijalizom s trajno prisutnom teškom hipokalemijom praćenom pseudoopstrukcijom debelog crijeva i sekretornom dijarejom, te ukazati na moguće rijetke uzroke trajne hipokalemije u anuričnih bolesnika s kroničnim bubrežnim zatajenjem i na uzročno-posljedične veze dugotrajne hipokalemije s promjenama na različitim organskim sustavima.

Ključne riječi: *Crijevna pseudoopstrukcija – etiologija; Crijevna pseudoopstrukcija – dijagnostika; Crijevna pseudoopstrukcija – terapija; Hipokalemija – etiologija; Kronične bolesti – terapija; Rizični čimbenici; Prikaz slučaja*