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Case Report

Acute Renal Failure after Ingestion of Polyethylene Glycol Electrolyte Lavage Solution for Bowel Preparation in a Chronic Spinal Cord Injury Patient: A Case Report

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Intravenous pyelography (IVP) is a common tool for evaluating the upper urinary tract in spinal cord injury patients. To obtain a proper image, bowel preparation is required. Among the regimens for bowel preparation, polyethylene glycol (PEG) electrolyte lavage solution has a good cleansing quality and fewer side effects. Nonetheless, adverse effects of the regimen, though rare, have been reported. We describe a spinal cord injury patient who suffered from acute renal failure as a result of PEG-related toxicity, after taking oral PEG electrolyte lavage solution for bowel preparation. A 57-year-old woman who had sustained spinal cord injury for 11 years was admitted for orthopedic problems and the follow-up of urinary system. Her serum blood urea nitrogen, creatinine, and electrolytes were within normal ranges on admission. She took 500 mL of PEG electrolyte lavage solution for bowel preparation. Mild vomiting and skin rash were noted 30 min later. Moreover, oliguria developed within the next 20 h so she was diagnosed with acute renal failure. The presence of metabolic acidosis and urinary calcium oxylate crystals were noted, so PEG-related oliguric acute tubular necrosis was suspected. The above symptoms were similar to those seen with ethylene glycol intoxication. We conclude that bowel preparation with PEG lavage solution may be associated with severe renal complications, and that physicians should be aware of possible adverse effects when administering the agent. (Tw J Phys Med Rehabil 2009; 37(1): 45 – 50)

Key Words: renal failure, bowel preparation, polyethylene glycol

INTRODUCTION

In earlier decades, urinary and renal complications were the leading causes of mortality among survivors of spinal cord injury (SCI). [1] Nowadays, urological complications remain common and important morbidities in patients after SCI. [2] Complications such as vesicoureteral reflux, renal failure, and nephrolithiasis may present without symptoms in early stages, but can have serious consequences if left untreated. [3] Therefore, regular follow-ups of urological function are recommended for

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patients after SCI. The American Paraplegia Society recommends annual follow-ups for the first five to ten years after injury. [4] If the patient continues to do well, the follow-up interval can be changed to every other year. The recommended tests include serum creatinine and an assessment of upper and lower urinary tracts via nuclear renal scans, plain abdominal radiographs, intravenous pyelography, renal ultrasound, or computerized tomography, if necessary. Among them, intravenous pyelography (IVP) has been the principal radiological technique used to provide detailed information concerning caliceal anatomy, kidney size and shape, and the presence of renal stones. [5]

To obtain a proper image, pre-examination bowel preparation is important. The most frequently used methods for bowel preparation include stimulant laxatives (bisacodyl), hyperosmotic laxatives (lactulose, sorbitol, and mannitol), oral gastrointestinal lavage solutions (polyethylene glycol, or PEG), and laxatives containing magnesium cations or phosphate anions. Among them, PEG electrolyte lavage solution is effective in achieving colon cleansing. Compared to oral laxatives containing sodium phosphate, it is recognized as a safer regimen, though it may not be better tolerated. [6]

PEG intoxication had been reported among patients who drank PEG, or to whom PEG was applied. [7,8] Herein, we describe a SCI patient who developed acute renal failure after taking 500 mL PEG electrolyte lavage solution for bowel preparation. The clinical course is reported and the possible patho-mechanism is discussed.

CASE REPORT

This 57-year-old woman had a traffic accident on April 25, 1995 that caused thoracic spine fracture. She received an internal fixation of the thoracic spine and was paraplegic (ASIA A, level at T4) after the injury. She initially voided by suprapubic tapping and then by indwelling catheterization since 1998 for the convenience of care. She received regular check-ups for urinary systems, including blood tests (blood urea nitrogen, or BUN; serum creatinine; and 24-hour creatinine clearance), intravenous pyelography (IVP), and voiding cystourethrography (VCUG), every one to two years. The most recent follow-up, in 2003, showed normal BUN (8.3 mg/dL) and creatinine (0.8 mg/dL) levels, as well as an acceptable 24-hour creatinine clearance rate (76.4 mL/min). There was no vesicoureteral reflux or hydronephrosis noted by IVP and VCUG. Otherwise, she had been a hepatitis C virus carrier and denied systemic disease. Her regular medication included Dulcolax (biascodyl) 5mg qd, Befon (baclofen) 10mg hs, and Genclone (zoplicone) 7.5 mg hs. She denied any previous drug or food allergy.

She was admitted to our ward for a delayed union of right bi-malleolar fracture and cellulitis at the left foot, which developed after an accidental fall from her wheelchair on November 14, 2006. On December 6, she received open reduction and internal fixation for her right bi-malleolar fracture, and debridement and wound closure for the left fourth toe. She had a symptomatic pyuria one day after the operation and intravenous Cefazolin was prescribed initially. Fever subsided two days later. Because urine culture yielded *Pseudomonas aeruginosa* and multi-drug-resistant *Escherichia coli*, the antibiotic was shifted to oral Ciproxin on December 9, according to the drug susceptibility test. She was scheduled for an IVP study after pyuria was brought under control. Klean-Prep (PEG lavage solution) was prescribed and the patient took 500 mL at 17:30 on December 10. However, subjective dyspnea (respiratory rate, 20/min), general discomfort, and skin itching developed about 30 min later. Multiple tiny erythematous papules at the bilateral upper extremities were also observed. Oxygen was supplied via nasal cannula and Venan (Diphenhydramine) 30 mg was given intramuscularly. The skin rash disappeared at 20:00, but the patient had nausea and mild vomiting twice. She complained of odynophagia, and oral Acetaminophen (500 mg) was prescribed.

Unfortunately, the next morning, the patient noted a reduced volume of urine from her Foley tube. Her urine output in the following 20 h was only 50 mL. Her consciousness remained clear, though she had complaints of general malaise. Blood pressure (BP) was 90/70 mmHg, similar to her baseline condition, and the body temperature was 37.9°C. Laboratory studies indicated leukocytosis, increased C-reactive protein, improved pyuria, and an elevated creatinine (Table 1). Acute renal failure (ARF) was diagnosed, based on Acute Kidney Injury Network criteria: an abrupt absolute increase in the serum creatinine concentration, of ≥0.3 mg/dL from baseline, or

oliguria of less than 0.5 mL/kg per hour for more than six hours. [9] Renal sonography at 17:00 showed no hydronephrosis, no renal stones, and normal bilateral kidney sizes. In the evening, her BP dropped to 70/50 mmHg. Shock was suspected and an inotropic agent (Levophed, or norepinephrine bitartrate) was used. The patient was transferred to the medical intensive care unit (ICU) on the same day at 22:00 for further care. Laboratory exams executed at night showed a urea nitrogen level of 19.5 mg/dL, an increased creatinine level of 2.5 mg/dL, a lactate level of 2.06 mmol/L, and an anion gap of 11.2 mEq/L (Table 1). A central venous catheter was inserted and the pressure was 12 cmH_2O. Urine output in the first 6 h after admission to the ICU increased to 250 mL (intake, 1,312 mL). The inotropic agent was discontinued at 0:00. The next day, urine output had returned to normal limits (2,220 mL in 24 h), blood pressure had returned to baseline, and the serum total IgE level was within normal limits (13.2 IU/mL). Blood gas on December 12 showed minimal metabolic acidosis (pH 7.33, O_2 96.9 mmHg, CO_2 43.5 mmHg, HCO_3^- 22.3 mmol/L). Urine creatinine was 17.6 mg/dL and urine sodium was 44 mmol/L. The fractional excretion of sodium (FE_{Na}) was 6.4%. Intrinsic renal failure, possibly with acute tubular necrosis, was diagnosed (Table 2). She was transferred back to the rehabilitation ward one day later, on December 13, after her condition was stabilized. Subsequent laboratory exams showed a urea nitrogen level of 33.9 mg/dL and a creatinine level of 3.3 mg/dL (Table 1). Urine analysis on December 13 showed proteinuria and calcium oxalate crystals. The serum creatinine level decreased to 1.1 mg/dL on December 25.

DISCUSSION

We presented a case who developed acute renal failure after ingesting 500mL PEG electrolyte lavage solution for bowel preparation. Although the patient had a coexisting urinary tract infection, supportive evidence suggested that PEG was partially responsible for the deterioration of renal function. Since PEG solution is one of the most commonly used bowel preparation regimens, [10] it is important that physiatrists be aware of such an unusual adverse effect while administering this agent.

PEG, an ethylene glycol polymer, is an osmotic agent that helps soften stool and stimulate bowel move-

Table 1. Laboratory examination of the patient

Date	WBC K/μL	CRP mg/dL	BUN mg/dL	Cre mg/dL	Na mmol/L	K mmol/L	Cl mmol/L	Ca mmol/L
2007/12/5	6,120	0.75	8.8	0.7	136	4.3	102	2.18
2007/12/11, AM*	15,010	5.07	16.1	1.8	130	4.3	96	2.02
2007/12/11, PM	16,190		19.5	2.5	125	3.9		
2007/12/13	6,730		26.6	3.3	128	4.4		

WBC, white blood cell; CRP, C-reactive protein; BUN, blood urea nitrogen; Cre, creatinine; Na, sodium; K, potassium; Cl, chloride; Ca, calcium

*17 hours after ingestion of PEG solution

Table 2. Differential diagnosis of oliguric acute renal failure and patient's data [16]

Diagnosis	U/P_{Cr}	U_{Na}	FE_{Na} (%)	U osmolality
Prerenal azotemia	>40	<20	<1	>500
Oliguria ATN	<20	>40	>1	<350
Patient data	5.33	44	6.4	–

ATN, acute tubular necrosis; FE_{Na}, fractional excretion of sodium; P, plasma; U, urine; Cr, creatinine; Na: sodium

ments by retaining water in the stool. The main ingredients of Klean-Prep powder contain 6 g of PEG 3350 per 100 mL and other electrolytes, including sodium sulfate, sodium bicarbonate, sodium chloride, and potassium chloride. The molecular weight (MW) of PEG 3350 is 3,000–3,700 Dalton. The Arabic number behind "PEG" usually indicates its molecular weight. Common side effects of PEG are mainly noted in the gastrointestinal system, including nausea, vomiting, bloating, and abdominal pain. [11] Nevertheless, few adverse effects in other organ systems have been reported. Urticarial reaction and eczema have occurred following the use of PEG-containing oral colon lavage preparations and dermal applications. [7, 12] Acidosis and coma were noted in a patient 5 h after ingestion of 2 L of PEG 400. [13] The toxicity and reported adverse effects of PEG are determined by the molecular weight of the PEG compound. The absorption of solid products (MW 3,000 Dalton or greater) are mostly negligible. [10] However, fatal renal failure had been described in nine patients receiving repeated applications of Furacin soluble dressing for burn care, as Furacin contains 63% PEG 300, 5% PEG 1000, and 32% PEG 4000. In those cases, death occurred 12–27 days after initiation of therapy. [7]

The adverse effects of PEG share some common features with intoxication of ethylene glycol, which is a common ingredient among automotive antifreeze solutions and industrial solvents. The laboratory features of ethylene glycol intoxication include high anion-gap metabolic acidosis, wide osmolal gap, and hypocalcemia. [14] The liver metabolizes most of the ethylene glycol via alcohol dyhydrogenase, with the final metabolite being oxalic acid (oxalate). Oxalate combines with calcium to form calcium oxalate crystals, which precipitate and are toxic to the kidneys. [14]

The toxicity of ethylene glycol is presented in three clinical stages. [15] The first stage (0.5–12 h after ingestion) is characterized primarily by direct effects on the central nervous system and gastrointestinal tract. Patients may have nausea, vomiting, hematemesis, abdominal pain, or compensatory tachypnea due to metabolic acidosis. Large anion and osmolal gaps accompany acidosis. The presented case also reported nausea, vomiting, and subjective dyspnea, but blood gas showed no metabolic acidosis. The second stage (12–24 h after ingestion) is characterized by worsening metabolic acidosis and multiorgan failure. It is during this stage that ethylene glycol is metabolized into toxic acid compounds. Acute respiratory distress syndrome (ARDS) or cardiogenic pulmonary edema may develop, and systemic hypocalcemia due to oxalate chelation of calcium can also cause cardiac arrhythmias and seizures. The majority of mortality occurs during this stage. Our patient had oliguria and elevated creatinine in this stage, but the clinical course did not progress to multiorgan failure. The third stage (24–72 h after ingestion) is characterized by renal toxicity due to deposition of calcium oxalate and consequential acute tubular necrosis and renal failure. Hemodialysis may be required initially, but renal function typically recovers to normal. For the current patient, a urine analysis 30 h after ingestion showed positive oxalate crystals. Her urine output did not return to normal range until 30 h after ingestion, while serum creatinine did not recover until 15 days after ingestion.

The clinical presentation of our patient was consistent with the aforementioned manifestations of ethylene glycol intoxication, though the signs and symptoms were milder. Therefore, acute renal failure secondary to PEG toxicity was highly suspected; nevertheless, other causes of oliguric acute tubular necrosis (ATN) should not be ruled out. The cause of ATN may have been renal ischemia, nephrotoxicity, or even anaphylaxis. [16] Among them, anaphylaxis is the least possible, because the patient did not have an objective airway or systemic symptoms and signs that could be attributed to anaphylactic shock. In the current patient, the serum IgE level and eosinophil count were not suggestive of an anaphylactic episode. Whether ATN was induced or aggravated by renal ischemia, caused by sepsis or by dehydration, should be considered. It was possible that both conditions were responsible for acute renal failure. The patient had mild pyuria, leukocytosis, and increased C-reactive protein, which were suggestive of a potential risk of sepsis. Besides, PEG is an osmotic agent that results in diarrhea, which can deplete intravascular fluid. Therefore, a physician should prescribe agents more cautiously, if a patient has renal insufficiency or infection that is not completely under control.

Little has been discussed about the risk factors for renal complications after polyethylene glycol application.

Nevertheless, liver plays an important role in metabolism of polyethylene glycol. Moreover, the cases of renal insufficiency may also be more liable to the renal complication. Therefore, we suggest that patients with impaired poor liver or renal functions should be especially closely monitored.

CONCLUSION

We reported a case of a patient who developed acute renal failure after bowel preparation with PEG electrolyte lavage solution. The case had good recovery after early intervention and intensive management. Close monitoring of fluid status is recommended when physicians prescribe the agent for patients who are at risk of renal function deterioration.

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慢性脊髓損傷患者於腸道準備中服用聚乙二醇溶液導致急性腎衰竭：病例報告

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靜脈腎盂造影是評估脊髓損傷患者上泌尿系統常用的影像檢查。患者接受檢查前，通常需要進行腸道準備以確保良好的影像品質，而腸道準備所使用的製劑中，以聚乙二醇電解質溶液(商品名刻見清)較少有嚴重副作用，較爲安全。然而，仍有少數報告其併發症。本病例報告描述一位脊髓損傷患者，爲了腸道準備而服用聚乙二醇電解質溶液，不料併發急性腎衰竭。一位 57 歲女性慢性脊髓損傷患者，住院接受骨骼傷害之治療與泌尿系統追蹤檢查，剛入院檢查時，血液中的尿素氮、肌酸酐與其他電解質皆在正常範圍。在腸道準備過程中，她口服 500 毫升的聚乙二醇電解質溶液，約半小時後，產生了輕微的嘔吐與上肢紅疹，二十個小時後，患者尿量減少，檢查結果證實爲急性腎衰竭。檢驗報告另發現了輕微的代謝性酸中毒，尿液中有新產生的草酸鈣晶體沉積，上述徵候皆與乙二醇中毒的症狀相似。藉此例報告，建議於腸道準備過程中，應留意可能的腎併發症，危險性較高的病人需監測其體液狀態。（台灣復健醫誌 2009；37(1)：45 - 50）

關鍵詞：腎衰竭(renal failure)，腸道準備(bowel preparation)，聚乙二醇(polyethylene glycol)

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