

CASE REPORT

급성신부전을 동반한 급성대장가성폐색

표정의, 민양원, 이풍렬

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Effective and Safe Use of Neostigmine in Treatment of Acute Kidney Injury Associated with Colonic Pseudo-obstruction after Cardiac Surgery

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Neostigmine can successfully decompress patients with acute colonic pseudo-obstruction (ACPO) who are unresponsive to conservative therapy. However, neostigmine is contraindicated in renal failure, so it is underused in ACPO patients with renal failure who would be otherwise appropriate candidates. We described the first successfully treated case of acute kidney injury (AKI) with neostigmine in a patient with ACPO. A 72-year-old man who underwent a coronary artery bypass graft surgery 11 days prior presented to the emergency room with abdominal distension, peripheral edema, and dyspnea on exertion. Plain abdominal radiographs and abdomen computed tomography scan showed diffuse colonic dilatation without obstruction. Serum creatinine level was increased five-fold over baseline. We diagnosed the patient as ACPO with AKI. With conservative treatment, renal function failed to improve because the ACPO was not corrected. Administration of neostigmine rapidly resolved ACPO and renal function, avoiding more invasive procedures such as colonoscopic decompression and hemodialysis. Neostigmine appears to be an effective and safe treatment option for ACPO patients with renal failure. Prospective large-scale studies should be carried out to determine the safety and efficacy of neostigmine in ACPO patients with renal failure. (**Korean J Gastroenterol 2016;67:103-106**)

Key Words: Neostigmine; Colonic pseudo-obstruction; Acute kidney injury

INTRODUCTION

Patients presenting with acute colonic pseudo-obstruction (ACPO) have underlying medical and surgical predisposing conditions.¹ Coronary artery bypass graft (CABG) surgery is reported as a rare cause of ACPO.² Pharmacological or colonoscopic decompression is indicated for patients unresponsive to conservative treatment, as they may rapidly undergo further distension.³ Neostigmine is rapidly effective, provides immediate relief, and is well tolerated and

safe.^{4,5} However, the medication should be administered with caution due to the anticholinergic side effects, including bradyarrhythmia. Patients with severe renal insufficiency may have an increased or prolonged vagomimetic response; thus, its use is contraindicated in such cases.^{1,3,4,6} Acute kidney injury (AKI) may be exacerbated or develop because of the ACPO.^{2,7,8} However, because neostigmine is contraindicated in renal insufficiency, there is no clinical data guiding the treatment of ACPO with AKI. We described a case of ACPO with AKI after CABG surgery, which dramatically resolved with

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rapid return of renal function without hemodialysis after neostigmine administration.

CASE REPORT

A 72-year-old male with a history of type II diabetes mellitus, hypertension, chronic renal disease, and prostatectomy for prostate cancer underwent CABG surgery for three-vessel disease 11 days before visiting the emergency room (ER). Results of the pre-operative blood analyses were within normal limits, except for anemia with hemoglobin/hematocrit of 8.7 g/dL (24.9%) and estimated glomerular filtration rate that had declined at a rate of 52.9 mL/min with a serum creatinine of 1.3 mg/dL. From day 4 after surgery, the patient complained of infrequent bowel movements and on day 6 after surgery he was discharged from the hospital with prescribed laxatives (bisacodyl). After discharge, he had no bowel movement and experienced abdominal distension. His urine output decreased gradually and he developed peripheral edema and dyspnea on exertion, which prompted his visit to the ER.

On arrival at the ER, the patients' vital signs were as follows: body temperature 36.2°C, pulse rate 70 beats/min, respiratory rate 24 breaths/min, and blood pressure 117/56 mmHg. Physical examination revealed 2+ pitting edema in both lower legs without crackles on the pulmonary examination. The bowel sounds were diminished and the abdomen was markedly distended, but the patient complained only of mild abdominal pain and there was no sign of peritoneal

inflammation. Rectal examination showed normal sphincter tone and no apparent tumor. Laboratory tests revealed an elevated white blood cell count at 13,010/mm³, blood urine nitrogen at 104.2 mg/dL, and creatinine at 5.31 mg/dL. A plain abdominal radiography (Fig. 1A) revealed significant diffuse colonic dilatation with a maximal diameter of 11.5 cm in the cecum. A non-contrast CT scan followed, to rule out mechanical obstruction, and showed dilated colonic segments full of flatus and feces, with no organic obstruction.

Based on these findings, we suspected ACPO. A nephrologist was consulted for the evaluation of AKI. Urinalysis was negative and urine microscopy was nondescript. Lower than normal blood pressure, dry tongue, and CT scan of dilated colonic segments full of feces suggested pre-renal AKI associated with third space loss, ACPO, and worsened pre-existing chronic kidney disease. Treatment of the underlying cause of renal failure was recommended for the patient, instead of hemodialysis.

Therefore, supportive measures were undertaken including nil per os with fluid and electrolyte supplements, and placement of a rectal tube to decompress the dilated colonic segments. Despite supportive measures for 24 hours, no passage of flatus or stool was observed. Furthermore, the abdominal distention failed to resolve and serum creatinine progressively increased to 5.54 mg/dL. We concluded that renal function failed to improve because the underlying cause, ACPO, was not corrected. Therefore, we decided to administer intravenous neostigmine. The patient was continuously monitored for electrocardiographic and vital signs.

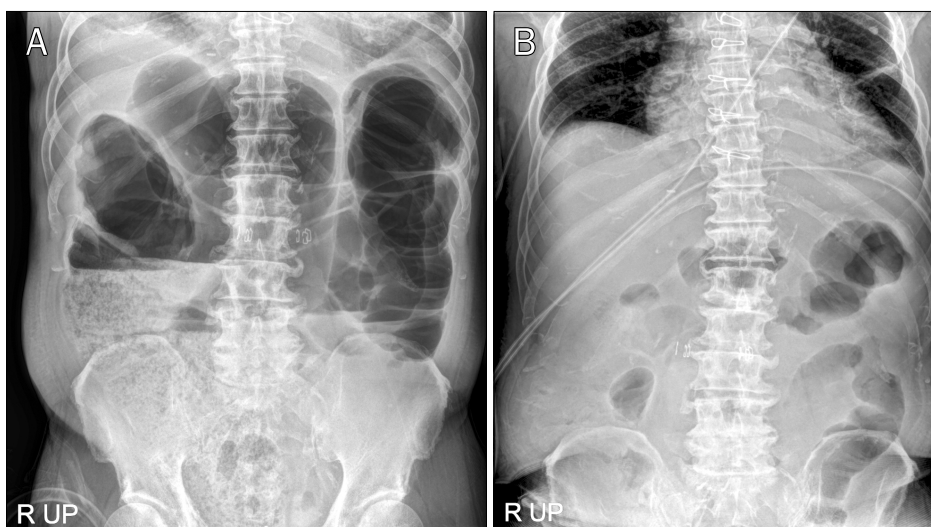


Fig. 1. Plain abdominal radiographs. (A) Upon arrival at the emergency room, plain abdominal radiograph demonstrated diffuse dilated loops and dilatation of the cecum up to 11.5 cm in diameter. (B) A plain abdominal radiograph obtained 24 hours after administration of neostigmine showed evacuation of stool and complete resolution of bowel distension.

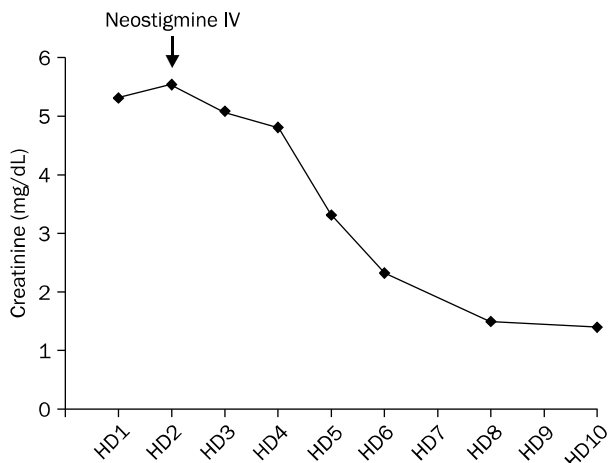


Fig. 2. Time course of serum creatinine. Creatinine level increased up to 5.54 mg/dL and rapidly decreased after administration of neostigmine. Six days after treatment with neostigmine, the patient's renal function recovered to basal level. HD, hospital day.

A physician administered 2 mg of intravenous neostigmine, atropine at the bedside. Twenty minutes later, we observed the passage of stool and gradual relief of the abdominal distention. The patient did not manifest bradycardia during the one hour observation period. AKI also rapidly resolved after the resolution of ACPO (Fig. 2). On the tenth day after admission, the patient was discharged from the hospital and reported no abdominal problems upon follow-up.

DISCUSSION

ACPO is a rare complication with an incidence of 4.6 per 10,000 cases undergoing CABG surgery.² Although the frequent use of beta-blocker or a history of recent myocardial infarction in patients who undergo CABG surgery may increase the risk of bradycardia,³ rapid and effective treatment is generally possible with neostigmine.⁹ Therefore, continuous cardiac monitoring is required for detection of bradycardia that may require treatment with atropine as well as for anticholinergic side effects. In addition, a slow intravenous infusion of neostigmine may lower the risk of bradycardia.¹⁰

The success rate of neostigmine treatment in patients unresponsive to conservative treatment ranges from 73% to 94% after the first dose, and up to 100% after the second dose.¹¹ Although colonoscopic decompression is successful in 77% of patients, colonoscopy is technically difficult, not always successful, and may cause complications such as

perforation. Additionally, colonic distention may recur in up to 40% of patients, despite initial successful decompression.² Furthermore, the cost of colonoscopy is substantially higher than that of parenteral neostigmine. Surgical intervention is associated with high morbidity and mortality rates.⁸ Therefore, colonoscopic or surgical decompression needs to be reserved for situations wherein conservative treatment fails.

Although neostigmine was associated with a favorable safety profile in the reported clinical trials, caution should be used when administering the medication. Webb¹² first reported a case of a child with renal failure who developed type I second-degree atrioventricular block after neostigmine administration. Since then, many studies indicate that renal insufficiency (serum creatinine > 3 mg/dL) contraindicates its use.^{1,3,4,6} Renal excretion accounts for approximately 50% of plasma clearance of neostigmine and therefore, it is not recommended in cases of severe renal insufficiency, since elimination half-life is significantly prolonged and serum clearance decreases.¹²⁻¹⁴ Thus, reports on the use of neostigmine alone in ACPO with AKI are rare. Instead of neostigmine, such patients undergo hemodialysis,⁹ or colonoscopic decompression.^{15,16} One case report described an ACPO patient with AKI who received conservative treatment and subsequent hemodialysis.⁹ Neostigmine was used to avoid further deterioration, and ACPO and renal failure were resolved. Thus, neostigmine can avert the need for hemodialysis in ACPO patients with AKI. Furthermore, no life-threatening side effects related to use of neostigmine in ACPO have been reported, although the risk in the presence of renal insufficiency might be different. In a randomized clinical trial of 21 patients, only two had symptomatic bradycardia requiring atropine.⁴ In addition, a review of 51 studies indicated that only four patients experienced bradycardia requiring atropine, which also resolved without significant complication.⁵

A recent review of ACPO¹⁷ did not include renal insufficiency as a contraindication for neostigmine, as dose adjustments are recommended according to creatinine clearance.¹⁸ We administered neostigmine without dose adjustment to the study patient with renal insufficiency, since the adjusted dose may have been insufficient to relieve ACPO and because anticholinergic side effects can be controlled with atropine. However, dose adjustment to 1 mg and addi-

tional 1 mg in the event that the previous dose was ineffective might have been an effective and safer choice.

In conclusion, when ACPO is the cause of AKI, a vicious cycle of worsening AKI and ACPO can occur if the ACPO is not resolved. As expected, administration of neostigmine rapidly resolved ACPO and AKI without any significant complications. For the appropriate patient, neostigmine with cardiac monitoring could be an effective, safe, and inexpensive treatment option of ACPO with renal failure. Further prospective large studies are required to determine the efficacy and safety of neostigmine in ACPO patients with renal failure.

REFERENCES

1. Saunders MD. Acute colonic pseudo-obstruction. *Best Pract Res Clin Gastroenterol* 2007;21:671-687.
2. Tenofsky PL, Beamer L, Smith RS. Ogilvie syndrome as a post-operative complication. *Arch Surg* 2000;135:682-686; discussion 686-687.
3. De Giorgio R, Barbara G, Stanghellini V, et al. Review article: the pharmacological treatment of acute colonic pseudo-obstruction. *Aliment Pharmacol Ther* 2001;15:1717-1727.
4. Ponc RJ, Saunders MD, Kimmey MB. Neostigmine for the treatment of acute colonic pseudo-obstruction. *N Engl J Med* 1999;341:137-141.
5. Kayani B, Spalding DR, Jiao LR, Habib NA, Zacharakis E. Does neostigmine improve time to resolution of symptoms in acute colonic pseudo-obstruction? *Int J Surg* 2012;10:453-457.
6. Loftus CG, Harewood GC, Baron TH. Assessment of predictors of response to neostigmine for acute colonic pseudo-obstruction. *Am J Gastroenterol* 2002;97:3118-3122.
7. Anuras S, Shirazi SS. Colonic pseudoobstruction. *Am J Gastroenterol* 1984;79:525-532.
8. Vanek VW, Al-Salti M. Acute pseudo-obstruction of the colon (Ogilvie's syndrome). An analysis of 400 cases. *Dis Colon Rectum* 1986;29:203-210.
9. Guler A, Sahin MA, Atilgan K, Kurkluoglu M, Demirkilic U. A rare complication after coronary artery bypass graft surgery: Ogilvie's syndrome. *Cardiovasc J Afr* 2011;22:335-337.
10. Abeyta BJ, Albrecht RM, Schermer CR. Retrospective study of neostigmine for the treatment of acute colonic pseudo-obstruction. *Am Surg* 2001;67:265-268; discussion 268-269.
11. De Giorgio R, Knowles CH. Acute colonic pseudo-obstruction. *Br J Surg* 2009;96:229-239.
12. Webb MD. Type I second-degree AV block after neostigmine administration in a child with renal failure. *Anesth Prog* 1995;42:21-22.
13. Cronnelly R, Stanski DR, Miller RD, Sheiner LB, Sohn YJ. Renal function and the pharmacokinetics of neostigmine in anesthetized man. *Anesthesiology* 1979;51:222-226.
14. Murphy GS, De Boer HD. Reversal (Antagonism) of neuromuscular blockade. In: Miller RD, ed. *Miller's anesthesia*. 8th ed. London, UK: Elsevier Health Sciences, 2014:995-1027.
15. Saunders MD. Case-based management of acute colonic pseudo-obstruction. *American Society for Gastrointestinal Endoscopy Leading Edge* 2011;1:1-6.
16. Strodel WE, Dent TL, Nostrant TT, Eckhauser FE, Campbell DA, Marks WH. Treatment alternatives in renal failure and renal transplantation patients with nonobstructive colonic dilatation. *Transplantation* 1983;36:37-40.
17. Camilleri M. Acute colonic pseudo-obstruction (Ogilvie's syndrome). [Internet]. UpToDate [updated 2015 Mar 26; cited 2015 Sep 1]. Available from: <http://www.uptodate.com/contents/acute-colonic-pseudo-obstruction-ogilvies-syndrome>
18. Aronoff GR. Drug prescribing in renal failure: dosing guidelines for adults and children. 5th ed. Philadelphia: American College of Physicians, 2007.