

# Cardiac arrest complicating neostigmine use for bowel opening in a critically ill patient

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## Clinical record

A 16-year-old woman with cerebral palsy underwent an elective scoliosis repair. She had previously undergone several orthopaedic procedures without complication.

The surgical procedure and anaesthesia were uncomplicated. The patient was extubated at the end of the procedure and transferred to the intensive care unit for postoperative management, as planned. The early postoperative course was complicated by respiratory failure requiring intubation and ventilation. Bilateral pleural effusions were drained, and a pneumothorax was treated.

Regular paracetamol and large doses of morphine and tramadol were administered to control pain. During the first 7 days in the ICU, the patient's bowels did not open despite management with docusate (Coloxyl), sennosides a and b (senna), Kiwi Crush digestive enhancer, glycerol (glycerine) suppositories and phosphate enemas. There was no clinical evidence of mechanical bowel obstruction. Neostigmine was administered intravenously to achieve bowel opening. This was commenced at a dose of 2.5 mg to be administered over 1 hour. Routine monitoring with electrocardiography, pulse oximetry and invasive arterial blood pressure was in use.

After 40 minutes of neostigmine administration, there was a progressive bradycardia, followed by asystole. Closed chest cardiac massage was performed for less than

## ABSTRACT

Absence of bowel opening is common among critically ill patients. Neostigmine can be used to achieve stool passage after other treatments have been ineffective. Here, we report a case of cardiac arrest complicating neostigmine use in a 16-year-old woman with cerebral palsy who was being treated in the intensive care unit after orthopaedic surgery. Bradycardia is a recognised complication of neostigmine administration; however, cardiac arrest has not been reported previously.

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1 minute before spontaneous return of circulation. No medications were given for management of the cardiac arrest, and the neostigmine infusion was discontinued. The patient's condition remained stable after the cardiac arrest, with no further arrhythmia or haemodynamic instability.

The patient was extubated 11 days after the operation. After a period of rehabilitation, she made an uncomplicated recovery and achieved a satisfactory functional result from her surgery.

**Table 1. Previous reports of bradycardia following neostigmine use among critically ill patients**

Study	Condition	Dose*	No. of patients	No. with bradycardia (%)
van der Spoel et al, 2001 <sup>1</sup>	CIRCI	0.4–0.8 mg/hour for 24 hours	24	0
Abeyta et al, 2001 <sup>3</sup>	ACPO	2 mg "bolus"	10	1 (10%)
Loftus et al, 2002 <sup>4</sup>	ACPO	2 mg over 3–5 min	18	2 (11%)
Sgouros et al, 2006 <sup>5</sup>	ACPO	2 mg over 3–5 min	30	2 (7%)
Turégano-Fuentes et al, 1997 <sup>6</sup>	ACPO	2.5 mg over 60 min	16	1 (6%)
Mehta et al, 2006 <sup>7</sup>	ACPO	2 mg over 15 min	19	2 (10%)
Trevisani et al, 2000 <sup>8</sup>	ACPO	2.5 mg over 2–3 min	28	0
Paran et al, 2000 <sup>9</sup>	ACPO	2.5 mg over 1 hour	11	0
Hutchinson & Griffiths, 1992 <sup>10</sup>	ACPO	2.5 mg over 1 min	11	0
Rosman et al, 2008 <sup>12</sup>	Spinal cord injury	2 mg IM (with 0.4 mg glycopyrrolate)	7	0
Rubiales et al, 2006 <sup>13</sup>	Constipation in advanced cancer	0.25–1.25 mg SC every 8 hours	8	0
<b>Total</b>			<b>187</b>	<b>8 (4%)</b>

ACPO = acute colonic pseudo-obstruction. CIRCI = critical illness-related colonic ileus. IM = intramuscular. SC = subcutaneous. \* Intravenous unless otherwise indicated.

## Discussion

Neostigmine is a cholinesterase inhibitor that acts by increasing the concentration of acetylcholine at the neuromuscular junction, increasing gut contractions.

Neostigmine use to achieve stool passage, after other treatments have been ineffective, has been described for critically ill patients.<sup>1,2</sup> Neostigmine is a treatment with a well established role in the management of acute colonic pseudo-obstruction in non-ICU settings.<sup>3-10</sup> Its use has also been described for bowel management in patients with autonomic neuropathy,<sup>11</sup> spinal cord injury,<sup>12</sup> advanced cancer<sup>13</sup> and severe constipation.<sup>14</sup> A double-blind, placebo-controlled trial examined neostigmine use for promoting defecation in critical illness-related colonic ileus.<sup>1</sup> Here, critical illness-related colonic ileus was defined as non-passage of stools among critically ill patients with absent colonic prokinetic movements, a normally functioning upper gastrointestinal tract and no evidence of mechanical obstruction.

A variety of dosing regimens for relief of acute colonic pseudo-obstruction or critical illness-related colonic ileus are described. Adverse events associated with neostigmine use include abdominal cramps, excessive salivation, bronchospasm, sweating, nausea and vomiting, hypotension and bradycardia. The reported incidence of bradycardia ranges from zero to 11%.<sup>1,3-13</sup>

Dosing regimens and incidence of bradycardia are summarised in Table 1. Cardiac arrest has not previously been reported.

Coadministration of atropine appears not to block the muscarinic effect of neostigmine on bowel activity.<sup>15</sup> When compared, glycopyrrolate and atropine showed similarly low efficacy in preventing neostigmine-induced colonic activity.<sup>16</sup> This raises the question of whether coadministration of glycopyrrolate or atropine could reduce the risk of bradycardia during neostigmine administration without reducing its ability to achieve bowel opening for critically ill patients.<sup>17,18</sup> The incidence of significant bradyarrhythmia when administering neostigmine means that cardiac monitoring is essential, and that atropine or glycopyrrolate should be immediately available for treatment of bradyarrhythmia.

## Conclusion

We have reported the rare event of cardiac arrest complicating neostigmine use to achieve bowel opening in a critically ill young woman in the ICU. The dosing regimen was comparable with those described elsewhere (Table 1). Although cardiac arrest itself has not previously been described in this circumstance, symptomatic bradycardia has been reported. Further work is required to determine whether there is a role for routine administration of atropine or glycopyrrolate with neostigmine.

## Competing interests

None declared.

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## References

- 1 van der Spoel JI, Oudemans-van Straaten HM, Stoutenbeek CP, et al. Neostigmine resolves critical illness-related colonic ileus in intensive care patients with multiple organ failure — a prospective, double-blind placebo-controlled trial. *Intensive Care Med* 2001; 27: 822-7.
- 2 Nesbitt I. Guidelines for the management of constipation in adult critical care. Newcastle upon Tyne, UK: NHS Trust, 2004.
- 3 Abeyta BJ, Albrecht RM, Schermer CR. Retrospective study of neostigmine for the treatment of acute colonic pseudo-obstruction. *Am Surg* 2001; 67: 265-9.
- 4 Loftus CG, Harewood GC, Baron TH. Assessment of predictors of response to neostigmine for acute colonic pseudo-obstruction. *J Gastroenterol* 2002; 97: 3118-22.
- 5 Sgouros SN, Vlachogiannakos J, Vassiliadis K, et al. Effect of polyethylene glycol electrolyte balanced solution on patients with acute colonic pseudo-obstruction after resolution of colonic dilatation: a prospective, randomized, placebo controlled trial. *Gut* 2006; 55: 638-42.
- 6 Turégano-Fuentes F, Muñoz-Jiménez F, Del Valle-Hernández E, et al. Early resolution of Ogilvie's syndrome with intravenous neostigmine. *Dis Colon Rectum* 1997; 40: 1353-7.
- 7 Mehta R, John A, Nair P, et al. Factors predicting successful outcome following neostigmine therapy in acute colonic pseudo-obstruction: a prospective study. *J Gastroenterol Hepatol* 2006; 21: 459-61.
- 8 Trevisani GT, Hyman NH, Church JM. Neostigmine. Safe and effective treatment for acute colonic pseudo-obstruction. *Dis Colon Rectum* 2000; 43: 599-603.
- 9 Paran H, Silverberg D, Mayo A, et al. Treatment of acute colonic pseudo-obstruction with neostigmine. *J Am Coll Surg* 2000; 190: 315-8.
- 10 Hutchinson R, Griffiths C. Acute colonic pseudo-obstruction: a pharmacological approach. *Ann R Coll Surg Engl* 1992; 74: 364-7.
- 11 Bharucha AE, Low PA, Camilleri M, et al. Pilot study of pyridostigmine in constipated patients with autonomic neuropathy. *Clin Auton Res* 2008; 18: 194-202.
- 12 Rosman AS, Chaparala G, Monga A, et al. Intramuscular neostigmine and glycopyrrolate safely accelerated bowel evacuation in patients with spinal cord injury and defecatory disorders. *Digest Dis Sci* 2008; 53: 2710-3.
- 13 Rubiales AS, Hernansanz S, Gutierrez C, et al. Neostigmine for refractory constipation in advanced cancer patients. *J Pain Symptom Manage* 2006; 32: 204-5.
- 14 Ong SP, Choong CF. Neostigmine in the treatment of severe constipation. *Intern Med J* 2007; 37: 836-7.
- 15 Wilkins JL, Hardcastle JD, Mann CV, Kaufman L. Effects of neostigmine and atropine on motor activity of ileum, colon, and rectum of anaesthetized subjects. *BMJ* 1970; 1: 793-4.
- 16 Child CS. Prevention of neostigmine-induced colonic activity — a comparison of atropine and glycopyrronium. *Anaesthesia* 1984; 39: 1083-5.
- 17 Vavilala MS, Lam AM. Neostigmine for acute colonic pseudo-obstruction [letter]. *N Engl J Med* 1999; 341: 1622.
- 18 Abbasakoor F, Evans A, Stephenson BM. Neostigmine for acute colonic pseudo-obstruction [letter]. *N Engl J Med* 1999; 341: 1622. □