CASE REPORT

Neostigmine and glycopyrronium: a potential safe alternative for patients with pseudo-obstruction without access to conventional methods of decompression

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SUMMARY

Intestinal pseudo-obstruction mimics bowel obstruction. However, on examination, no mechanical cause is identified. This condition will often resolve when managed conservatively, yet in some cases decompression is required to avoid the serious complications of bowel ischaemia and perforation. This is performed endoscopically, and due to the invasive nature and limited access to this service, an alternative treatment option is deemed appealing. Neostigmine has good efficacy in the decompression of pseudo-obstruction but is hindered by its wide side effect profile. In this context, neostigmine requires careful monitoring, which limits its appeal. This side effect profile is minimised when neostigmine is administered in conjunction with glycopyrronium. This case demonstrates the novel use of neostigmine and glycopyrronium in decompression of the bowel in a patient with pseudo-obstruction. Furthermore, it highlights its value, particularly when conventional techniques for decompression are not accessible.

BACKGROUND

Intestinal pseudo-obstruction, also known as Ogilvie's syndrome, is a condition that presents with colon dilatation in the absence of a mechanical or anatomical obstruction. It is commonly seen in hospitalised patients, predominantly, postorthopaedic, bowel or pelvic surgery and in those with metabolic disturbances.^{1,2} To date, the incidence of the disorder remains unknown as spontaneous resolution in patients is often observed.² Caecal perforation, a life-threatening complication is reported in 15%–20% of cases² and is associated with a 40%–50% mortality risk.

Although patients may be managed conservatively with a nasogastric tube, bowel rest and reversal of precipitating factors, a subset of patients will require decompression to avoid bowel perforation and its sequelae. Currently, this is performed by flexible or rigid sigmoidoscopy, but access to such services is often limited (eg, out of hours or in smaller centres).

Neostigmine methylsulfate is a reversible cholinesterase inhibitor, which is indicated in the management of symptomatic myasthenia gravis and in general anaesthesia for the reversal of

non-depolarising neuromuscular agents.² Neostigmine is effective in the treatment of ileus and pseudo-obstruction. However, its cardiac side effects of bradycardia, heart block and life-threatening arrhythmias make it relatively undesirable.³ Furthermore, patients receiving this drug require continuous cardiac monitoring.

Glycopyrronium is used as a reversal agent in general anaesthesia to reverse the neuromuscular block produced by non-depolarising muscle relaxants.⁴ It is unable to permeate the blood brain barrier, has a relatively short half-life and does not hinder the advantageous gastrointestinal effects of neostigmine.⁵ As a result, administration of the combination glycopyrronium and neostigmine to treat pseudo-obstruction enables the former to inhibit the cardiac side effects of the latter without impairing its beneficial effects on the bowel.^{1,5}

CASE PRESENTATION

An 80-year-old male presented as an acute admission with abdominal distension, nausea, diarrhoea and lethargy. Importantly, no abdominal pain was reported. His medical history included stroke, ischaemic heart disease, hypertension, aortic aneurysm (5.1 cm), parastomal hernia repair and pacemaker, and he had previously undergone a low anterior resection for a rectal adenocarcinoma (Dukes C) with an ileostomy, which was reversed 1 month prior to admission.

The patient was a non-smoker, who lived independently. He reported occasional alcohol consumption and had no family history of relevance.

On physical examination, he had a distended abdomen, which was non-tender with audible bowel sounds. Per rectum examination was normal. His vital signs were normal.

INVESTIGATIONS

Initial blood tests revealed a profound hypokalaemia (2.0 mmol/L) and a raised C-reactive protein (169 mg/L); all other blood tests were unremarkable. A plain abdominal radiograph demonstrated dilated loops of small and large bowel (figure 1).

Further imaging via CT demonstrated a diffusely dilated colon (figure 2). More specifically, the caecum was 12.5 cm in diameter with proximal

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Figure 1 Plain abdominal film demonstrating grossly dilated loops of large bowel.

small bowel collapse. No specific cause of obstruction was identified.

DIFFERENTIAL DIAGNOSIS

Large bowel obstruction in the context of a competent ileocaecal valve results in perforation of the caecum if left untreated. Identification of a mechanical cause is therefore pertinent to determine further management. Given the patient's history of colonic resection for malignancy, it was imperative to exclude an obstruction secondary to malignancy. Cross-sectional imaging and flexible sigmoidoscopy found no mechanical cause. The absence of pain and systemic toxicity made the diagnosis of toxic megacolon an unlikely differential.

The clinical presentation of painless abdominal distension and profound hypokalaemia, together with the absence of systemic toxicity and absence of vomiting, made colonic pseudo-bowel obstruction the most likely diagnosis.

TREATMENT

Initial management involved electrolyte replacement, intravenous fluids and nasogastric tube placement. Despite this, the patient's abdomen became increasingly distended and required decompression with flexible sigmoidoscopy within 24 hours of his admission. This provided relief for 6 days and was continued on close monitoring and replacement of his electrolytes. Total parenteral nutrition was commenced to provide optimal nutrition.

At day 7, he had a recurrence of painless abdominal distension that failed to improve with conservative management. A new abdominal X-ray was performed and demonstrated dilated loops of large bowel in keeping with his known presentation of pseudo-obstruction. Intravenous neostigmine and glycopyrronium (2.5 mg and 0.5 mg/mL, respectively) at a dose of 1 mL were administered over 30 s. This provided immediate symptomatic relief, resulting in bowel evacuation and resolution of abdominal distension on serial examination. The patient remained on cardiac monitoring for the duration of drug administration and 4 hours subsequently given his pre-existing cardiac disease. No cardiac events were recorded.

Figure 2 CT scan of the abdomen and pelvis confirming large bowel distension.

OUTCOME AND FOLLOW-UP

The patient's symptoms of tense abdominal distention and abdominal pain were successfully managed with the combination of neostigmine and glycopyrronium administration. There were no immediate or delayed side effects reported.

DISCUSSION

While neostigmine is known to have gut-stimulating effects, it is not routinely used by surgeons in the management of pseudo-obstruction due to its wide side effect profile. Such effects include bradycardia, heart block and life-threatening arrhythmias.⁶ As a result, endoscopy has been used as an alternative when available.

When given in combination, glycopyrronium inhibits the neostigmine-related cardiac side effects.^{5,6} However, as glycopyrronium has limited gastrointestinal activity, the desired neostigmine effect of enhancing gastric motility is preserved. This combination has been successful in bowel stimulation following spinal cord injuries.⁷

This case demonstrates the safe and effective use of neostigmine and glycopyrronium in the treatment of pseudo-bowel obstruction in a single patient. While no side effects were observed in our patient, the adverse cardiac side effects of neostigmine and the antimuscarinic effects of glycopyrronium including difficulty in micturition, dry mouth and flushing require adequate monitoring.^{3,4}

To date, there have been no large-scale trials investigating neostigmine alone or the combination of neostigmine–glycopyrronium as an alternative treatment to endoscopic decompression. Further research is required to educate and establish this combination as a viable treatment alternative.

Learning points

- ▶ The management of pseudo-obstruction with colonic dilation poses a challenge to clinical teams.
- ▶ Neostigmine has demonstrated good efficacy in decompression of pseudo-obstruction, although it may have serious side effects and should not be used unless monitoring is available.
- ▶ Neostigmine and glycopyrronium given in combination is a non-invasive, safe and effective management option for treating pseudo-obstruction.
- ▶ Further research is required in this area.

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