

Acute colonic pseudo-obstruction: a pharmacological approach

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Acute colonic pseudo-obstruction is a functional disorder that closely mimics mechanical large bowel obstruction, and in which inadvertent laparotomy carries a high mortality.

Eleven such patients were treated by pharmacological manipulation of the autonomic innervation to the colon with guanethidine and neostigmine. Eight responded to treatment with passage of flatus and/or stool within 10 min with complete resolution of symptoms. In three patients the treatment failed. Postural hypotension occurred in only one patient and no other serious side-effect was apparent.

This pharmacological approach to the management of acute colonic pseudo-obstruction is suggested as an alternative to the other treatment options of colonoscopic decompression or surgery, when conservative management has failed.

Acute colonic pseudo-obstruction is a condition characterised by symptoms, signs and plain radiographic appearances of acute large bowel obstruction in the absence of a mechanical blockage. The exact pathophysiology of acute colonic pseudo-obstruction has not been elucidated, but it is generally accepted to be an adynamic ileus of the colon due to inhibition of parasympathetic innervation relative to sympathetic innervation. It is classified among the functional bowel disorders in which ineffective propulsion results from neuromuscular abnormalities of the bowel.

Acute colonic pseudo-obstruction occurs most commonly in the elderly (1,2). The typical patient is usually already hospitalised with a serious illness. Pseudo-

obstruction may also follow trauma such as burns (3), and extra-abdominal surgery—particularly total hip replacement. It has been reported after caesarian section in the younger female (4). If, as in the majority of cases, there is a predisposing illness, the condition is described as secondary acute colonic pseudo-obstruction. Sometimes there is no identifiable predisposing factor—primary acute colonic pseudo-obstruction.

Patients with acute colonic pseudo-obstruction should be treated conservatively with the aim of eliminating or reducing factors known to contribute to the condition. Any electrolyte or metabolic disorder is corrected and medical illnesses are sought and treated. Conservative management is advocated initially because it is successful in the majority (>85%) of cases in a mean of 3 days (5–9). Surgical intervention for acute colonic pseudo-obstruction is associated with a high mortality (1,10,11).

Conservative management requires careful monitoring and support; this is time-consuming and labour intensive. While awaiting resolution, the distended patients are at risk of caecal perforation, respiratory embarrassment, and nutritional depletion, as well as being uncomfortable and immobilised. Therefore, any method of safely hastening resolution by deflation would be both therapeutic and cost-effective. A pharmacological approach was conceived with the aim of shortening the natural history of acute colonic pseudo-obstruction. The rationale for pharmacological manipulation of the autonomic innervation to the colon derives from studies on small bowel paralytic ileus by Neely and Catchpole over 20 years ago (12,13). They reported a regimen of guanethidine and prostigmine to treat small bowel ileus and succeeded in restoring peristalsis in 30 patients (14).

A pharmacological method of shortening the natural history of acute colonic pseudo-obstruction seems to be worth considering. Our experience with this approach is presented.

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Patients and methods

In a 4-year period (1987–1991), 11 patients were treated for acute colonic pseudo-obstruction by pharmacological manipulation. A few patients with pseudo-obstruction were seen in whom it was judged that the administration of autonomic-modulating drugs could be detrimental to an unstable cardiac condition and these were not included in the study.

Data were collected prospectively and details of age, sex, duration of symptoms, serum urea and any predisposing factors, are shown in Table I. Other serum electrolytes were normal. All patients had the clinical and plain radiographic appearances of acute large bowel obstruction. The patients had abdominal pain, gross abdominal distension and absolute constipation. All patients had a mechanical obstruction excluded by an emergency contrast enema examination in which contrast flowed beyond the apparent site of obstruction.

All patients were managed conservatively with a policy of nil by mouth, intravenous infusion, and nasogastric tube decompression. Fluid and electrolyte imbalances were corrected, and any associated medical conditions were treated. A decision to treat by pharmacological manipulation was reached, with the patients' consent, only after predisposing factors had been corrected, and conservative management was judged to have failed after at least 48 h of conventional treatment.

Pharmacological treatment was provided as follows:

- 1 20 mg of guanethidine (an adrenergic blocker) in 100 ml of normal saline infused intravenously over 40 min.

- 2 2.5 mg of neostigmine (a parasympathomimetic) given over 1 min, after the guanethidine infusion.

Doses of drugs used were derived from Neely and Catchpole's experience. The blood pressure was checked every 10 min, and the treatment would have been stopped if the systolic pressure had dropped to below 90 mmHg. This did not occur in any of the patients. A flatus tube was inserted into the rectum to assist collection of the effluent.

Results

The results are shown in Table I.

In eight of the 11 patients, there was rapid passage of flatus and/or faeces with clinical improvement in distension and symptoms. In six patients, deflation occurred within 5 min, and in two this occurred within 10 min. No recurrence of pseudo-obstructive features occurred during the hospital stay of the patients. All eight successfully treated patients had some predisposing factor.

Serious side-effects were noted in only one patient—postural hypotension occurred when a 76-year-old lady sat upright on a commode shortly after the treatment. One other patient developed quite distressing excessive salivation.

There was one late death—a 74-year-old lady suffered a right-sided cerebrovascular accident 13 days after successful treatment for pseudo-obstruction, and died 2 days later with bronchopneumonia. It is difficult to assess whether the treatment had any influence on this event.

Table I. Patient details and results of treatment

Age/Sex	Duration of symptoms (days)	Serum urea (mmol/l) [NR 2.5–7.5]	Associated conditions	Time to passage flatus/stools (min)	Comments
74 F	2	6.4	Atrial fibrillation, femoral embolectomy	1	Complete resolution
72 F	3	7.8	Asthma with chest infection	10	Complete resolution
64 M	5	5.9	Total hip replacement	3	Complete resolution
46 F	5	8.8	Chest injury with multiple fractures	5	Complete resolution
78 F	4	10.4	Diabetes mellitus	5	Complete resolution
76 F	3	9.1	Congestive cardiac failure	2	Postural hypotension, complete resolution
64 M	2	6.6	Hypothyroid, on thyroxine	1	Complete resolution
82 F	2	12.4	None	Treatment failed	Settled spontaneously in 2 days
68 F	2	7.9	None	Treatment failed	Decompressed colonoscopically
81 F	2	9.6	None	Treatment failed	Settled spontaneously in 2 days
78 M	7	6.8	Above-knee amputation	8	Excessive salivation, complete resolution

In three patients, no predisposing factor was evident and the treatment failed. One was decompressed colonoscopically, and two resolved with continued conservative management for a further 2 days.

Discussion

Our study can be criticised for not containing a control group. However, acute colonic pseudo-obstruction is too uncommon for an individual clinician to encounter adequate numbers of cases to mount a placebo-controlled trial of drug treatment; or a trial of drug treatment versus another treatment option, such as colonoscopic decompression. We encountered only 11 cases over 4 years in four different hospitals. Furthermore, the dramatic response in the eight successfully treated cases, was convincing evidence of a temporal relationship between the drug treatment and the deflation of the patients with resolution of symptoms. Six patients 'deflated' rapidly and completely within 5 min of the neostigmine infusion, and in a further two patients this occurred within 10 min. There was no observed change during the guanethidine infusion but only after the neostigmine was administered. This supports current theory that pseudo-obstruction is due to parasympathetic suppression rather than sympathetic overactivity. A further study is required to assess whether neostigmine alone would be as effective. Neostigmine alone has been used successfully for the treatment of idiopathic megacolon (15).

When conservative management of acute colonic pseudo-obstruction fails, other treatments tried include purgation, enemas, flatus tube decompression, colonoscopic decompression, surgery, and treatment with other drugs. It is difficult to compare our results with those of other methods of treatment because all reports are retrospective reviews with differences in patient selection, criteria for intervention, and outcome measures. Recognising this difficulty, our results compare favourably with the other treatment options in terms of efficacy and morbidity. Purgation, enemas, flatus tube decompression and transverse loop colostomy are ineffective (2). Caecostomy is of unpredictable efficacy and operative mortality is about 20% (10,11). Resection is indicated when perforation or intestinal ischaemia is present; in this situation, mortality approaches 50% (1,10,11).

Colonoscopic decompression has been advocated as the treatment of choice for acute colonic pseudo-obstruction (16). First reported by Kukora and Dent (17), many other reports testify to its efficacy of 70–80% (18–21). However, there is an overall repeat procedure rate of about 15%, colonic perforation rate of about 2%, surgical intervention rate of about 17%, and mortality rate of about 1% (18–21). Sloyer *et al.* (9) have challenged the need for colonoscopic decompression, emphasising that conservative management was successful in 96% of their cancer patients with acute colonic pseudo-obstruction. They emphasise that reports of colonoscopic decompression do not demonstrate a clear advantage over conservative management.

Drug therapy is an alternative method for hastening the resolution of acute colonic pseudo-obstruction. It can be argued that our 'cocktail' of guanethidine and neostigmine is crude and non-selective, thus leading to unacceptable extra-gastrointestinal effects. The ideal drug for treatment of acute colonic pseudo-obstruction should specifically enhance colonic motility with no extra-gastrointestinal effects. The prokinetic agent, cisapride, has been used in the treatment of chronic constipation (22), chronic idiopathic intestinal pseudo-obstruction (23), and acute colonic pseudo-obstruction (24). We have tried oral cisapride in two of our patients (before the guanethidine and neostigmine treatment), and we did not observe any change. This may be because we used the oral formulation—the successfully treated patient was given cisapride intravenously (24). Erythromycin, which is a motilin agonist, has also been reported recently for the treatment of a case of pseudo-obstruction (25).

Bowel-selective prokinetic agents will be a major therapeutic advance for acute colonic pseudo-obstruction. However, the guanethidine and neostigmine regimen was associated with acceptable morbidity in our series. There were no deaths attributable to the treatment, no caecal perforations, and the only significant adverse effect was an episode of postural hypotension which quickly resolved on lying the patient flat.

In conclusion, our good results, with minimal morbidity in carefully selected patients with secondary acute colonic pseudo-obstruction, lead us to recommend this pharmacological approach as an alternative to the other treatment options of colonoscopic decompression or surgery when conservative management has failed, or when expeditious resolution of the condition is required.

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Invited comment

This is an interesting and helpful contribution to the management of patients with colonic pseudo-obstruction. It is important to note the exclusion of patients with an unstable cardiac condition and possible side-effects of postural hypotension.

The original work by Neely and Catchpole achieved limited popularity possibly because of fear of anastomotic dehiscence. This fear is removed in patients with colonic pseudo-obstruction and it will be interesting to read

follow-up accounts to seek the regimen proposed here achieve more success in a group of patients who are otherwise destined to spend many uncomfortable days in an expensive hospital bed.

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