Review Article

Colonic Pseudo-obstruction: Contemporary Concepts and Practice

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Abstract: Acute colonic pseudo-obstruction is characterised by massive colonic distension without distal mechanical obstruction. It affects a wide variety of patients who often have multiple comorbidities, which makes studies on pseudo-obstruction difficult to perform and interpret. Few advances have been made in recent years in our understanding and management, which remain challenging. This article explores and provides interpretation of the key studies and concepts that have shaped our management of this condition.

Keywords: Colonic pseudo-obstruction; Ogilvie syndrome; neostigmine; decompression; caecostomy

Introduction

Acute colonic pseudo-obstruction was first described by Sir William Heneage Ogilvie in 1948, hence its eponymous name: Ogilvie's syndrome[1]. Ogilvie described two cases of malignancy causing interruption of sympathetic tone. Although inconsistent with pathophysiological concepts today, this gave rise to the idea of autonomic imbalance as a cause for colonic distension. Key management issues have always been the exclusion of mechanical obstruction and the reduction of caecal diameter to avoid perforation.

There are two management guidelines, with the latest released recently[2, 3]. They provide detailed overviews of the evidence in the management of pseudo-obstruction, but do not provide in-depth interpretation of the key studies. There is little new evidence in the most recent guidelines. This review aims to clarify the key studies on the management of acute colonic pseudo-obstruction as well as some finer points in management.

Definitions

Acute colonic pseudo-obstruction is an acute symptomatic form of megacolon, which simply describes colonic dilatation over 12 cm in the caecum, over 8 cm in the ascending colon, over 6 cm in the transverse colon or over 6.5 cm in the rectosigmoid colon[4]. Acute pseudo-obstruction should be distinguished from toxic megacolon, which may have inflammatory or infective causes, as well as chronic megacolon.

Chronic megacolon may be separated into problems arising in colonic inertia or rectosphincteric dyssynergy[4]. Causes may be acquired or congenital. Small bowel may be involved. Acquired causes include neurologic, systemic connective tissue disorders, metabolic, medication-induced or idiopathic. Chaga's disease is one such example, where infection with *Trypanosoma cruzi* causes destruction of the enteric nervous system. Idiopathic causes include non-familial visceral neuropathy (sporadic hollow visceral neuropathy or chronic idiopathic intestinal pseudo-obstruction). Congenital cases present in younger patients and are caused by various enteric and visceral neuropathies, of which Hirschsprung's disease is the most well-known[5].

Aetiology & Outcomes

Acute colonic pseudo-obstruction is associated with hospitalisation for acute medical or surgical illness (**Table 1**). The plethora of case reports in the literature is testament to the large number of possible underlying illnesses and the difficulty of studying treatment options in a heterogeneous patient group.

Table 1. Adapted from Table 2 of AGSe Guidelines[3]

Causes and Pre-disposing Factors of Acute Colonic Pseudo-Obstruction
Surgical
Intra-abdominal surgery Other (lumbar/spinal and other orthopaedic, obstetric, gynaecologic, urologic surgery)
Trauma
Retroperitoneal trauma Spinal cord injury
Medical
Advanced age Sepsis Inflammatory conditions Neurologic conditions Hypothyroidism Cardiac or respiratory disorders electrolyte imbalance (hypokalaemia, hypocalcaemia, hypomagnesaemia) Medications (opioids, tricyclic antidepressants, phenothiazides, antiparkinsonian drugs, anaesthetic agents) Renal insufficiency

The incidence and outcomes for acute pseudo-obstruction are difficult to measure. Much of what we know about associations and outcomes arises from a landmark retrospective study in 1986 by Vanek et al on 400 patients with acute pseudo-obstruction[6]. Non-operative trauma, obstetrics and gynaecology, orthopaedics, abdominal-pelvic surgery, infection, cardiac disease and neurological causes each contributed approximately 10% of cases. In surgical patients, it usually occurred 4 to 5 days postoperatively[6].

The mortality rate was 14% in those managed non-operatively and 36-44% in those managed surgically with perforated or ischaemic bowel. Patient comorbidities contributed significantly to mortality. While this is an older study prior to the use of neostigmine, pseudo-obstruction remains a condition associated with significant morbidity and mortality. Other studies estimate the risk of spontaneous perforation to be 3-15% with a mortality of 50% when this occurs[7].

Pathophysiology

The exact mechanism of acute pseudo-obstruction remains poorly understood. Current theory favours a relative excess of sympathetic over parasympathetic tone, leading to reduced contractility in the distal affected colon. This leads to a functionally obstructing distal colon and a relaxed and dilated proximal colon. However, the response of pseudo-obstruction to cholinergic agents like neostigmine suggests that the cause is due to excessive parasympathetic suppression rather than sympathetic over-activity[8].

Dilatation in most cases of pseudo-obstruction has a cut-off at the splenic flexure (56%), followed by sigmoid and descending colon (27%) and hepatic flexure (18%)[6]. This supports the theory of interruption to the parasympathetic fibres from S2 to S4 that leads to an atonic distal colon and a functional proximal obstruction[6]. The splenic flexure is the point at which parasympathetic innervation changes from the vagus nerve to the sacral nerves. However, there are cases of acute pseudo-obstruction where there has been no such interruption to these parasympathetic fibres.

The neurotransmitters associated with imbalance may include stimulatory ones such as acetylcholine, neurokinin A and substance P, or inhibitory ones such as vasoactive intestinal polypeptide and nitric oxide[9]. The lack of animal models for acute colonic pseudo-obstruction makes study of its pathophysiology difficult.

Based on Laplace's law, increasing the radius ($\mathbf{r}$) of the colon increases the tension (T) experienced by the colonic wall for a given intraluminal pressure (P). This leaves the caecum most vulnerable to ischaemia with subsequent perforation. Therefore, consideration of caecal diameter is important in management.

Diagnosis

Clinical Signs and Symptoms

Abdominal distension is the chief complaint, but it is non-specific. Evidence of chronicity, recurrent episodes and clinical

context helps to differentiate acute pseudo-obstruction from chronic and toxic megacolon. Symptoms may include nausea, vomiting, abdominal pain and constipation. Diarrhoea may occur paradoxically in some patients, but this should prompt consideration of *Clostridium difficile* infection as a cause of toxic megacolon.

The likelihood of ischaemia or perforation should be clinically assessed. Findings cannot be taken in isolation due to their lack of specificity. Abdominal tenderness, whilst invariably present in patients with ischaemia or perforation, may also occur in their absence[6]. It is common for the inflammatory markers such as the white cell count to be elevated regardless of ischaemia, so they are not predictive of ischaemia. Nevertheless, a finding of marked tenderness, fever and elevated inflammatory markers is highly suspicious for ischaemia or perforation.

Radiology

Imaging is crucial to establish a diagnosis of pseudo-obstruction and to rule out a mechanical cause. An initial plain abdominal radiograph is easy to obtain, can exclude other causes of abdominal distension, can diagnose perforation and provides a baseline caecal diameter for serial radiographs. It cannot reliably distinguish between a mechanical and functional obstruction[10].

Computed tomography (CT) scan has largely replaced the contrast enema study for the diagnosis of a large bowel obstruction[11, 12]. It is more readily available and gives more information. Oral contrast is not required, but intravenous (Iv) contrast is helpful in determining bowel viability. The presence of a transition point that is gradual rather than abrupt without an associated mass is typical for pseudo-obstruction, whilst an abrupt transition point with a mass lesion suggests a malignant obstruction[13]. Colonic distension is usually gaseous rather than faeculent in pseudo-obstruction. Diagnostic difficulty arises when there is focal mural thickening at the transition point without an obvious mass. Pericaecal stranding and caecal wall thickening are concerning for caecal ischaemia, whilst intramural gas suggests necrosis. Small bowel dilatation occurs occasionally and relates to an incompetent ileocaecal valve.

Use of rectal contrast during the CT scan is controversial. Critics fear the dehydrating effects of the hyperosmolar enema and the inability of elderly patients to hold the contrast long enough. Advocates consider the potential therapeutic effect[14] and its ability to better define the transition point. CT scan has 91% sensitivity and specificity in diagnosing large bowel obstruction without the use of rectal contrast[12]. However, this accuracy is only achievable through re-positioning the patient into a prone or lateral decubitus position to shift intra-colonic air during the CT scan to clarify a transition point. If a mechanical obstruction cannot be excluded on a CT without rectal contrast, then further study with contrast enema or even colonoscopy is warranted.

Radiological assessment of caecal diameter is important because of its association with perforation. In the retrospective study by vanek *et al*, no perforations occurred with a caecal diameter of less than 12cm, whilst 23% of those with a diameter greater than 14 cm suffered perforation or ischaemia[6]. The traditional 9cm caecal diameter cut-off arises from a study by Lowman and Davies[15]. They artificially inflated the caecum in 100 patients and noted that almost all had a diameter of 9 cm, thus concluding this to be the point of impending perforation. They then studied 19 patients with large bowel obstruction who had caecal diameters of over 9 cm: 12 had impending perforation and the remainder were perforated at surgery. Increased caecal diameter is a risk factor for perforation, but it should not be the sole determinant of management.

Management
Conservative Management

Despite the AGSe guidelines recommending just 24 hours of conservative therapy, most cases will resolve within three days[16]. Longer durations of conservative treatment will result in a greater proportion of patients resolving without intervention. However, the risk of perforation increases with duration of non-resolving symptoms. A time to decompression in excess of seven days is associated with a mortality rate of up to 73%, compared with 27% in those delayed four to seven days[6]. Therefore, duration of symptoms must be considered during clinical assessment and intervention after 48 hours without resolution would be reasonable if the caecal diameter is below 12cm and the patient is without signs of ischaemia or perforation[5]. Daily plain abdominal radiographs should be obtained to assess for worsening caecal distension. A

deterioration in clinical condition mandates prompt reassessment.

whilst both guidelines recommend a nasogastric tube in all patients with acute pseudo-obstruction[3], there is no evidence for this and it represents an aspiration risk. Therefore, selective use in patients with vomiting, nausea or gastric distension may be more appropriate. rigid sigmoidoscopy and rectal tube are also commonly used, but their therapeutic value is doubtful unless the distension extends to the rectosigmoid colon.

electrolyte disturbances, especially hypokalaemia, should be corrected. Underlying illnesses should be treated where possible. Any medications that inhibit colonic motility should be withheld: opioids, calcium channel blockers and anticholinergic agents. Bowel rest is recommended and gentle water enemas may be used, but the evidence for this practice is lacking[17]. Osmotic laxatives such as lactulose should be avoided due to increased gas production that may worsen colonic distension.

Decompressive Colonoscopy

Decompressive colonoscopy for the treatment of pseudo-obstruction that has failed conservative management has long since replaced tube caecostomy as the procedure of choice. It is inherently difficult and should be performed by an experienced endoscopist. The colon is unprepared and only minimal insufflation should be used where possible. For greatest efficacy, the hepatic flexure should be reached[18]. Once there, extensive suction of gas is recommended. A dual-channel colonoscope is preferable due to clogging of the suction channel.

The efficacy approaches 88% in patients non-responsive to conservative treatment after 48 hours, allowing for repeat therapy[18]. Perforation risk is about 2%. The advantages of decompressive colonoscopy over other modalities of decompression include the ability to exclude a distal obstructing lesion and to assess colonic mucosa for viability. A finding of necrosis mandates resection.

Placement of a decompression tube is controversial. Proponents recommend the insertion of a 140 cm enteroclysis tube with cut side-holes in the distal 20 cm at 2 cm intervals[19]. This is placed over a 480 cm Teflon-coated guidewire inserted through the colonoscopy. Alternatively, a ready-made kit such as the wilson-Cook® 14Fr Colon Decompression Set can be used. Fluoroscopy is necessary for guidance. This should be left in situ for about three days, placed on gravity drainage and flushed every six hours[3, 7]. Peristalsis will expel the tube - otherwise it should be removed manually. recurrence of up to 40% has been described in patients where no decompression tube was left[20, 21], although a more recent study seemed to show no such effect[22].

Neostigmine

Neostigmine is a reversible acetylcholinesterase inhibitor which promotes cholinergic activity in smooth muscle via muscarinic receptors[23]. Its use in acute colonic pseudo-obstruction was first described in 1993 in eight patients who had failed more than two days of conservative treatment[8]. All eight patients responded to a bolus of 2.5 mg IV neostigmine within 20 minutes, measured as the passing of flatus. Subsequent studies have proven its efficacy in pseudo-obstruction, but a sustained response is not guaranteed.

A meta-analysis from 2010 studied four randomised control trials (rCT) comparing neostigmine with placebo[24]. They found the overall effect of a single dose of neostigmine to be 89% compared with 15% for placebo in the resolution of pseudo-obstruction. However, there was significant heterogeneity in study design and some patients had ileus rather than pseudo-obstruction, making interpretation of results difficult.

The evidence base for the use of neostigmine comes from the seminal RCT by Ponec et al, where patients were randomised to neostigmine or placebo after 24 hours of conservative treatment[25]. Immediate resolution was achieved using neostigmine in 91% (10 of 11) with a median time of four minutes, with resolution measured as the passing of flatus or stool. Two of these patients (11%) had a recurrence of pseudo-obstruction requiring decompressive colonoscopy to give an overall success rate of 73%. In comparison, two of the 10 patients who received placebo treatment eventually responded to conservative measures, although many of the remainder had subsequent resolution with open label neostigmine administered three hours later. It is uncertain how many of these patients would have resolved without neostigmine if given a longer period of conservative management.

4

Use of a second dose of neostigmine when required is often described, but its use and timing remain uncertain[26]. Iv neostigmine has a short onset of action (<20 mins) and is short-acting (<2 hours)[7]. However, it has a half-life of 80 minutes and 50% of excretion depends on the kidneys[27]. Therefore, repeat doses must be used cautiously in patients with renal impairment.

The optimal initial dose and timing remain controversial[9]. whilst a 2mg bolus dose of Iv neostigmine may seem a more practical option, symptomatic bradycardia is thought to be more frequent than with an infusion[28]. Factors associated with non-response to neostigmine include use of anti-motility medications and electrolyte disturbances. Post-surgical patients are associated with greater response to neostigmine[26].

The most significant side effects are abdominal pain in over half of the patients, sialorrhoea and vomiting. Bradycardia is found in around 6% of patients undergoing neostigmine treatment[24]. The potential for bradycardia during the administration of neostigmine means cardiac monitoring should be applied and atropine (1 mg Iv) immediately available if required. Therefore, the contraindications are patients on beta-blockers and those with asthma or recent ischaemic heart disease.

Subcutaneous neostigmine has been tried and proposed as a safe alternative to Iv neostigmine[29]. It has been used without cardiac monitoring. If proven to be efficacious and safe in the near future, it would be highly advantageous over IV neostigmine.

Both guidelines recommend neostigmine as first line intervention after conservative treatment has failed[2, 3]. There is a perception that decompressive colonoscopy carries more risk to the patient than neostigmine[30]. Other reviews have suggested neostigmine treatment to be equivalent to decompressive colonoscopy depending on local resources[5]. One study found decompressive colonoscopy to be superior to neostigmine[22]. They found that colonoscopy was 75% effective after a single intervention compared with 55% for neostigmine. Furthermore, the risk of perforation was the same in both groups. However, this study was retrospective, the mean time to diagnosis was eight days, and some patients had crossover treatment. A RCT comparing neostigmine with decompressive colonoscopy is needed. Until then, the availability of adequate cardiac monitoring, appropriate staff and potential for repeat interventions needs to be weighed against the cost and availability of endoscopy.

Other Agents

Methylnaltrexone has been successfully used in a patient who failed to respond to two doses of neostigmine[31]. This patient was on opioids, and responded rapidly to this *mu* opioid receptor antagonist that does not cross the blood-brain barrier. Use of subcutaneous methylnaltrexone has been studied in RCTs on opioid-induced constipation in patients with advanced illness[32]. It has been shown to be efficacious, and there may be a role in pseudo-obstruction associated with opioid-use. Other agents that have been tried in acute pseudo-obstruction include erythromycin, metoclopramide, 5-HT4 derivatives (prucalopride) and pyridostigmine[9].

Preventing Relapse

relapse after decompression has been found to occur in up to 40%. Polyethylene glycol (PEG), an osmotic laxative, has been shown to prevent relapse after decompression in a RCT[33]. Thirty consecutive patients were randomised to receive either PeG or placebo (flour, sugar or vanilla powder). They all had relapses after successful colonoscopic or chemical decompression. 29.5 g of PEG was prepared in 500mL of water and administered in two doses daily for one week. No patients receiving PeG suffered from relapse, compared with one third of those on placebo. PEG may reduce the rate of nitric oxide production, which is a major inhibitory neurotransmitter released by enteric neurones[34, 35].

Surgical Management

For patients with pseudo-obstruction refractory to non-operative management, a caecostomy may be performed through a limited incision or laparoscopy[36]. Stamm-style placement of a Foley catheter or similar is the usual practice. Percutaneous endoscopic caecostomy has also been used successfully[37], but there is no evidence for the superiority of any approach. Catheter displacement and skin protection may be problematic postoperatively[38].

In cases of colonic necrosis or perforation, resection of the affected colon should be performed. A diverting stoma should

be strongly considered rather than primary anastomosis, as many of these patients have multiple comorbidities.

Conclusion

Acute colonic pseudo-obstruction remains a poorly understood condition that is associated with high mortality if left untreated. Most cases will resolve without intervention, but some will require decompression. There is good evidence for the efficacy of both colonoscopic decompression and neostigmine. Operative management is uncommon and a number of options are acceptable.

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