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Current Approaches to Diagnosing and Managing Constipation in Advanced Cancer and Palliative Care

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Abstract

Constipation is common in advanced cancer. Despite this, clinicians' understanding of the underlying changes affecting the colon and the rest of the gastrointestinal tract are limited. Two case histories are used to illustrate the problems encountered when the current approaches to diagnosing and managing altered bowel habits are unsuccessful. An alternative paradigm in which to consider the problems of constipation encountered by some people with advanced cancer is proposed.

Introduction

CONSTIPATION IS COMMON and often distressing in advanced cancer. Similar to "depression," which has both common usage and a specific scientific definition, the term "constipation" is confusingly used to both describe a symptom and a diagnosis. This problem is exacerbated by the disparity between patients' and health professionals' opinions. Patients tend to report constipation as any of several changes in their bowel movements. This contrasts with clinicians who usually describe constipation in terms of the stool appearance and frequency.

In the wider community, two constipation subtypes are recognized: functional or primary and secondary.¹ Functional constipation affects up to nearly 30% of the total population.^{2,3} Unlike secondary constipation, functional constipation has a consensus and diagnostic definition, the Rome Criteria⁴ (Table 1). In contrast, no agreed standards for definition and diagnosis of secondary constipation exist. Within palliative care, constipation is usually considered a result of multiple insults.

When adopting a palliative approach to symptoms, the initial, most logical step is to identify the dominant underlying pathophysiology then correcting or modifying this if possible. Even for people with advanced disease, this includes appropriate investigations when tolerable. Approaching constipation in this framework is handicapped by the sparse evidence that objectively identifies risk factors and underlying mechanisms. As a result, current approaches to investigating

and managing constipation are poorly evidence based. These problems are highlighted here.

Case Histories

Case 1

A 60-year-old woman with metastatic peritoneal sarcoma presents with 7 days of poorly localized cramping abdominal pain, nausea, bloating, and infrequent passage of flatus and stool. These were new problems and previously she had functioning independently and not requiring any regular medications. In particular, she did not have a past history of constipation. A bowel obstruction was suspected. Physical examination revealed mild, diffuse abdominal tenderness, audible soft bowel sounds, and a collapsed empty rectum. Investigations did not show hypercalcaemia or other abnormalities. On plain radiograph, the bowel was not dilated, there were no fluid levels but fecal material was visible in the entire ascending colon.

On this basis, intestinal obstruction was excluded and she was diagnosed with constipation. She was given sodium phosphate stat orally and rectally. Regular oral polyethylene glycol with electrolytes (PEG + E) three times per day was commenced.

She did not pass stool leading to a second radiograph 24 hours later, which was unchanged. Oral PEG + E was continued, with little response, for 3 more days, after which she started passing small amounts of brown liquid.

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TABLE 1. ROME CRITERIA FOR FUNCTIONAL CONSTIPATION

Diagnostic criteria for functional constipation with criteria fulfilled for the last 3 months and symptom onset at least 6 months before diagnosis

1. Must include two or more of the following:
 - a. Straining during at least 25% of defecations
 - b. Lumpy or hard stools in at least 25% of defecations
 - c. Sensation of incomplete evacuation following at least 25% of defecations
 - d. Sensation of anorectal obstruction or blockage during at least 25% of defecations
 - e. Manual manoeuvres to facilitate for at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor)
 - f. Fewer than three defecations per week
2. Loose stools rarely present without the use of laxatives
3. Insufficient criteria for IBS

IBS, irritable bowel syndrome.
See Longstretch et al., 2006.

Case 2

A 55-year-old independently functioning woman with stage IV ovarian cancer presented 2 weeks after completing her first course of chemotherapy with a 2-day history of constant lower abdominal pain, nausea, vomiting, and reduced frequency of passing flatus and bowel motions. She also was not receiving regular opioid or anticholinergic medications and reported no past history of constipation. At presentation, her abdomen was mildly distended and tender, without guarding. Bowel sounds were soft to auscultation and her rectum was empty.

Her investigations were unremarkable. Abdominal radiograph excluded bowel obstruction in the absence of air/fluid levels, but fecal material was visible in the descending colon. She was diagnosed with constipation and commenced on twice-daily PEG + E and lactulose 20 mL, with daily Micro-lax[®] enemas (Johnson & Johnson Pacific Pty, New South Wales, Australia). There was little result and she remained nauseated, finding it difficult to tolerate anything orally. Another radiograph 48 hours later only showed fecal material in the colon. A third radiograph 4 days showed some air-fluid levels without dilatation.

Discussion

These scenarios are commonplace but highlight how limited current understanding is of the problems that affect the bowel in advanced cancer and how this is best diagnosed and managed.

Likely causes of constipation

Based on the prevalence of functional constipation, up to 30% of people will come to their life-limiting illness with this problem, suggesting that this may be either the predominant cause of their constipation, changed bowel habits, problems or at least a significant contributing factor potentially exacerbated by systemic or local factors associated with their illness. Other lists of factors that potentially contribute to constipation are readily available in palliative care.⁵ The evidence that underlies such lists are variable. Opioid analgesia

is perceived as one of the most common causes, and as a result, the most attributed cause of constipation in advanced cancer. This was not so in neither case, nor were other contributing medications such as those with anticholinergic effects use. Some contributing factors include altered mobility and oral intake and sites of disease. To date, the evidence supporting performance status is inconclusive. Decreased oral intake has better evidence in other parts of medicine than in palliative care. Both cases had peritoneal involvement. Anecdotally, such sites of disease in gynecologic cancers are widely accepted as cause of disturbed gastrointestinal motility. The literature describes changes in motility of people with upper gastrointestinal stromal tumors, with reports suggesting these malignancies arise from the Cajal cells of the myenteric plexus.⁶ Peritoneal metastases from adenocarcinoma of the bowel are suggested to exert increased intra-abdominal pressure leading to gut wall oedema, a problem that causes disturbed transit.⁷ Last, paraneoplastic effects on the myenteric plexus or smooth muscle through the actions of tumor-specific antibodies affect motility. Paraneoplastic intestinal pseudo-obstruction has been reported in small cell lung cancer, thymoma, ovarian cancer, breast cancer, and neuroblastomas secondary to circulating ANNA-1 antibodies. Constipation alone is a very rare paraneoplastic phenomena.⁸

Plain radiographs to diagnose constipation?

In both cases, radiographs revealed fecal matter occupying different colonic segments. There was no clinical or radiologic evidence of bowel obstruction, rectal fecal impaction, paralytic ileus, or pseudo-obstruction at presentation. Plain radiographs when reviewed by experienced clinicians are likely to provide an accurate diagnosis of obstruction 66%–83% of the time⁹ leading to diagnoses of “constipation” by exclusion. Perhaps it is more accurate to conclude that only “bowel obstructions” were excluded.

The practice of diagnosing constipation with a plain radiograph assumes that the appearance of stool in the colon at one time point provides a reproducible marker of the passage of stool through the colon. Within a functionally constipated adult population, systematically reviewing the role of plain radiographs to diagnosis constipation led to the conclusion that the evidence is insufficient to recommend this.¹⁰ Other observations refute single plain radiographs to diagnose constipation. A convenience sample of 100 volunteers from a constipation clinic failed to confirm significant correlations between the degrees of fecal loading on plain radiograph, self-reported constipation symptoms, and objective measures of colon transit times.¹¹ There were wide ranges of interobserver variability with exact agreement in 18% of reports and complete disagreement noted in 10% of reports. Last, retrospective examination of abdominal radiographs previously taken to diagnose constipation in 144 palliative care inpatients failed to identify a correlation between a fecal loading score and a clinical diagnosis of constipation.¹²

The radiograph offers little more than a “snapshot” of the colon at that time and it is not possible to conclude if the appearance of a single radiograph is a normal variant for this person or if the presence of colonic matter is pathologic, resulting either from impaired gut function due to the bolus of the fecal matter itself or if the fecal matter is accumulating as a result of another more complex pathology.

Lack of response to laxatives?

In both cases, responses to trials of laxatives was unsatisfactory. According to the product information, the passage of frequent liquid stool is to be within 30 minutes after administration of a single dose of sodium phosphate liquid.¹³ Rectal administration of sodium phosphate liquid should result in the passage of stool within 2 to 3 minutes.¹⁴ The onset of laxative action of PEG + E depends upon the severity of the constipation being treated but it is expected that by the end of 3 days, up to 90% of people should have a response.¹⁵ In contrast, despite the ongoing use of two to three sachets per day for at least 5 days each, neither of the cases had such a response. The recommended doses of lactulose for constipation are 15 to 30 mL daily. At this dose, relief of constipation should be expected in 24 to 48 hours,¹⁶ again a response not witnessed in the case presented here. Lastly, a response to a Microlax[®] enema should occur within 30 minutes of administration.¹⁷ Although it could be argued that the choices of laxatives were inappropriate and alternative combinations such as senna may have been more palatable for these people, there are very limited data to support the superiority of one agent over another in any palliative care situation.¹⁸

In a functionally constipated population, failing to respond to laxative trial would prompt other investigations to better categorize the problem, either obstruction, slow transit or pelvic floor dysfunction.¹⁹ Both cases excluded obstructions, an imperative based on their symptoms. However subsequent investigations may have been useful to better define what changes actually underpinned their presentations. Colon transit times may be simply and cheaply measured by combining orally ingested radioopaque markers with plain radiographs to calculate the transit hours.²⁰ More costly approaches include scintigraphy or colonic manometry. Other specialized, invasive tests are required for assessing pelvic floor dysfunction, including balloon expulsion, anorectal manometry, and defecography.³ This standard approach in gastroenterology has not been explored in the constipation advanced cancer, despite the prevalence and severity of the problem.

Adverse effects of laxatives?

In this vacuum of understanding, questions are raised as to whether there may be detrimental effects by treating the people with laxatives when the undying problem is not clearly defined. Despite the frequency with which people with advanced cancer are prescribed laxatives, the data to describe laxative's adverse effects in this frail population are still sparse¹⁸ and no identified studies report the use of laxatives in people similar to those described in this paper and their clinical outcomes. Some data are available from 388 very unwell, intubated intensive care patients without paralytic ileus or obstruction (mechanical, pseudo-obstruction) in whom the use of placebo was compared to either lactulose or polyethylene glycol to induce defecation.²¹ Higher incidences of paralytic ileus and acute intestinal pseudo-obstruction occurred in the lactulose-treated group (5 versus 1), but this not a statistically significant difference. An increased incidence of colonic distension was noted in lactulose group. This occurs secondary to metabolism of lactulose by colonic bacteria into short chain fatty acids with the byproducts of hydrogen,

methane, and carbon dioxide that accumulate when intestinal passage is delayed. As these people were intubated, it is not possible to explore how this was experienced. Whilst this study was not of people with advanced cancer, it was of people with impaired gut transit due to the identified risks of opioid analgesia, gut oedema and immobility.²² Although not mentioned, the incidence of functional constipation in the whole community suggests that at least some of the participants must have some preexisting gut pathology.

Conclusion

It seems very logical to better explore the problem of constipation in advanced cancer this by examining the paradigms that already exist in gastroenterology. This would allow a clearer and more objective understanding of how the passage of gut contents in this patient group is affected. In turn, this would begin a process to develop a system that allows classification and grading of the different scenarios. Ultimately, the major goal is to develop a structure where interventions can be tailored to the underlying problem.

There are challenges to this process including assessing the impact of multiple confounding factors that may complicate gut function in this group and the problems associated with progressive frailty with advancing disease. However, given the costs and burdens associated with constipation, it seems more unethical not to consider evidence-based alternatives that could lead to improved comfort and quality of life.

Author Disclosure Statement

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