



Review Article

Postoperative Ileus in the Elderly[☆]

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ARTICLE INFO

Article history:

Received 23 December 2012

Received in revised form

26 April 2013

Accepted 2 August 2013

Available online 7 March 2014

Keywords:

ileus,
old age,
surgery

SUMMARY

Postoperative ileus is among the most common complications after surgery. Aging is associated with an increased colonic transit time, and anesthetic disturbance to colonic motility is often aggravated in the elderly. Postoperative ileus increases morbidity, prolongs the length of hospital stay, and constitutes a significant economic burden on the healthcare system. Multimodal enhanced recovery protocols, or fast-track surgeries, have been developed to improve postoperative recovery. Patient education, avoidance of perioperative fluid overload, selective use of nasogastric decompression, early ambulation, adopting a minimally invasive approach, early initiation of clear fluids, and gum chewing are all possible measures to reduce postoperative ileus. Thoracic epidural anesthesia is a well-established technique to hasten recovery, whereas insufficient data are available to ascertain the safety and efficacy of opioid-sparing analgesia in the elderly. The evidence is clear that traditional prokinetic medications are not helpful in the treatment or prevention of postoperative ileus. Early results suggest that alvimopan is a promising agent to reverse opioid-induced ileus. Since postoperative ileus is a multifactorial condition, a concerted effort is therefore necessary to prevent or decrease the duration of postoperative ileus using multimodal strategies.

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1. Introduction

Longer life expectancy has led to a large increase in the number of surgical procedures performed in elderly patients. Older individuals have significantly higher rates per population of both inpatient and outpatient surgical procedures, compared with other age groups¹. With aging, functional decline of almost every organ system results in a decreased physiologic reserve and ability to compensate for stress. Studies have shown that older patients with comorbidities are at a higher risk of in-hospital complications following surgery^{2,3}. Postoperative disturbances of gastrointestinal function (postoperative ileus) are among the most significant problems after abdominal and other types of surgeries. In this article, we review the pathophysiology, clinical implications, and management of postoperative ileus in the elderly.

2. Pathophysiology of postoperative ileus

The pathophysiology of postoperative ileus is multifactorial. Normal bowel function can be affected by three main mechanisms: neurogenic, inflammatory mediators, and gastrointestinal hormones⁴. Operation and anesthesia change one or more of these mechanisms, rather than altering bowel motility. Opening of the peritoneal cavity and manipulation of the intestine are the main factors. However, other factors can influence neuromuscular functions such as anesthesia, postoperative pain medications, and even aging⁵.

Three nervous systems regulate the motility of the gastrointestinal tract: the parasympathetic nervous system, sympathetic nervous system, and intrinsic nervous system⁶. Parasympathetic activity increases gastrointestinal motility, whereas the sympathetic system inhibits bowel function. The third system, intrinsic nervous system, is different in the colon from that in the small intestine. Since the smooth muscle in the colon lacks gap junctions, the colon does not exhibit synergetically peristaltic movements as the small bowel does. Therefore, it may take more time for the colon to recover its motility postoperatively. It is well known that

[☆] The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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the recovery of bowel motility occurs in a stepwise fashion: the small intestine first, the stomach next, and the colon last. The entire gastrointestinal tract takes 3–5 days to recover after a major abdominal procedure^{7–9}.

The major cause of postoperative ileus is operation itself. Two different phases have been identified after abdominal surgeries⁴. The first or early phase is mainly neurologic, which is evoked by abdominal surgery immediately and subsides within the initial 3 hours. An incision of the skin or a simple laparotomy wound will interrupt gastrointestinal motility due to sympathetic activation. After surgery, the sympathetic system tends to be more active than the parasympathetic system, which results in decreased motility and ileus¹⁰. However, neural factors fade away once the abdomen is closed. Other factors such as immune mediators that are released subsequent to tissue damage or inflammation play more important roles in prolonged postoperative ileus¹¹.

The second phase begins 3–4 hours after surgery and persists to inhibit gastrointestinal motility. Its duration is dependent on the nature of surgery. Intestinal manipulation would activate the macrophages present in the intestinal muscularis externa¹². This results in the release of cytokines and chemokines and influx of leukocytes into the intestine. Interestingly, in a murine model, muscle strips from the intestine of rats with postoperative ileus showed remarkable inflammation and infiltrating leukocytes¹³. This observation was confirmed in human studies¹⁴, suggesting that prolonged postoperative ileus correlates with the degree of inflammation. Immunological modulation of gastrointestinal motility is becoming an important area of research focusing on various gastrointestinal dysmotilities.

3. Effects of aging on gastrointestinal motility

In the elderly, gastrointestinal functions, including digestion, absorption, motility, and sphincter function, and immunity undergo various changes^{15–17}. Changes in diet or nutritional stress lead to not only a decrease of function of the gastrointestinal tract, but also a loss of adaptability. These changes may contribute to symptoms and even the development of malnutrition in older patients. It is noteworthy that delayed gastric emptying may increase the contact time of medication or toxin, and is often exacerbated by anticholinergic medications¹⁸.

Changes in small- and large-bowel motor patterns are associated with aging. Age-related neuronal losses occur in both the myenteric plexus and the submucosal plexus of the intestines^{19,20}. In the small intestine, relatively minor effects on manometric patterns with a decreased frequency of contractions after eating, reduction in the frequency of the migrating motor complex, and reduced frequency of propagated clustered contractions are observed²¹. Madsen and Graff²² used the gamma camera technique to determine gastric emptying, and small intestinal and colonic transit rates in 16 elderly people. They concluded that no significant alterations were observed in gastric and small intestinal motility in old people, but normal aging seems to reduce the propulsive capacity of the colon. In addition, physical inactivity may prolong the colonic transit time in the elderly population²³.

Takahashi and colleagues²⁴ found that advanced age is associated with diminished gene expression, and synthesis and catalytic activity of neuronal nitric oxide synthase in rats. Nitric oxide released from the myenteric plexus enhances colonic transit and facilitates propulsion of the colonic contents by mediating descending relaxation. This further explains the mechanism of delayed colonic transit in older people. Constipation is not uncommon in older patients²⁵. Intriguingly, an increased density of opioid receptors was observed in the colon of aged guinea pigs²⁶.

This finding is in line with the clinical observation that anesthetic disturbance to colonic motility is aggravated in the elderly.

4. Clinical impacts of ileus

Although the surgical technique and devices have improved with time, postoperative ileus remains one of the most common complications after abdominal surgery. Postoperative ileus is a frequent cause of prolonged hospital stay. As mentioned earlier, postoperative ileus is more evident in the colon. Usually, motility of the stomach and small intestine returns to normal within 12–24 hours after abdominal surgery²⁷. Nonetheless, 48–72 hours are required for the return of normal colonic motility. On the average, postoperative ileus lasts about 2–4 days for open abdominal procedures, while the duration is usually less than 2 days in laparoscopic surgeries²⁸. Furthermore, secondary ileus may result from complications of surgery, such as an anastomotic leak, abscess, or peritonitis.

Symptoms of ileus include abdominal distention, cessation of defecation, postoperative nausea, vomiting, tenderness, and abdominal cramps. It can prolong postoperative recovery, and may increase morbidity and mortality during the hospitalization. Abdominal distention may increase the risks of ventral hernia and wound dehiscence. Postoperative nausea and vomiting affect enteral nutrition and increase the risk of malnutrition, resulting in impaired wound healing. The use of nasogastric decompression and prolonged intravenous injection, when necessary, decreases ambulation of patients, and may increase the risk of pulmonary complications and thromboembolism.

Postoperative ileus not only prolongs the hospital stay of patients, but also increases the economic burden on the healthcare system significantly. Economic consequences include increases in labor costs for nursing staff and costs associated with equipment and supplies for intravenous hydration or parenteral nutrition, laboratory and radiological tests, and increased length of hospitalization^{29,30}. If oral intake is not possible, total parenteral nutrition may be required. The cost of total parenteral nutrition is 3.5 times higher than that of enteral nutrition, excluding the costs associated with central venous catheter placement and its related complications³¹. Based on the Dindo-Clavien classification, postoperative ileus is a Grade II (sometimes Grade III or higher) surgical complication, which may compromise patient outcomes³². Efforts to minimize postoperative ileus can help diminish the financial loading on hospitals, private and governmental health insurers, and the society.

5. Perioperative management to prevent ileus

The pathogenesis of postoperative ileus involves inhibitory neural reflexes and inflammatory reactions from the site of intestinal injury. With an increased understanding of the various components of the pathophysiological responses, the concept of multimodal postoperative rehabilitation, or fast-track surgery, has emerged as an important approach to improve postoperative recovery. Fast-track surgery programs are also known as enhanced recovery after surgery, or rapid or accelerated recovery after surgery programs. This approach employs a multimodal perioperative care pathway with the aim of attenuating stress response to surgery and accelerating recovery. Program members typically include surgeons, nurses, anesthesiologists, pain specialists, ward nursing staff, social workers, occupational, and physical therapy staff. In addition, patient education is of great importance in these multimodal fast-track programs. The use of this fast-track protocol is feasible in elderly patients, which may decrease the incidence of complications and duration of hospital stay^{33,34}.

5.1. Intravenous fluids

Administration of excess perioperative fluid can lead to intestinal edema, which may prolong the duration of postoperative ileus³⁵. Moreover, many elderly people have impairment of cardiac and pulmonary functions, and are more vulnerable to perioperative adverse cardiac events^{36,37}. One prospective study showed that cardiovascular optimization using esophageal Doppler reduced ileus significantly³⁸. Therefore, anesthesiologists and surgeons should pay increased attention to perioperative fluid management to avoid postoperative fluid excess.

5.2. Nasogastric decompression

Insertion of a nasogastric tube for gastric decompression after almost all abdominal surgeries has been a traditional maneuver. It is considered to have advantages such as lowering the risk of aspiratory pneumonia, protecting the intestinal anastomoses, and shortening the postoperative ileus. However, many randomized studies and meta-analyses have suggested that a nasogastric tube should not be used routinely^{39,40}. Inappropriate use may contribute to unnecessary morbidity, including pharyngolaryngitis and respiratory infection.

5.3. Early ambulation

Ambulation of postoperative patients has been encouraged to stimulate intestinal motility, which may decrease the duration of postoperative ileus. On the contrary, splanchnic blood flow decreases during exercise, which may result in alterations in the normal gastrointestinal function. Reduced walking capacity is associated with a higher risk of mortality in older women⁴¹. Currently, there is no evidence showing that physical exercise improves colonic motility⁴². Regardless of no demonstrable effect on expediting the resolution of ileus, early postoperative ambulation is still encouraged to prevent atelectasis, pneumonia, and venous thromboembolism, while preserving strength and conditioning.

5.4. Minimally invasive surgery

The use of minimally invasive techniques theoretically produces less tissue trauma and inflammatory responses, resulting in reduced postoperative pain, less need for analgesia, and usually a shorter hospital stay⁴³. It is difficult to determine whether the improvement in postoperative ileus is a result of the reduction of the inflammatory response, reduction of postoperative pain and opiates use, or a combination of additional factors. Decades of successful laparoscopic procedures in older patients have proved that despite underlying comorbidities, geriatric patients tolerate laparoscopic procedures extremely well⁴⁴. A minimally invasive surgery represents a major opportunity to reduce postoperative ileus and enhance recovery in the elderly.

5.5. Early enteral feeding

It has been suggested that early postoperative enteral feeding via oral or nasogastric administration may diminish postoperative ileus. The rationale is based on the assumption that early feeding evokes the reflex for coordinated propulsive activity and elicits the secretion of intestinal hormones. Feeding is one of the leading items correlated with self-rated health⁴⁵. Nonetheless, studies have failed to demonstrate a reduction of ileus in patients receiving early enteral nutrition⁴⁶. The true effect of early feeding on the duration of postoperative ileus is probably modest, but early enteral nutrition after bowel surgery is generally safe and well tolerated⁴⁷.

5.6. Sham feeding (gum chewing)

The use of gum chewing in the postoperative period is a safe method to stimulate bowel motility⁴⁸. The proposed mechanism is through stimulating a cephalic-vagal reflex in which cholinergic stimulation of the enteric nervous system results in propulsion and by inducing the secretion of various gastrointestinal hormones. For its low cost, safety, and simplicity, it is an attractive modality to prevent postoperative ileus.

5.7. Epidural anesthesia

It is well established that a continuous epidural anesthetic infusion is preferable to systemic narcotics and reduces the duration of postoperative ileus^{49,50}. A combination of general anesthesia and thoracic epidural anesthesia has become the technique of choice at many institutions for major abdominal surgery. Epidural anesthesia blocks afferent and efferent inhibitory reflexes, pain signals, catecholamine releases, and stress response to surgical trauma. Systemic absorption of local anesthetics may also have anti-inflammatory effects. A thoracic epidural is needed to block the sympathetic outflow. Thoracic epidural blockade also causes mesenteric vasodilation and, theoretically, may increase splanchnic blood flow. Recent evidence suggests that beneficial effects are also observed in major laparoscopic procedures⁵¹.

5.8. Opioid-sparing analgesia

Postoperative pain decreases patients' interest in and ability for mobilization, and interferes with the performance of breathing exercises. Given the inhibitory effects of opioids on bowel motility, various opioid-sparing analgesic techniques have been developed. Most evidence comes from the use of nonsteroidal anti-inflammatory drugs. The advantageous effect of these drugs, apart from the sparing of opioids, may also be related to their anti-inflammatory properties⁵². However, in elderly patients, the incidence of the gastrointestinal intolerance, an adverse effect of nonsteroidal anti-inflammatory drugs, is not negligible. In this regard, combining analgesics that have multiple mechanisms of action with nonpharmaceutical approaches can be beneficial⁵³.

6. Pharmacological therapy

Postoperative ileus has many causes; therefore, in general, the effectiveness of most single-modality strategies is limited⁵⁴. A multimodal rehabilitation approach will be necessary to have major improvement in terms of early resolution of postoperative ileus⁵⁵. Although several prokinetic drugs are available, including cholinergic receptor agonists (bethanechol and neostigmine), benzamides (cisapride and metoclopramide), dopamine receptor antagonists (domperidone), β -adrenoceptor antagonists (propranolol), and macrolide antibacterials (erythromycin), none has been found to be effective in preventing or treating postoperative ileus⁵⁶. Cisapride has been withdrawn from the market because of several reports of life-threatening cardiac events.

6.1. Laxatives

Laxatives have a theoretical role in the treatment of postoperative ileus due to their stimulatory action on the gastrointestinal tract. Few nonrandomized and randomized studies have shown that colon-stimulating laxatives have a beneficial effect on gastrointestinal recovery^{57,58}. Despite limited clinical evidence, laxatives may be used as a part of a multimodal postoperative treatment regimen.

Table 1
Strategies to reduce or prevent postoperative ileus.

Perioperative management
Avoid administration of excess fluid
Nasogastric decompression only when necessary
Early ambulation
Minimally invasive surgery
Early enteral feeding
Sham feeding
Epidural anesthesia
Opioid-sparing analgesia
Pharmacological approach
Laxatives
Somatostatin
Opioid antagonists
Hyperosmolar water-soluble contrast medium

6.2. Somatostatin

Somatostatin and its synthetic analogue octreotide may stimulate intestinal motility by inducing consecutive bursts of propagated clustered motor activity⁵⁹. Anecdotal reports demonstrated that octreotide can shorten the duration of ileus in experimental animal models^{60,61}. However, the effect of somatostatin analogs on postoperative ileus has not been evaluated in clinical trials.

6.3. Opioid antagonists

The pain control mechanism of opioids is through μ -opioid receptors in the central nervous system. The same μ -opioid receptors are also present in the gastrointestinal tract, and activation of these peripherally located receptors impairs bowel motility. Peripherally selective gastrointestinal opioid receptor antagonists have been developed to block these receptors without reversing the central analgesic effects. A recent review evaluating the effects of alvimopan, methylnaltrexone, naloxone, and nalbuphine suggests that both alvimopan and methylnaltrexone can reverse opioid-induced increased gastrointestinal transit time⁶². Alvimopan is the first drug approved by the Food and Drug Administration (in May 2008) to reduce time to gastrointestinal recovery and hospital discharge^{63,64}. The incidence of adverse events, observed to be mild to moderate, is similar to that reported with placebo. However, alvimopan is not recommended for use in patients with severe hepatic impairment or end-stage renal disease.

6.4. Hyperosmolar water-soluble contrast medium

Oral administration of water-soluble, hyperosmolar, radio-contrast material plays an important role in the diagnosis and management of adhesive small intestine obstruction. It may also be helpful in the resolution of postoperative ileus because of its laxative properties^{65,66}. The benefit is not consistent among studies⁶⁷, but its use is generally safe if mechanical obstruction is absent. For patients presenting with prolonged postoperative ileus, this modality can be useful diagnostically and possibly therapeutically.

7. Conclusion

Prolonged postoperative ileus is an iatrogenic phenomenon with significant influence on patient morbidity, healthcare costs, and the length of hospital stay. Chronological age is no longer a contraindication for surgical treatment. While older patients are increasingly candidates for surgery, many elderly people have various comorbidities, and combinations of such pathological conditions affect their physical and mental functions. These factors significantly complicate treatment of postoperative ileus in geriatric surgery patients. Ileus is a multifactorial condition, requiring

meticulous assessment and correction of physiological disturbances with the implementation of multimodal enhanced recovery protocols (Table 1). New pharmacologic agents such as μ -opioid receptor antagonists are being developed and have shown promising benefits in accelerating patients' recovery. The primary goal is to improve the safety of patient care, speed up recovery, reduce postoperative complications and deconditioning, and maintain high quality of life in the geriatric population.

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