
Postoperative ileus: a preventable event

[Review]

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Abstract

Background: Postoperative ileus has traditionally been accepted as a normal response to tissue injury. No data support any beneficial effect of ileus and indeed it may contribute to delayed recovery and prolonged hospital stay. Efforts should, therefore, be made to reduce such ileus.

Methods: Material was identified from a Medline search of the literature, previous review articles and references cited in original papers. This paper updates knowledge on the pathophysiology and treatment of postoperative ileus.

Results and conclusion: Pathogenesis mainly involves inhibitory neural reflexes and inflammatory mediators released from the site of injury. The most effective method of reducing ileus is thoracic epidural blockade with local anaesthetic. Opioid-sparing analgesic techniques and non-steroidal anti-inflammatory agents also reduce ileus, as does laparoscopic surgery. Of the prokinetic agents only cisapride is proven beneficial; the effect of early enteral feeding remains unclear. However, postoperative ileus may be greatly reduced when all of the above are combined in a multimodal rehabilitation strategy.

Introduction

Postoperative ileus is generally defined as a transient impairment of bowel motility after abdominal surgery or other injury. Clinically, it is characterized by bowel distension, lack of bowel sounds, and lack of passage of flatus and stool. Symptoms include nausea, vomiting and stomach cramps, and ileus is thus a major contributory factor to postoperative discomfort. Resumption of a regular diet and mobilization is delayed, and hospital stay is thereby prolonged. Ileus has traditionally been accepted as an obligatory physiological response to abdominal surgery, but the purpose of this response in the elective surgical setting has not been established and no data suggest a beneficial effect of the delayed postoperative recovery of gastrointestinal motility. Various pathogenetic mechanisms have been proposed and several pharmacological interventions have been employed to resolve ileus, but so far no single technique or agent has been found effectively to eliminate the problem.

In recent reviews [1-5](#) both pathophysiology and pharmacological treatment have been described, but none of these papers has addressed recent advances in perioperative management (including choice of anaesthesia, pain management, nutrition and mobilization) in an integrated multimodal approach. The present review updates knowledge on the pathophysiology and pharmacological treatment of postoperative ileus, and brings these data into the broader context of a multimodal anaesthetic, analgesic, pharmacological and nutritional rehabilitation strategy in an attempt to reduce ileus and improve postoperative outcome.

Definitions and methods of assessment

Not all segments in the gastrointestinal tract are equally affected by postoperative ileus. The average paralytic state lasts between 0 and 24 h in the small intestine, 24 and 48 h in the stomach, and between 48 and 72 h in the colon after major abdominal surgery. The effective duration of ileus is, therefore, mainly dependent on the return of colonic motility and, in particular, motility of the left colon [6,7](#). Ileus most commonly occurs after intraperitoneal operations, but it may also occur after retroperitoneal and extra-abdominal surgery. The duration is related to the anatomical location of surgery and the longest duration is encountered after operation involving the colon [8,9](#). The difference between right-sided and left-sided colonic procedures on the duration of ileus remains uncertain [10-12](#). In experimental and clinical studies ileus has been demonstrated to be related to the degree of surgical manipulation and the magnitude of the inflammatory response [13](#).

The definition of ileus and methods of assessment are not well defined. As an objective indicator of resolution, assessment of electrical activity has been widely used, focusing on either the return of the migrating myoelectric complex (MMC) or qualitative changes in MMC patterns. However, the MMC reflects mostly fasted state activity and some investigators have found no correlation between return of the MMC or specific MMC pattern and the clinical resolution of postoperative ileus [6,14](#). A correlation between some of the widely used clinical endpoints, such as bowel sounds, passage of flatus and stool, is also controversial. Bowel sounds are non-specific because they may originate in the small bowel as well as in the large bowel, and also require frequent auscultation for assessment. Passage of flatus is highly dependent on reporting by patients, and the correlation between passage of flatus and propulsive bowel movements is unclear [6](#). Passage of stool, although manifest as a clinical sign, is not specific, as it may indicate only distal bowel emptying and not necessarily the function of the entire gastrointestinal tract. Other frequently used endpoints include measurements of intraluminal pressure, migration of radio-opaque markers and non-invasive electrical measurements, such as percutaneous registration of electrical activity. Several investigators have found the clinical resolution of ileus to be relatively independent of these technical variables [15,16](#). As no single objective variable has yet been found accurately to predict resolution of ileus, the most adequate definition of resolution probably depends on a combined functional outcome of normalization of food intake and bowel function.

Pathogenesis of postoperative ileus

Inhibitory neural reflexes

Several inhibitory reflexes in the gastrointestinal tract have been proposed to mediate postoperative ileus, including somatovisceral and viscerovisceral reflexes [1](#). Three anatomically distinguishable reflexes seem to be involved: ultrashort reflexes confined to the wall of the gut, short reflexes involving the prevertebral ganglia, and long reflexes involving the spinal cord. The long reflexes are probably of most importance, since several experimental studies have shown spinal anaesthesia, abdominal sympathectomy and other nerve-cutting techniques to prevent or reduce the development of ileus [2,3](#).

Other experimental studies have demonstrated that selective degradation of splanchnic afferent neurones with capsaicin reduces ileus [17,18](#). This applies to both systemic administration and direct application at the prevertebral ganglia; perivagal administration is without effect [17](#). Furthermore, ablation of vagal fibres may not influence gastrointestinal transit after injury in contrast to spinal afferent fibre ablation [17](#). Several experimental studies suggest that the afferent reflexes originate primarily from the peritoneum and that skin incisions alone, unlike incisions through the peritoneum, do not provoke ileus [19,20](#).

In summary, inhibitory sympathetic reflexes are of major importance in the pathogenesis of ileus. This has substantial clinical implications as these reflexes are subject to modification by epidural blockade.

Neurotransmitters and inflammatory factors

A surgical operation elicits a stress response that is generally considered to be of combined endocrine and inflammatory origin. Although many neurotransmitters and neuropeptides are found locally in the gastrointestinal tract and might possibly contribute to ileus, they may also be released systemically following noxious stimuli or local inflammatory responses (the wound). So far, few comparative studies are available, but plasma changes in motilin and substance P may be related to depressed postoperative gastrointestinal motility [21](#). These findings, however, do not exclude the importance of local release of these substances.

Numerous transmitters and peptides are involved in regulating gastrointestinal motility and so may be involved in ileus. Nitric oxide, vasoactive intestinal peptide (VIP) and substance P have been established as inhibitory neurotransmitters in the intrinsic gut nervous system. Experimental studies have shown that VIP and substance P receptor antagonists, as well as inhibitors of

nitric oxide synthesis, improve postoperative gastrointestinal transit [19,22,23](#). Induced endotoxaemia in dogs leads to increased concentrations of products of VIP and nitric oxide synthesis combined with decreased gastrointestinal motility [24,25](#). Calcitonin gene-related peptide also inhibits postoperative gastric emptying and gastrointestinal transit, acting on specific peripheral receptors, possibly located in splanchnic afferent nerves or ganglia [17,26](#). Several studies have demonstrated that corticotrophin releasing factor (CRF) is involved in the pathogenesis of ileus, as intracisternal and intraventricular injection of CRF may delay postoperative gastrointestinal transit, which subsequently may be reversed by administration of specific CRF antagonists [27,28](#). Finally, opioids are well established as modulators of transmission in the central and peripheral nervous systems, leading to inhibition of gastric emptying and non-propulsive smooth muscle contraction with an increase in intraluminal pressure throughout the gastrointestinal tract [29,30](#). This effect is predominantly mediated by mu receptor agonists. Recent experimental studies have shown that selective peripheral kappa agonists may reverse ileus and gut paralysis following surgery or chemical peritonitis [31-33](#). Interestingly, experimental studies have also documented improved visceral pain relief by kappa agonists [32](#).

Little work has focused on the role of local inflammatory responses and cellular events in mediating ileus. Bauer's group has demonstrated, in a series of experimental studies, that the local inflammatory response is related to the extent of surgical trauma and degree of ileus [13](#). The effect may be mediated by leucocyte-derived nitric oxide [23](#), and is prevented by reducing the number of inflammatory cells locally [34](#). Furthermore, the paralytic gut response to surgery seems to be biphasic, consisting of a short temporary initial paralysis, followed by a longer-lasting impairment of muscle activity paralleling the local tissue concentration of inflammatory cells [35](#).

In summary, various neurotransmitters and inflammatory factors are known to be involved in the pathogenesis of postoperative ileus. However, their relative roles, as well as the hierarchical order and cooperation of these substances in the initiation and resolution of ileus, remain obscure.

Perioperative management

Anaesthesia

All anaesthetics used for induction or maintenance of general anaesthesia may depress gastrointestinal motility [36](#). However, the choice of general anaesthetic technique may have insignificant effects on ileus as even prolonged general anaesthesia in surface surgery does not lead to any clinically relevant reduction in bowel motility. The potential contributory effect of nitrous oxide to ileus has been evaluated in several clinical trials comparing nitrous oxide with isoflurane or propofol in abdominal surgery; it has not been found to be of clinical significance [37-39](#). A single dose of neural blockade with spinal or epidural anaesthetic alone or as a supplement to general anaesthesia does not influence the duration of ileus [40](#). The role of intraoperative short-acting opioids (alfentanil, remifentanil) on ileus is unknown, but is unlikely to be of clinical significance.

Analgesia

As noted above, it is well established that a surgical noxious stimulus leads to activation of inhibitory sympathetic splanchnic reflexes, and that the choice of analgesic technique may affect several aspects of the surgical stress response, including these inhibitory reflexes [40](#). After major abdominal surgery effective dynamic pain relief may be obtained only by a continuous epidural infusion that includes local anaesthetics [41](#). Analgesic treatment that includes opioids may prolong ileus, and the use of opioid-sparing analgesia with non-steroidal anti-inflammatory drugs (NSAIDs) or other analgesics (balanced analgesia) may reduce ileus.

Epidural analgesia

Theoretically, epidural blockade with local anaesthetics may improve postoperative ileus by several mechanisms: blockade of afferent and efferent inhibitory reflexes, efferent sympathetic blockade with concomitant increase in splanchnic blood flow, and anti-inflammatory effects via systemic absorption of local anaesthetics [42,43](#). Several randomized studies in patients undergoing abdominal procedures have evaluated the effect of epidural thoracic local anaesthetics compared with systemic opioids [44-51](#) ([Fig. 1](#)). Thus, in six of eight studies epidural bupivacaine significantly reduced ileus. In one statistically negative study [44](#) the duration of epidural analgesia was only 24 h, whereas in all other studies it was administered for between 48 and 72 h. In the other small, statistically negative study [51](#) a low thoracic (Th9-12) epidural blockade was used, which may not permit sufficient dermatomal blockade of noxious stimuli to improve gastrointestinal motility.

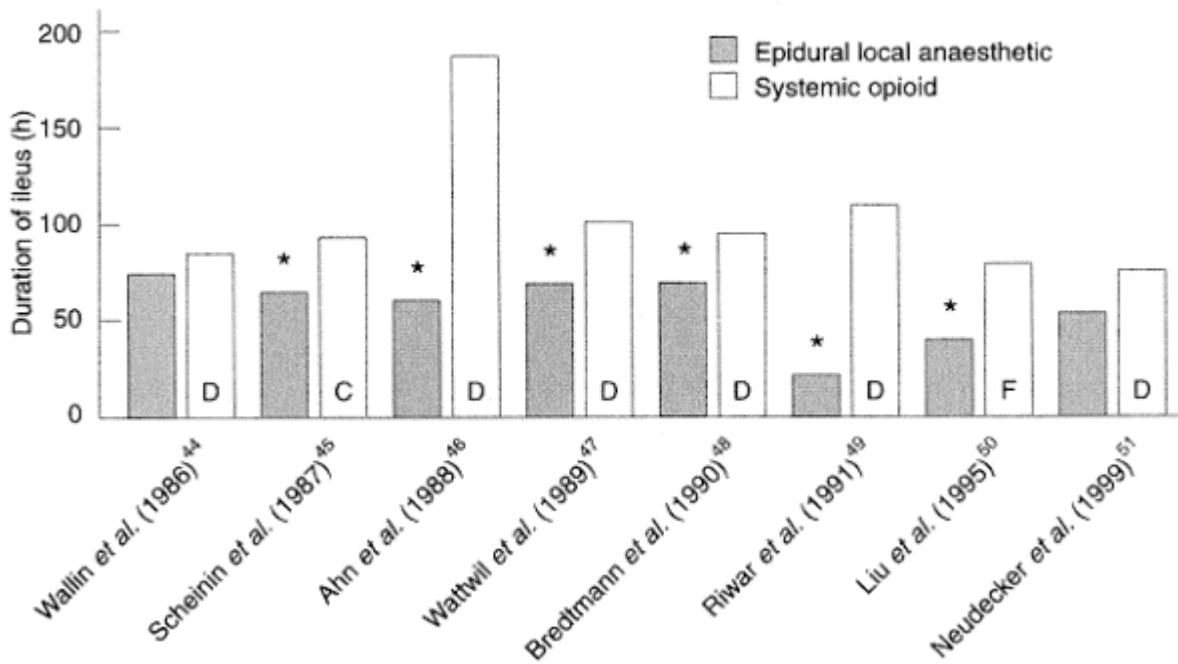


Fig. 1 Randomized clinical trials assessing the effect of epidural local anaesthetic *versus* systemic opioid on postoperative ileus. In all studies colonic surgery was performed, except Wallin *et al.*⁴⁴ (cholecystectomy) and Wattwil *et al.*⁴⁷ (gynaecological surgery). The various endpoints (defaecation (D), combination score (C) and flatus (F)) used to assess resolution of postoperative ileus are indicated. The combination score is defined as a combination of flatus and defaecation. In studies with assessments of both flatus and defaecation, defaecation was given a higher priority than flatus. * $P < 0.05$

Compared with epidural opioid or epidural bupivacaine plus low-dose opioid, epidural bupivacaine also led to a reduction in the duration of ileus [45,50,52,53 \(Fig. 2\)](#). Furthermore, the combination of epidural opioid plus low-dose bupivacaine may also reduce ileus compared with epidural or systemic opioid [50,53-58 \(Fig. 3\)](#). In one randomized study in hip surgery [59](#), the combination of intraoperative plus postoperative lumbar epidural local anaesthetics reduced ileus compared with general anaesthesia plus postoperative intravenously administered analgesia.

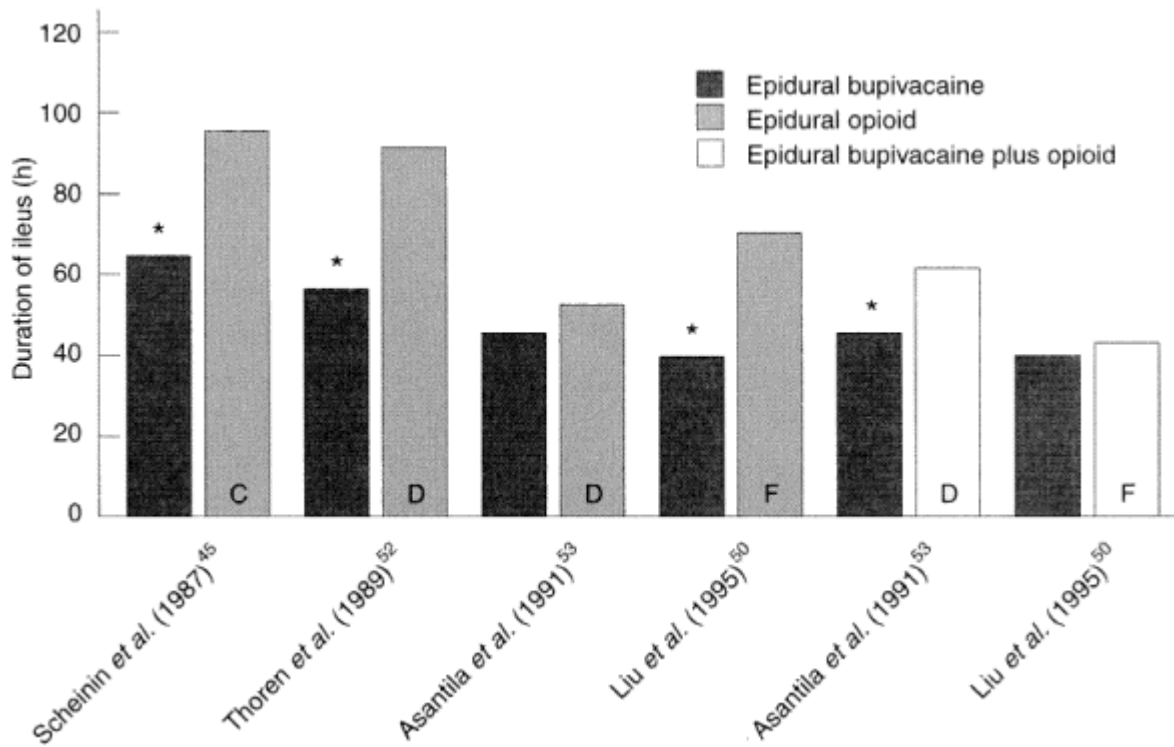


Fig. 2 Randomized clinical trials assessing the effect of epidural local anaesthetic *versus* epidural opioid or epidural local anaesthetic plus opioid on ileus. Two studies [45,50](#) were colonic and two studies [52,53](#) were gynaecological. The various endpoints (combination score (C), defaecation (D) and flatus (F)) used to assess resolution of ileus are indicated. The combination score is defined as a combination of flatus and defaecation. In studies with assessments of both flatus and defaecation, defaecation was given a higher priority than flatus. * $P < 0.05$

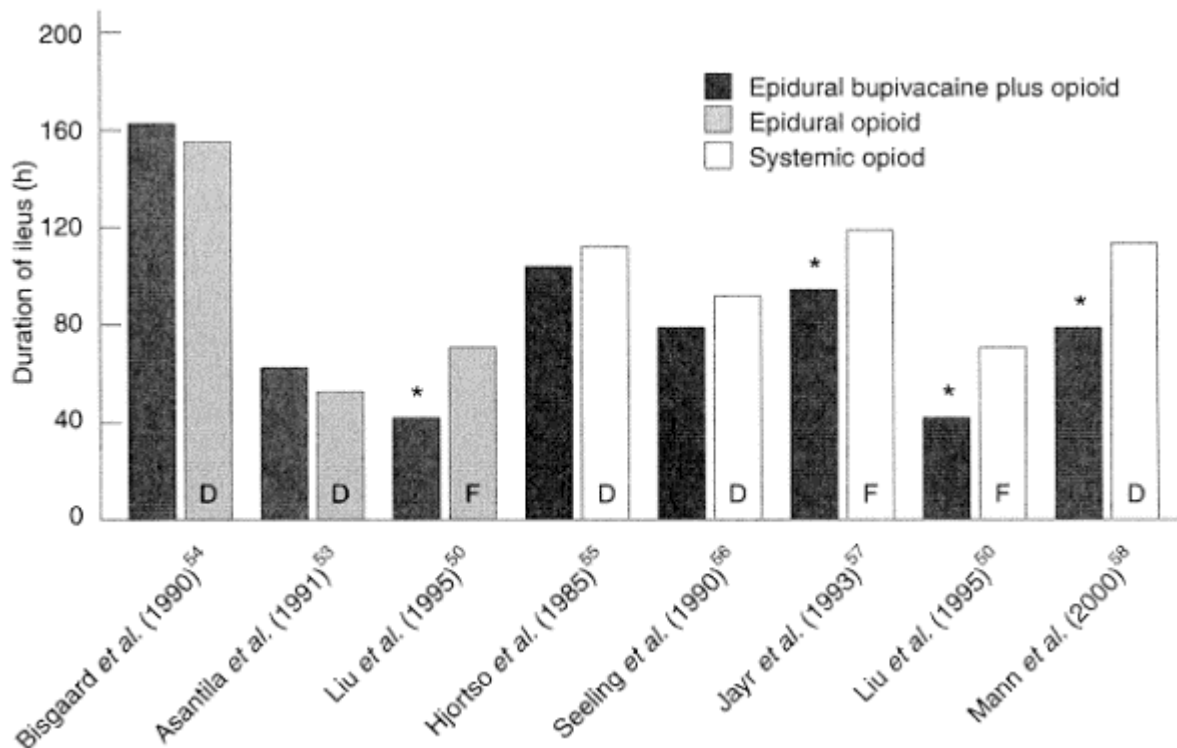


Fig. 3 Randomized clinical trials assessing the effect of a combination of epidural local anaesthetic and opioid *versus* epidural or

systemic opioid on ileus. In the studies demonstrating a positive effect of epidural local anaesthetic, thoracic epidural infusion was used. In the remaining four studies, epidural blockade was lumbar or not specified precisely. In all studies except that of Asantila *et al.*[53](#) (hysterectomy), major abdominal (not specified) and/or colonic procedures were performed. The various endpoints (defaecation (D), combination score (C) and flatus (F)) used to assess resolution of ileus are indicated. The combination score is defined as a combination of flatus and defaecation. In studies with assessments of both flatus and defaecation, defaecation was given a higher priority than flatus. * $P < 0.05$

The established positive effect of epidural local anaesthetic administration is related to the segmental visceral afferent/efferent blockade which, in abdominal surgery, can be obtained only by thoracic application of the local anaesthetic. Not surprisingly, studies using lumbar or low-thoracic epidural administration of local anaesthetics have not demonstrated the positive effects of epidural analgesia on ileus [44,51,54,55](#).

Experimental studies have shown that local anaesthetics inhibit the development of chemical peritonitis following hydrochloric acid administration [60](#) and shorten bowel paralysis after ischaemia [61](#). However, clinical studies using intraperitoneal or systemic (intravenous) administration of local anaesthetics have been inconclusive with regard to both analgesic effects [62](#) and to any potentially advantageous effect on the resolution of postoperative ileus [16,62,63](#).

Opioid analgesia [✚](#)

It is well known from experimental studies that opioids have a profound inhibitory effect on resting and post-traumatic gastrointestinal motility [30,31](#). These effects are primarily seen during systemic opioid administration with intravenous patient-controlled analgesia, conventional intramuscular opioid administration or epidural opioid administration [11,29](#). Pain relief apart, there is a major difference between the effects on ileus of these opioid administration techniques and techniques involving local anaesthetics.

Findings from experimental studies demonstrate that kappa opioid agonists may provide sufficient visceral analgesia [32](#) as well as reduce ileus [31,33](#), but this has not been studied in the clinical setting. The effects of a kappa opioid agonist (fedotozine) on pain and bowel function in a nonsurgical setting, irritable bowel syndrome, have been negative [64](#). Recent studies in chronic methadone users suggest that peripheral opioid antagonists (methylnaltrexone) may reverse the opioid-mediated inhibition of gastrointestinal function [65](#), with possible future implications in the surgical setting.

Opioid-sparing analgesia [✚](#)

Based on knowledge of the inhibitory effects of opioids on gut motility, various opioid-sparing analgesic techniques have been developed to avoid the undesirable sequelae of opioid administration in the postoperative period (drowsiness, nausea and vomiting, inhibition of bladder function)[66](#). One of the most established techniques of obtaining a 20-30 per cent sparing of opioid is pain relief with NSAIDs [67](#). In both experimental and clinical studies, the administration of NSAIDs and the subsequent opioid-sparing effect has, in most but not all studies, resulted in less nausea and vomiting and improvement in overall gastrointestinal motility [15,20,68-70](#). Similar effects have been obtained with different types of NSAIDs, although no data are available to compare cyclo-oxygenase (COX) 1 *versus* COX-2 inhibitors. The advantageous effect of NSAIDs, apart from the sparing of opioid, may also be related to a direct anti-inflammatory effect mediated by the inhibition of prostaglandin synthesis [68](#). The effect of other types of opioid-sparing analgesia (ketamine, paracetamol, tramadol, etc.) has not been finally established.

Nasogastric intubation [✚](#)

The insertion of a nasogastric tube has been the traditional supportive treatment for postoperative ileus, but it does not shorten time to first bowel movement or time to effective oral food intake [71,72](#). Many randomized clinical studies and a meta-analysis have concluded that a nasogastric tube should not be used routinely, and that unnecessary use may contribute to postoperative morbidity such as atelectasis, pneumonia and fever [71,72](#).

Mobilization [✚](#)

Contrary to popular belief, physical exercise does not improve colonic motility in healthy volunteers [73](#). Neither does mobilization of itself shorten the duration of postoperative ileus; recovery of myoelectrical activity is similar in patients mobilized from day 1 compared with day 4 after major abdominal surgery [74](#). However, the commonly practised prolonged immobilization after surgery has never been proven to be beneficial [75](#). In fact, prolonged bedrest may enhance the risk of postoperative complications and prolong recovery [41,76](#), and so should be avoided for reasons other than recovery of gastrointestinal function.

Early postoperative oral feeding [77](#)

Food intake elicits a reflex response that is propulsive in action. Several intestinointestinal reflexes connecting various parts of the gastrointestinal tract respond to food intake, producing coordinated propulsive activity [77](#). In addition, the presence of food stimulates the secretion of various intestinal hormones, with an overall stimulating effect on gastrointestinal motility [77](#).

Traditionally, oral feeding has been delayed after laparotomy until any ileus has resolved clinically. At that point a liquid diet is administered, gradually progressing to solid food. Patients undergoing major abdominal procedures often have at least 4 or 5 days of semistarvation or total starvation. This is unfortunate because semistarvation contributes to catabolism and so to fatigue and prolonged convalescence [41](#). Furthermore, several randomized clinical studies have shown that early enteral nutrition may improve immune function and reduce postoperative and posttraumatic infectious complications [78](#).

Early uncontrolled studies by Moss [79](#) found that ileus was resolved within 48 h when patients received immediate enteral nutrition. Unfortunately, it has been only recently that the traditional restriction of early post-operative oral intake has been questioned seriously; several trials have shown the institution of early enteral feeding both to be safe [80-86](#) and to reduce postoperative ileus ([Fig. 4](#)). One study of 80 patients undergoing colorectal surgery and randomized to either early enteral feeding or conventional fasting showed that the early fed group tolerated a regular diet 3 days before the later fed group. The former were discharged from hospital 2 days before the traditionally fed group [88](#). Another study of 96 gynaecological patients demonstrated that an earlier fed group tolerated solid diet 1 day before a group receiving traditional feeding; the former were discharged 1 day sooner too [87](#). Two other studies involving gynaecological patients have similarly demonstrated a reduction in ileus in early fed groups [89,90](#), although in one of these studies [89](#) the positive effect was noted in only some of the assessed variables (return of bowel sounds and hospital stay).

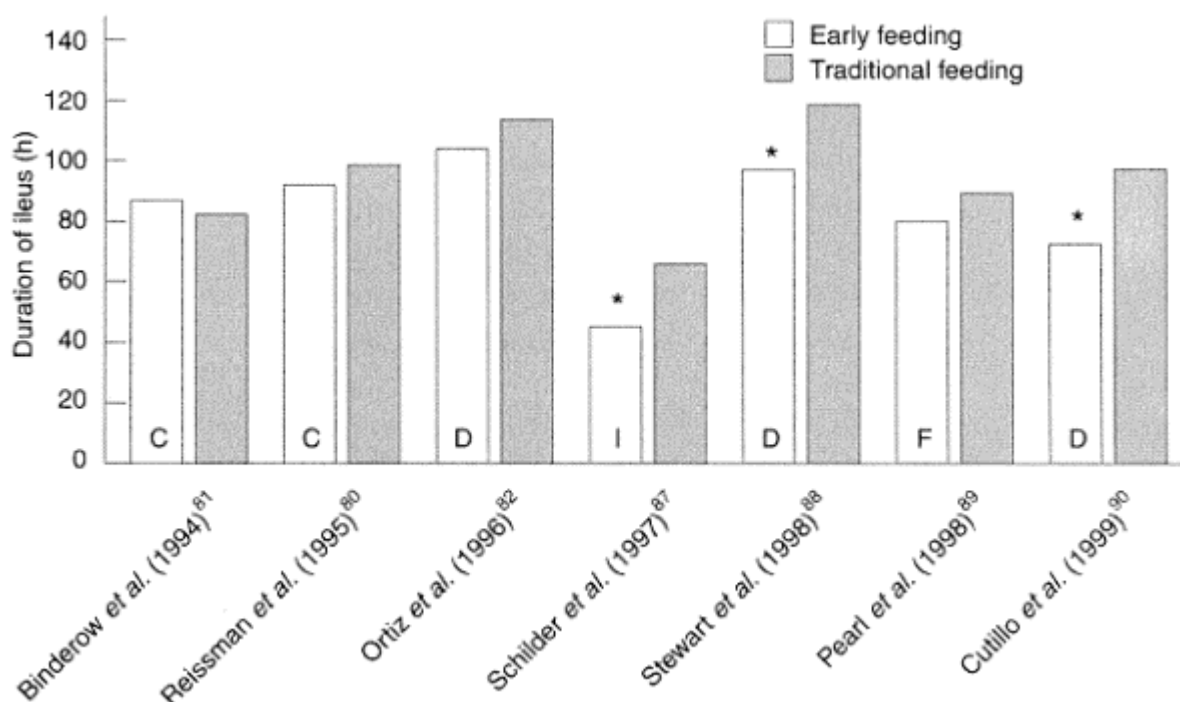


Fig. 4 Randomized clinical trials assessing the effect of early enteral nutrition *versus* traditional feeding (consisting of no oral intake until clinical resolution of ileus or of only liquid oral intake) on resolution of ileus, except Heslin *et al.* [91](#), which is

discussed in the text. Three studies [87,89,90](#) were performed in gynaecological patients and the rest in abdominal (not specified or colonic) surgery. As indicators of ileus various endpoints (combination score (C), time to tolerate regular food (I), passage of flatus (F) and defaecation (D)) were used. The combination score is defined as a combination of flatus and defaecation. In studies with assessments of both flatus and defaecation, defaecation was given a higher priority than flatus. * $P < 0.05$

In contrast, two other recent trials [91,92](#) investigating the effect of early oral feeding have demonstrated no difference in either length of ileus or hospital stay. In one of these studies impairment of pulmonary function and postoperative mobilization with early oral feeding was noted [92](#). Of importance, however, in these and other oral feeding studies is that the type of analgesia was rarely reported and, when mentioned, usually consisted solely of opioids and rarely of epidural local anaesthetics [80-85](#). Thus the established stimulatory effect of solid food on intestinal motility may not have been obvious as the profound inhibitory effect of opioids on motility may have dominated. The proven beneficial effects of continuous epidural local anaesthetics, opioid-sparing analgesics and cisapride have unfortunately not been incorporated in previous controlled clinical studies of early enteral nutrition. Future well designed studies are required to evaluate the potential benefits of early enteral nutrition when combined with regimens aimed at early resolution of postoperative ileus.

Laparoscopic surgery [4](#)

Experimental studies comparing laparoscopic with open cholecystectomy have shown that the laparoscopic approach improves gastric emptying and fasted state gastrointestinal motility [14,93](#). However, ileus is clinically non-existent after laparoscopic cholecystectomy [94](#) and so these results are not applicable to major abdominal procedures. In experimental studies in colonic surgery, the laparoscopic technique leads to earlier return of gastrointestinal motility as well as earlier normalization of myoelectrical activity and bowel movement compared with open colectomy [95,96](#). The mechanisms involved may include reduced activation of inhibitory reflexes and local inflammation due to a reduction in surgical trauma [13](#).

In clinical studies, earlier resolution of ileus has been demonstrated following laparoscopic colonic surgery. Four prospective randomized clinical studies comparing laparoscopic and open colonic techniques have shown a reduction in postoperative ileus with the laparoscopic method in two of three studies in which it was assessed [97-99](#) ([Fig. 5](#)). However, in a broader context the difference between laparoscopic and conventional abdominal surgery with respect to ileus remains to be clarified; expectations may have led to treatment bias favouring earlier food intake and less routine use of nasogastric tubes in laparoscopic groups.

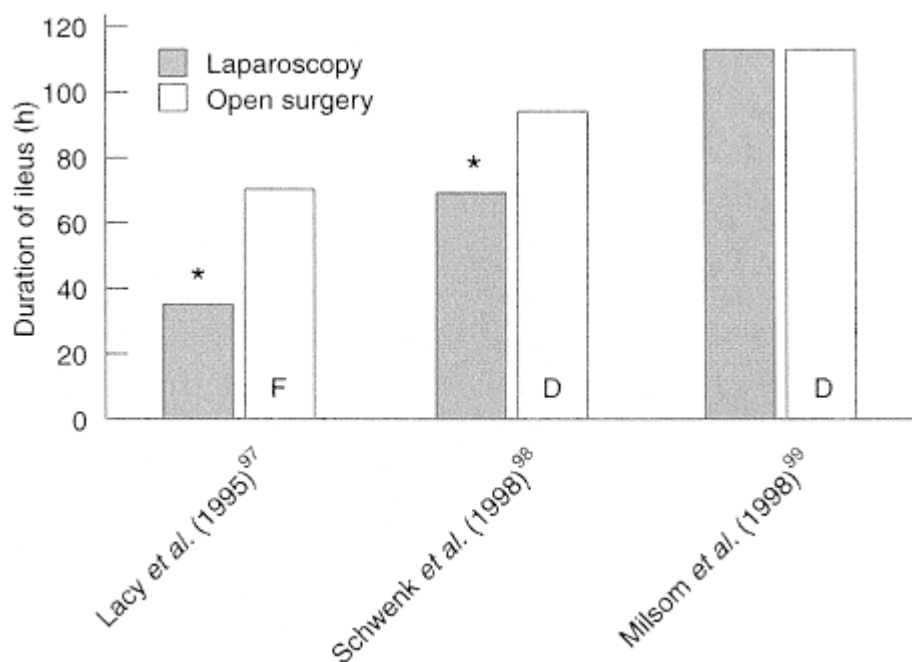


Fig. 5 Randomized clinical trials comparing the effect of laparoscopic *versus* open colonic surgery on ileus. F=flatus, D=defaecation. * $P < 0.05$

Prokinetic agents [†]

Cisapride [†]

Cisapride enhances acetylcholine release from the intrinsic plexus and acts as a serotonin receptor agonist; it may stimulate all aspects of gastrointestinal motility [100](#). Nine randomized controlled clinical trials have been performed on postoperative patients [101-109](#) (Fig. 6). In one study, however, patients (neonates) were included only after an initial 10-day period of ileus [109](#). In four studies cisapride significantly reduced ileus; it was administered intravenously in three of them. In one of these studies [107](#) 43 per cent of patients undergoing various abdominal operations had flatus 2 h after the intravenous administration of cisapride 4 mg, compared with 12 per cent in the control group. In another study on postoperative patients [108](#) 55 per cent had flatus 4 h after the intravenous administration of cisapride 8 mg, compared with 29 per cent of patients receiving placebo. In only one clinical trial [105](#) was cisapride administered orally; ileus was reduced from 4.8 to 3.7 days. In three of the four remaining (negative) studies, cisapride was administered rectally. These results suggest that the beneficial effect of cisapride on ileus depends on the route of its administration, favouring intravenous or, possibly, oral administration in the postoperative period. However, adverse cardiac effects may occur with cisapride, which may therefore be contraindicated in high-risk patients [110](#).

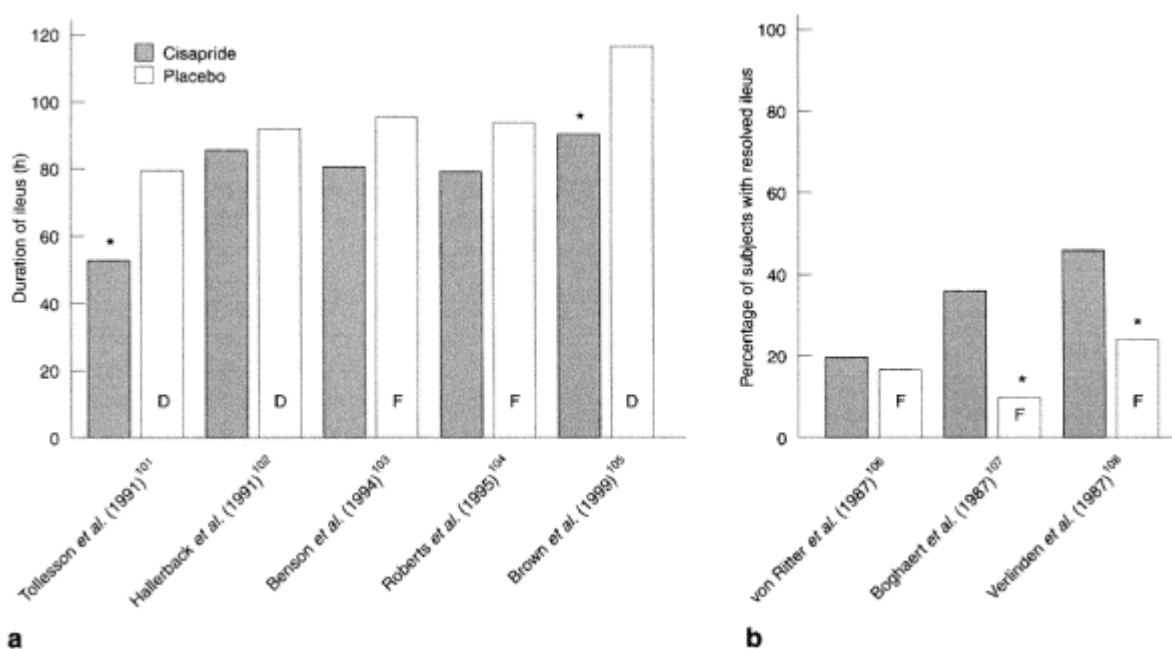


Fig. 6 Randomized clinical trials evaluating the effect of cisapride on **a** duration of ileus and **b** percentage of subjects with resolved ileus. Various indicators of postoperative ileus (flatus (F) and defaecation (D)) and were used as well as various doses of drug (4-30 mg administered for between 1 and 7 days) and various routes of administration (intravenous, rectal and oral). In all studies, patients underwent various abdominal (not specified) or colonic procedures. In studies with assessments of both flatus and defaecation, defaecation was given a higher priority than flatus. * $P < 0.05$

Ceruletide [†]

Ceruletide is a synthetic peptide whose cholecystokinin antagonist activity may stimulate gastrointestinal motility. In two clinical placebo-controlled studies ceruletide has been found to reduce ileus slightly [111,112](#). However, side-effects such as nausea and vomiting, which may require additional antiemetic treatment, limit the potential use of ceruletide. Further studies are necessary on other cholecystokinin antagonists before clinical recommendations can be made.

Erythromycin [†]

Erythromycin stimulates the motilin receptor and so may induce a MMC. However, the only existing prospective clinical randomized study found no effect of postoperatively administered erythromycin on ileus after abdominal surgery [113](#).

Metoclopramide [†]

Metoclopramide may potentially influence gastrointestinal motility by acting as a dopamine antagonist, as well as by direct and indirect effects on cholinergic and serotonergic receptors throughout the gastrointestinal tract. Six controlled clinical studies exist in patients undergoing abdominal surgery to assess the effect of metoclopramide on ileus. In three of the studies endpoints such as bowel sounds, food intake and defaecation were assessed [114-116 \(Fig. 7\)](#). Of the remaining three studies, one assessed ileus with a functional combination score [117](#). In another [118](#), the study population was divided according to the median drug dose received, and in the third study [119](#) the number of patients with bowel sounds in each group was counted after 2 days. Despite the variety of endpoints, none of these studies has demonstrated a significant effect of metoclopramide on the resolution of postoperative ileus.

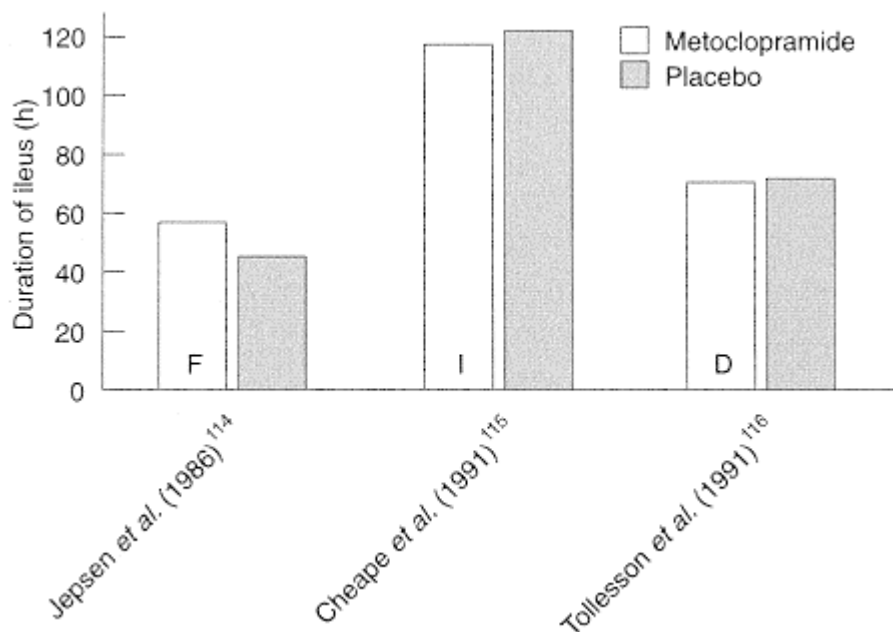


Fig. 7 Effect of metoclopramide on ileus. Three of the existing six clinical trials are shown. The remaining three studies are discussed only in the text, owing to the great variety of endpoints assessed and statistical analyses. Surgery was aortic [114](#), various abdominal [115](#) or cholecystectomy [116](#). Indicators of ileus were flatus (F), time to solid food intake (I) and defaecation (D)

Somatostatin [†]

Somatostatin is known to inhibit the secretion of gastrointestinal hormones. In experimental studies the somatostatin analogue, octreotide, has been shown to enhance colonic transit and to restore interdigestive myoelectrical complexes [21,120](#). The effect of somatostatin analogues on postoperative ileus has not been investigated in clinical studies.

Adrenoblockers [†]

Although inhibitory reflexes mediated by sympathetic visceral afferents are important in the development of ileus, the effect of adrenoblocking agents in reducing ileus in the clinical setting has been rather limited [121,122](#). It is probably clinically insignificant.

Laxatives [†]

Despite the wide use of laxatives with prokinetic effect in non-surgical patients, no randomized clinical study exists to assess the possible beneficial effect of postoperative laxatives on ileus. In fact only one clinical study (unblinded and nonrandomized) has assessed the effect of postoperatively administered laxatives (magnesia and bismol suppositories) and this was in 20 consecutive

gynaecological patients [123](#). The duration of ileus in the treated group (time to flatus and bowel movement) was 3 days. Furthermore a 50 per cent reduction in length of hospital stay (4 *versus* 8 days) was noted.

Conclusion [↑](#)

Several prokinetic drugs are available, but so far none has been found effective in the elimination or reduction of postoperative ileus, with the exception of cisapride. However, as a sole agent, cisapride is likely to be of limited clinical relevance, although it may be useful in conjunction with other techniques.

The future [↑](#)

In the future we must consider a multimodal concept of controlling perioperative pathophysiology, postoperative ileus and rehabilitation. The pathogenesis of ileus involves mainly inhibitory neural reflexes, and inflammatory mediators and neurotransmitters from the site of intestinal injury. Effective pain relief with continuous thoracic epidural local anaesthetics is the most important method of reducing ileus. It appears that several techniques, when studied individually, may reduce the duration of ileus without eliminating the problem. A rational treatment would therefore be a combination of avoidance of the routine use of nasogastric tubes, the use of a continuous thoracic epidural local anaesthetic regimen for at least 48 h, the use of additional opioid-sparing analgesia, and routine early oral nutrition. Other additional methods may be supportive, for instance cisapride and the use of a laparoscopic technique. Unfortunately, no randomized studies are available to document the validity of this multimodal concept, but several case series suggest that such an approach may significantly reduce, or even eliminate, ileus after colonic surgery.

Sixty consecutive patients scheduled for elective open colorectal surgery participated in an accelerated rehabilitation programme. Their median age was 74 years and 33 per cent were American Society of Anesthesiologists grade III or IV. Analgesia consisted of continuous thoracic epidural blockade with local anaesthetics over 48 h, combined with systemic paracetamol and ketorolac. Nasogastric tubes were removed immediately after surgery and oral food intake was started on the day of operation. The patients were mobilized within 8 h of surgery. The median hospital stay of these unselected patients was 2 days and ileus was considered to be significantly reduced, as 95 per cent of the patients tolerated normal food and had defaecation within 48 h of operation [124,125](#). Similar results have been found in a group of 17 patients undergoing elective colonic surgery; 12 passed stool within 48 h, despite the fact that several patients received morphine after operation [126](#). Thirty-nine patients undergoing laparoscopic colonic surgery participated in a similar programme and 35 had normal bowel function on day 2 after operation [127,128](#). The combination of epidural anaesthesia and analgesia and of a standardized care protocol has also been found to reduce the duration of postoperative ileus and hospital stay by 1 day, compared with other analgesic techniques, in patients undergoing elective colorectal surgery [50,129](#).

In conclusion, these preliminary findings suggest that a multimodal rehabilitation approach may result in a major improvement in terms of early resolution of postoperative ileus. Further trials are needed to document efficacy with respect to different types of operation, safety and the potential for reducing overall postoperative morbidity and cost.

Acknowledgements [↑](#)

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