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POSTOPERATIVE ILEUS: ARE THERE ANY CHANGES IN ITS MANAGEMENT?

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Abstract

Postoperative ileus (POI) is an inevitable adverse consequence of abdominal and other surgical procedures. Prolonged POI can lead to slow postoperative recovery, add to the patients discomfort and ultimately prolonged hospitalization and increased costs. It is believed that POI occurs as a result of inhibitory neural reflexes and inflammatory processes. The potential influence of endogenous opioids, in addition to exogenous opioids on the pathogenesis of POI has become more evident. The traditional routine use of nasogastric suction and the effects of prokinetic agents has been studied more and either challenged or refuted. Current treatment modalities, which are well studied includes the use of epidural long-acting local anaesthetics, early enteral feeding, multimodal postoperative care pathway, and less invasive surgical procedures. Recent research showed the usefulness of the newly introduced medications among the most promising is the peripherally acting *μ-opioid antagonist*.

Introduction

The latin word ***ileus*** originated from the Greek term ***Ieleos*** – intestinal colic, which is derived from the verb ***eilein*** – to squeeze or roll up tight[1]. This term obviously, is not accurate description of postoperative ileus, since it is functional rather than a mechanical disorder. Because of the lack of an accepted definition, ***postoperative ileus (POI) is known as a transient impairment of gastrointestinal (GI) motility after abdominal or other surgery***[2]. It is clinically characterized by abdominal distension, lack of bowel sounds, accumulation of gas and fluids in the bowel, and delayed passage of flatus and daefecation that might result in nausea and vomiting. Although accepted as inevitable, POI does not seem to serve any useful purpose. On the contrary prolonged POI contributes to several undesirable consequences to the patient, and increase hospital stays and subsequent health-care costs.

Physiological control of Gastroinestinal motility

Normal bowel function requires the coordination of motility, mucosal transport, and evacuatory reflexes[3]. GI motility is an integrated process of the electrophysiological activity of smooth muscle cells, neural input from the intrinsic and autonomic nervous system, hormonal interactions, and coordinated smooth muscle contraction. The basic motor apparatus of the gut consists of both muscular and nervous components that act as contractile units. Although it has a specific structure, there are variations among the different parts of the intestine to better accommodate the specific function of each part[3].

Functional movement and motility

The gut exhibit two fundamental patterns of movements: ***propulsion*** and ***mixing.*** The propulsion pattern is ***peristalsis,*** which is seen in the

oesophagus and small intestine. It is the coordinated contractions of the circular and longitudinal muscles, which cause GI contents to be pushed distally. The main stimulus of peristalsis is distension by a food bolus that causes stretching of the smooth muscle of the bowel wall. The common type of ***mixing*** motility is segmental contractions especially seen in the small intestine allowing mixing of the ingested material with the digestive enzymes.

Postoperative gastrointestinal function

Postoperative ileus affects all parts of the GI tract[4]. After operation, the motility of the GI tract is characterised by disorganized activity and lack of coordinated propulsion[3]. Because the components of GI tract differ in electrical and mechanical activity therefore they recover differently from the process of postoperative ileus.

Research performed over the last three decades has established the electrical and manometric pattern of recovery of the intestinal function after surgery reasonably well. In many cases, these experiments were performed on small number of patients in whom electrodes were implanted in the bowel wall during laparotomy[5]. General opinion suggests that duodenal motility does not stop (or stops very briefly) after surgery. The electrical rhythm in the stomach immediately after operation is irregular and disorganized, but it returns to normal in 24 to 48 hours[3,4,6].

It is believed that small intestinal function returns in 4 to 8 hours, to 24 hours after surgery[4,5]. However, recent studies have shown that this early motor activity is disorganized and rarely results in a normal, coordinated motility. This state may last 3 to 4 days, after which the small bowel resumes normal motor activity[7].

The colon is the last portion of the GI tract to return to normal function, which generally occurs 48 to 72 hours after surgery[8]. The passage of stool, which normally occurs one to two days after passage of gas, does not necessarily indicate resolution of the ileus since it depends on the type of the procedure performed, the condition and contents of the bowel before the procedure, dietary factors, and the patient's bowel habit[3].

Pathophysiology of postoperative ileus

The duration of postoperative ileus correlates with the degree of surgical trauma and is most extensive after colonic surgery[9]. However, it may develop after all types of surgery, including extraperitoneal surgery as demonstrated in a recent review of 21,589 patients undergoing lower extremity arthroplasty, in which 0.32% of patients developed postoperative ileus[10].

The pathophysiology of postoperative ileus is multifactorial and involves ***Inhibitory Neural Reflexes*** and ***Neurotarnsmitters and Inflammatory Factors.***

Inhibitory Neural Reflexes: Three nervous systems control the motility of the gastrointestinal tract[10]: the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS), which extrinsically regulate motility, and the intrinsic nervous system (INS)[10,11]. The PNS acts to increase intestinal motility, whereas activation of the SNS inhibits bowel function.

Many believe that the duration of postoperative ileus is related to the length of the high sympathetic state, which is thought to sustain intestinal peristalsis such as during surgical stress[11]. The INS is structurally different in the colon than in the small intestine[11]. The smooth muscle in the colon lacks gap junctions and does not function as a peristaltic syncytium, as does the small intestine[11]. Therefore,

contraction and motility of colonic cells are more dependent on the extrinsic nervous system for regulation. A longer duration of high sympathetic outflow would then prolong the duration of postoperative ileus[9].

Neurotransmitters & Inflammatory Factors: The degree of ileus corresponds to intestinal inflammatory response. The inflammatory mediators released as a part of stress response contributes to the development of postoperative ileus[12]. Gut paralysis was found to be biphasic, with nitric oxide (NO) as an important mediator of initial paralysis[13]. Furthermore, intestinal manipulation was found to lead to increased mucosal permeability, resulting in the hypothesis that the endogenous bacterial products may act synergistically with the inflammatory response in the development of postoperative ileus[14].

PERIOPERATIVE MANAGEMENT

Anaesthesia and Analgesia

Various types of anaesthesia have different effects on bowel motility[2,9]. The effect of anaesthetic agents is strongest on the region of the bowel, which depends most on neural integration. In theory, epidural local anaesthetic can block afferent and efferent sympathetic reflexes, increase splanchnic blood flow, and have anti-inflammatory effects[15]. Epidural anaesthetics have the added benefit of blocking the afferent stimuli that trigger the endocrine metabolic stress response to surgery and, thus, inhibit the catabolic activity of hormones released during this process[16].

Thoracic epidurals significantly reduce ileus when compared to systemic opioids therapy in patients undergoing abdominal surgery[17].

Comparing epidural bupivacaine with epidural opiods, there was a significant reduction in the duration of postoperative ileus in the first group of patients without significantly adversely affecting pain relief[18]. The location of the epidural is important; low thoracic and lumbar administration was not shown to be beneficial on postoperative ileus[15,17].

It has been known for some time that exogenous opioids reduce motility and contribute to POI with its most profound effect on the colon[9,19]. Recent studies[4,20] show that endogenous release of morphine occurs after an operation, and although their contribution to POI is incompletely understood, the fact that naloxone administration increases colonic transit time suggest that endogenous opioids may have an inhibitory effect on GI transit[4,19].

Treatment

There is no single, specific treatment for POI. Traditionally, the treatment consisted of routine nasogastric decompression, intravenous fluids, correction of electrolyte imbalances, and expectant observation. Additional measures may include the use of prokinetic agents, early enteric feeding, early mobilization, and the use of minimally invasive surgery. The efficacy of each individual modality is difficult to assess due to the wide variety of trials with different endpoints, a multitude of procedures, numerous treatment regimens and protocols, and also the lack of a common definition of POI[3]. Nevertheless, some conclusions can be made.

Fluids and Electrolytes: The appropriate postoperative intravenous replacement of fluids and electrolytes is important for maintaining renal, cardiovascular, and also GI function. There is a trend of shift from "wet" to "dry" regimens, but standard procedure-specific guidelines are lacking[21]. While some trials supported the concept of restricting the

postoperative fluids and electrolytes intake[22], stating that this practice results in fewer complications, whereas others have demonstrated the opposite[23]. The correct amount of intravenous fluids and the dose of electrolytes are probably between strict restriction and liberal regimens keeping in mind the general status and condition of the patient and any co-existing medical conditions, the type and length of surgical procedure since both dehydration and over hydration may cause fluid and electrolytes imbalances that might lead to a variety of complications, including GI dysfunction.

Ambulation: Although early postoperative ambulation should be encouraged to prevent atelectasis, pneumonia, and deep venous thrombosis, it has not been proved by studies that it enhance bowel movement and decrease the duration of POI[9,24].

Nasogastric Tube: The insertion of a nasogastric (NG) has been the traditional supportive treatment for POI; however, its use does not shorten time to first bowel movement or effective oral intake[25]. A meta-analysis of 26 trials with a total of 3,964 patients[25] of selective versus routine placement of an NG tube after elective laparotomy found that patients without routine postoperative NG tube had fewer episodes of fever, atelectasis, and pneumonia as well as a faster return to oral intake. However, patients treated without an NG tube had an increased incidence of abdominal bloating and vomiting, but without an overall increase in postoperative complications. Additional analysis revealed that for every patient requiring an NG tube for postoperative bloating, nausea, and vomiting, 20 patients did not. In another study of patients who had cystectomy it had been found that those cases who were treated with metoclopramide and early NG tube removal had fewer episodes of atelectasis, more rapid return of bowel sounds, and an earlier tolerance of solid food[26].

Early Postoperative Feeding: Study comparisons between early and delayed enteral feeding are difficult because of the types of surgeries, various control groups used for comparison, prospectively randomized groups versus retrospective reviews, differences in parameters used to assess the presence and resolution of POI, varying thresholds of placement, replacement, and duration of NG tubes, and types of anaesthetics used[9]. However, most patients tolerated oral feeding without a significant increase in the rate of POI or increase in postoperative complications, including vomiting with aspiration, anastomotic leaks, and intra-abdominal abscess[9].

Laparoscopy: The use of minimally invasive techniques produces less physical tissue trauma, compared with open surgery, resulting in reduced postoperative pain, less need for postoperative analgesia, improved pulmonary function, early enteral feeding, and usually shorter hospital stay[27]. Although it was documented that laparoscopic procedures is associated with lower levels of cytokines (interleukin-1 beta and interleukin-6) and C-reactive protein[28], the beneficial effect of laparoscopy on the postoperative course is probably multifactorial.

Pharmacologic agents: Numerous drugs in various classes have been suggested and studied as potentially beneficial in improving postoperative ileus including a variety of prokinetic agents, laxatives, non steroidal anti inflammatory drugs (NSAIDs), and GI hormone analogues. However, many were found to have no beneficial effect and therefore have no place in the treatment of POI[3]. Laxatives were used

as part of a multimodal postoperative treatment regimen as it will be discussed later, with encouraging results. NSAIDs have a potential of dual effect on resolving POI both by their analgesic and anti inflammatory characteristics and by indirectly reducing the dose of used opiates[29].

Alvimopan is a novel selective peripherally acting μ-opioid antagonist. The biological rationale for the use of a μ-opioid antagonist is based on increased understanding of the role of opiate receptors in the peripheral modulation of gut functions, and the new insights in the pathophysiology of diseases and conditions such as POI[30]. As mentioned above, endogenous opiates alter gut functions and this is easily understood when one considers the dramatic changes in gut functions caused by commonly used μ-opioid agonists such as codeine or morphine[30]. Given the association between the POI with the use of opiate analgesia, the use of selective opiate antagonists has been proposed in the management of POI without inhibition of the pain-relieving effect of the opiate[31]. Two large phase III studies have now been published demonstrating efficacy of alvimopan in the management of POI[32,33]. Wolff et al[33] evaluated 510 patients scheduled for bowel resection or radical hysterectomy who were randomized (1:1:1) to receive alvimopan 6mg, alvimopan 12mg, or placebo orally 2 h or more before surgery, then twice a day until hospital discharge or for up to 7 days. Time to recovery of gastrointestinal function was accelerated for the alvimopan 6mg and alvimopan 12mg groups with a mean difference of 15 and 22 h, respectively, compared with placebo. The time to hospital discharge order written was also accelerated in the alvimopan 12-mg group with a mean difference of 20 h compared with placebo. The incidence of adverse events was similar in all treatment groups, with the most common adverse effects being nausea, vomiting and abdominal distension. Patients who were treated with epidural analgesia or nonopioid analgesic were withdrawn from the study. Alvimopan adds no benefits in these patients since a different mode of pain control is employed in which opiates seldom used[33].

Multimodal approach: Basse et al[34] published their results supporting the multimodal approach in patients underwent segmental colectomy. The regimen used included thoracic epidural anaesthesia for 48 hours, omission of a nasogastric tube, one liter of fluid orally on the day of surgery, mobilization within eight hours of surgery, use of Milk of Magnesia, and an alteration in the incision (curved or transverse) to minimize pain and pulmonary dysfunction. The end results showed that 95 of 100 patients evaluated have had defaecated within 48 to 72 hours, and most patients were able to go home after 48 hours (median hospital stay, 2 days). To confirm these results, in a subsequent analysis[35], patients received radioactive indium in the stomach and were observed with scans at 24 and 48 hours postoperatively. In two repeats, all 12 patients/volunteers who were evaluated had postoperative defaecation within 48 hours. The bowel function of the operated patients was comparable to that of the control group.

Others[5] advocated utilizing **C**ontrolled **R**ehabilitation with **E**arly **A**mbulation and **D**iet **(CREAD)**. This was studied in patients undergoing laparotomy with intestinal resection, and the authors compared the results with the traditional postoperative care offered previously at their institution[5]. Patients who are included in the CREAD regimen are seen by the colorectal nurse manager and given written information on the expected

postoperative milestones. Intravenous, patient-controlled anaesthesia systems are used for all patients. Epidural anaesthesia and analgesia are not used. Orogastric tubes placed during anaesthesia are removed prior to extubation. Patients are permitted to walk and are offered liquids on the evening of surgery. Analgesia is supplemented with ketorolac 30mg, intravenously every 6 h as needed. On postoperative day 1, patients are encouraged to walk at least one circuit of the nursing floor (approximately 60 m) up to five times, to sit out of the bed between walks and to perform regular, incentive spirometry. They are allowed non-carbonated liquids and if they are tolerating oral fluids, are offered solid food that evening, without waiting for signs of intestinal function. Oral analgesia (oxycodone) is started on postoperative day 2 if either liquids or diet are being tolerated, and the patient-controlled analgesia is discontinued. Discharge criteria include that the patient passes flatus or stool, is comfortable on oral analgesia, can stand and walk independently and has tolerated three, successive solid meals. An effort is made to ensure that patients are satisfied with discharge plans, or they are kept for an additional 12-24 h until they are fully reassured. The study concluded that patients receiving CREAD have a shorter hospital stay, without adverse effects on patient's satisfaction, pain scores or complication rates. Patients under 70 years of age derive the optimal benefit, and increased surgeon experience improves outcome[5].

CONCLUDING REMARKS

Postoperative ileus continues to be a significant problem after abdominal and other types of surgeries. It has multiple pathogenic mechanisms, of which neural reflexes seem to be the most important, coupled by inflammatory mediators and administration of opioids. The contribution of endogenous opioids in POI is probably an area of future study. Currently, the important factors that could affect the duration and recovery from POI include limitation of the narcotic use, and using alternative medications such as NSAIDs. Placing a thoracic epidural with local anaesthetic when possible appears to reduce time to recovery from POI; however, this approach has not been shown to provide clinical benefit to patients following multimodal postoperative care pathway. Selective use of nasogastric decompression and correction of electrolyte imbalances also is important. Laparoscopy reduces the time taken to recover from POI; however, this surgical approach is not indicated or feasible in all patients undergoing abdominal surgery.

The advent of new therapeutic approaches relating to fluid administration, or novel medications such as μ-opioid antagonists, may influence POI and further improve outcomes after major abdominal surgery.

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