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REVIEW ARTICLE

Epidural Anesthesia with Opioids in Open Colorectal Surgeries is not Related to Postoperative Ileum

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Abstract

Purpose of review: This is a short review describing recent data on the use of opioids in epidural anesthesia on abdominal surgery. It is known that postoperative pain has nociceptive, inflammatory and neuropathic components and must be prevented. The period following abdominal surgery is particularly challenging because it has other side effects related to the surgery, in addition to pain. Limiting these unwanted consequences requires a multidisciplinary team. Opioids remain the leading postoperative pain management drugs despite their known side effects, which are dose-dependent and may vary according to the route of administration. Sedation, dizziness, nausea, vomiting, and constipation are often related to opioid use. Since constipation or ileum are also directly related to abdominal surgery, temporary changes in gastrointestinal motility are inevitable after open surgeries. As such, there is concern that opioid-based anesthesia could make it worse and even increase postoperative morbidity and mortality.

Recent findings: Several studies involving open colorectal surgery have shown that epidural analgesia, with or without opioid administration, is more effective in treating postoperative pain than intravenous analgesia, thus, this article intends to conduct a literature review to assess whether the association of opioids and local anesthetics in epidural analgesia for colorectal surgery increases the incidence and intensity of postoperative ileus.

Summary: This review found no convincing evidence that the use of intrathecal opioids increases the incidence of postoperative ileus, in addition, it was shown to be an effective pain management tool, as expected.

Keywords

Opioid analgesics, Ileum, Epidural anesthesia, Laparotomy, Colorectal surgery

Key Points:

- Side effects of opioids are dose dependent but may also vary according to the route of administration.
- Data show that epidural opioids are effective and when this route is used there is a lower incidence of post-surgical ileus.
- Studies show that epidural analgesia, with or without opioids, is more effective in treating postoperative pain than intravenous analgesia.

Introduction

Postoperative pain comprises a combination of unpleasant sensory, emotional, and mental experiences associated with metabolic and immunological neuroendocrine alterations resulting from surgery, anesthesia, and psychological stress [1]. During abdominal surgery, tissue damage occurs coupled with nociceptive stimuli from the skin, subcutaneous tissue, viscera, and neural structures, followed by sympathetic and neuroendocrine activation, with tachycardia, arterial hypertension, hyperglycemia, immunosuppression, decreased regional blood flow, and increase platelet aggregation [2]. At the surgical

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incision site, inflammatory mediators are released, the pain threshold of peripheral nerve endings is reduced, and neuronal damage is inevitable [3]. There are several predictors of postoperative pain occurrence and intensity, such as pain before surgery, anxiety, younger patients, obesity, use of high doses of opioids before or even during surgery, prolonged surgical time, and site. For instance, thoracic surgery is the most strongly correlated to the presence of postoperative pain [4]. Rawal, et al. concluded that more than 80% of patients experience postoperative pain and less than 50% receive adequate treatment [5]. Inadequate pain management delays patient recovery and rehabilitation, increases the risk of complications and hospital costs. Pogatzky, et al. concluded that acute postoperative pain turns into persistent postoperative pain in 10 to 50% of patients, being classified as severe in 2 to 10% of these patients [6].

In this context, opioids remain the leading drugs in postoperative pain management. A North American study showed that approximately 95% of surgical patients are treated with opioids [5,7]. However, when it comes to analgesia for abdominal surgery, there are still numerous controversies in literature research. Opioids are considered potent analgesics and the association of opioids with local anesthetics has a synergistic benefit when compared to the use of isolated local anesthetics [8], this practice is known as multimodal anesthesia, and when employed can improve analgesia and reduce side effects [9,10].

Postoperative ileus is a smooth muscle paralysis of the gastrointestinal tract that most commonly occurs after intraperitoneal surgery. The immediate postoperative period is characterized by intestinal obstruction, abdominal distension, and absence or reduction in bowel sounds. The risk of developing postoperative ileus is associated with the type of surgery performed, is more commonly linked to abdominal and genitourinary interventions, the use of intravenous or oral opioids and the presence of gastrointestinal tract pathologies, such as Crohn's Disease [11]. Opioid-induced constipation (OIC) is one of its many symptoms and probably the most common when associated with open surgery. Opioids lead to decreased neuronal excitability and fewer neurotransmitter release, resulting in a general inhibitory effect on cells, the main effect being reduced formation of cyclic adenosine monophosphate. Besides, opioids affect motility and secretion in the gastrointestinal transit which is mainly controlled by the myenteric plexus and relies on neurotransmitters activation by acetylcholine [11,12]. Although confirmation is needed in other species, a recent study in rats suggested that the effect on the gut may vary according to the specific opioid used [13].

A comprehensive literature search was performed on PubMed, Scielo, Lilacs, Medline and Cochrane Central Register. The following keywords were used: Ileum, colon, colorectal, postoperative open surgery, epidural, morphine, opioids, postoperative pain. Publications in English, French, Spanish and Portuguese languages were included.

Text of Review

Abdominal surgery main complications

Postoperative ileum is an interruption of normal peristaltic bowel movements, with intestinal content stasis lasting approximately 72 to 96 hours. The presence of pain, surgical stress, sympathetic hyperactivity, surgical manipulation of the intestine, intestinal neuroinflammatory processes, and the use of systemic opioids are associated with postoperative ileus duration [8]. Open colorectal surgeries are often associated with prolonged and high-intensity postoperative pain, mainly related to mobilization. Ineffective postoperative analgesia prolongs the postoperative ileum and postpones hospital discharge [14]. As an example, cytoreductive surgery performed with hyperthermic intraperitoneal chemotherapy (HIPEC), is considered one of the abdominal surgeries with the highest incidence of postoperative pain. This technique has improved the prognosis of colorectal cancer, but it is also highly associated with difficult pain management. Despite the known and expected coagulation disorders in these cases, an Italian study showed no complications related to neuraxial anesthesia during this type of surgery, providing adequate pain relief with the use of epidural anesthesia associated with opioids [15].

Analgesia and anesthesia in abdominal surgeries

Regional analgesia in abdominal surgeries is often recommended in Recovery after Enhanced Surgery (ERAS) protocols for postoperative pain relief, early patient recovery and consequent reduction in hospital stay [16]. Epidural analgesia presents itself as an excellent option for pain management in open colorectal surgery. Data from several randomized controlled trials and meta-analyses comparing the various postoperative analgesia techniques have shown that epidural analgesia offered superior pain control associated with other benefits such as reduced postoperative ileus duration, better functional recovery, and quality of life. Some studies even indicated a reduced incidence of metastasis recurrence and a longer survival time [8,17-19]. Several controlled clinical trials at the Cochrane reviews evaluated the best analgesic technique that would allow effective postoperative pain control, fewer adverse effects, and early hospital discharge and recovery, epidural analgesia with local anesthetics, associated or not with opioids, was considered the gold standard, providing pain relief and early mobilization of patients. Intravenous administration of opioids for the treatment of postoperative pain was linked to cardiac and respiratory complications, prolonged ileus and

delayed patient recovery [19]. M.C Lin, et al, compared epidural analgesia with local anesthetic and opioid with intravenous analgesia with an opioid for the treatment of postoperative pain in colorectal surgery. Nausea and vomiting were the main adverse effects presented by patients who received intravenous morphine, however, when opioids are associated with the epidural analgesia with local anesthetic they are considered very effective and had fewer adverse effects [20]. Dragana Radovanoviéc, et al. conducted a study comparing thoracic epidural analgesia with patient-controlled intravenous analgesia after colorectal surgery and evaluated bowel function recovery, pain intensity, patient satisfaction and postoperative complications, and length of hospital stay. In this study, postoperative ileum recovery was resolved earlier in patients who received epidural analgesia. An evacuation was established within the first 48 hours in more than 80% of the patients who received epidural analgesia and in only 36.7% of patients who received intravenous analgesia. The resumption of food intake was also achieved earlier in the first group and pain intensity was significantly lower, which increased patient satisfaction. Moreover, the incidence of postoperative delirium increased significantly in patients who received intravenous analgesia. Finally, there were no statistically significant differences between groups regarding adverse effects such as nausea and vomiting, excessive sedation or respiratory depression [21]. Accordingly, the study by Flisberg, et al. demonstrated that epidural analgesia was very effective in controlling postoperative pain with a reduction in the incidence of adverse effects such as respiratory depression and sedation, compared to venous analgesia with morphine [22]. A randomized controlled clinical trial by Phillippe Jouve compared epidural anesthesia and preperitoneal analgesia in open colorectal surgery, fifty patients were randomized to receive epidural analgesia or continuous wound infiltration for 48 hours and were treated according to ERAS recommendations, patients undergoing epidural anesthesia had lower resting pain scores over the first three days and lower dynamic pain scores during mobilization, which remained true at hospital discharge. The average length of hospital stays, return of bowel function and tolerance to complete diet was also shorter in the epidural analgesia group, urinary retention did not differ between groups [23]. Among the various methods of postoperative analgesia in patients undergoing open abdominal surgery, epidural analgesia is accepted as the gold standard for postoperative pain relief. However, as important as the analgesia method, the agents of choice play a crucial role in the success of pain management and the presence of adverse effects. Local anesthetics are often used for epidural analgesia; however, they have the potential to cause hemodynamic instability. To reduce these side effects and improve analgesia, adjuvants are often added, with opioids being the most commonly used. Chesterman, et al. evaluated the use of epidural morphine associated with local anesthetic for postoperative analgesia in cesarean sections. The authors concluded that epidural morphine not only provided postoperative pain relief but also reduced the incidence of ileus [24]. Studies on the risk of postoperative ileus in abdominal surgeries showed that only preoperative opioid use, but not intraoperative or postoperative use, was statistically associated with ileum [25]. Intravenously administered morphine appears to cause disturbances in intestinal motility and subsequently induces constipation. However, the epidural administration of morphine associated with bupivacaine seems to facilitate the recovery of the ileum after surgery, suggesting the existence of a different effect on intestinal motility that can be explained by the indirect analgesic effect of epidural morphine on the central nervous system [24]. Although several studies have evaluated the effects of epidural analgesia on gastrointestinal motility after colorectal surgery, its benefits are difficult to demonstrate in practice. Several factors can interfere with the results, such as the amount and types of medication administered through the epidural catheter, surgical technique, and surgery time. Some factors have been related to early postoperative ileus recovery with epidural analgesia, such as pain relief, sympathetic blockade, blockage of nociceptive afferent fibers and increased blood flow to the colon, in addition to a decrease in the consumption of systemic opioids, which reduces their adverse effects [8,20]. Frantzides, et al. evaluated the effects of intravenous, intramuscular, and epidural morphine on colon myoelectric activity during ileal recovery. The authors noted that morphine, when administered intravenously and intramuscularly, interrupts the recovery of colonic motility. However, epidural morphine did not affect colon myoelectric activity [26]. Nakayoshi, et al. examined and compared the effects of epidural analgesia and intravenous analgesia with morphine on intestinal motility in an animal model. Epidural morphine had different effects than intravenous morphine in the recovery of intestinal motility in an animal model in open colorectal surgeries, with a decrease in postoperative ileus with the administration of epidural morphine [27]. Opioids administered into the epidural space are routinely used for pain relief after a wide variety of abdominal surgeries. They have great advantages over epidural analgesia performed with only local anesthetics, such as better quality of analgesia and lower incidence of adverse effects [28].

Conclusion

Opioids can be administered by a variety of routes, such as oral, intravenous, epidural, and intrathecal and the adverse effects are contingent on the route in which they were administered. Intravenously administered

morphine increases the incidence of ileus. On the other hand, studies show that, if used in epidural analgesia, it does not have pronounced intestinal effects, improves postoperative pain control, decreases hospital stay, and can be used safely in colorectal surgeries. Other studies are needed to guarantee the best route of administration for opioids avoiding undesirable effects on the abdominal procedures.

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Conflicts of Interest

There are no conflicts of interest.

Declaration of Interest

The authors declare no conflicts of interest.

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