Postoperative Pain Management in Patients With Ulcerative Colitis

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Inflammatory bowel disease (IBD) is a group of chronic inflammatory disorders of the gastrointestinal tract including ulcerative colitis (UC) and Crohn's disease. Pain management can be challenging in patients with IBD because there are limitations on the use of analgesics. Use of nonsteroidal anti-inflammatory drugs is not recommended in patients with IBD because there is risk of relapse of IBD and an overall increase in disease activity. Opioids, although frequently used for treating severe acute pain, can have additional risks and complications in patients with IBD such as ileus, toxic megacolon, and narcotic bowel syndrome. Furthermore, little information is available in the literature on pain management in these patients undergoing noncolorectal surgery. This report describes 2 patients with UC in whom postoperative pain following oral and maxillofacial surgery was managed by intravenous patient-controlled analgesia with pentazocine. Apart from the development of acute dystonia in 1 case that was likely due to the use of droperidol for prevention of postoperative nausea and vomiting, postoperative pain was well controlled by pentazocine in both patients without any complications or UC exacerbations.

Key Words: Inflammatory bowel disease; Ulcerative colitis; Postoperative pain management; Pentazocine.

Inflammatory bowel disease (IBD) describes a group of disorders involving chronic relapsing inflammation of the gastrointestinal tract including ulcerative colitis (UC) and Crohn's disease (CD).[1] The etiology of these diseases is still not completely understood. So far, combined influences have been considered, including reduced host microbiota diversity, immune response accommodative insufficiency, and environmental factors (smoking, foods, drugs, social stress, and genetic susceptibility).[1] Pain management is often challenging in these patients, especially in the perioperative period,[2] due to limitations on pharmacologic analgesic options for patients with IBD. Generally, the first analgesics considered for patients undergoing oral and maxillofacial procedures are acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and/or cyclooxygenase-2 (COX-2) inhibitors administered alone or in combination.[3,4] Weak or strong opioids are also commonly used as additional analgesic adjuncts if treating moderate to severe postoperative pain. However, NSAIDs are generally not recommended in patients with IBD because of the risk of relapse of IBD and an overall increase in disease activity, as well as the general risk of further injury to the gastrointestinal mucosa.[5] Therefore, NSAIDs are used cautiously or are contraindicated in patients with IBD.[6,7] Use of COX-2 inhibitors, which may be associated with a lower risk of IBD exacerbations, remains controversial because of potential side effects, such as cardiovascular adverse events.[8,9] Moreover, opioid agonists are generally not recommended in patients with IBD because of the risks of ileus, toxic megacolon, and narcotic bowel syndrome.[7] This is because opioids negatively affect gut motility by increasing the nonpropagating segmentation component of peristaltic activity and inhibiting the propagated peristaltic wave via agonistic activity involving the mu-opioid receptor.[10] Given these ongoing concerns, no standard has been established for the management of postoperative pain in patients with IBD undergoing noncolorectal surgery.

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Oral acetaminophen is essential for acute postoperative pain management for patients with IBD undergoing routine dental or oral and maxillofacial surgery procedures. As NSAIDs are generally unavailable, if acetaminophen alone is ineffective, then combined administration with a weak opioid or tramadol can be useful. Pentazocine, which acts mainly as a kappa-opioid receptor agonist but also as a partial mu-opioid receptor agonist/antagonist, is widely used to treat moderate to severe postoperative pain in Japan.[11] Based on its mechanism of action, pentazocine may have weaker side effects in patients with IBD than a full mu-opioid agonist such as morphine or fentanyl.[12]

This paper describes 2 patients with UC in whom postoperative pain after oral and maxillofacial surgery was successfully managed by intravenous patient-controlled analgesia (IV-PCA) with pentazocine. Written informed consent was obtained from both patients for publication of this report.

CASE PRESENTATIONS

Case 1

The patient was a 22-year-old man (height 172.0 cm, weight 65.6 kg, body mass index [BMI] 22.2 kg/m^2) with a diagnosis of skeletal mandibular prognathism who was scheduled for bilateral sagittal split osteotomies. He had no remarkable preoperative medical history, and all routine preoperative laboratory data were within normal limits. He was not on any routine medications and had no known allergies. Physical examination was otherwise unremarkable, and the airway examination did not reveal any notable findings indicating a high risk for a difficult airway. However, a week before admission, the patient suddenly developed bloody diarrhea and severe lower abdominal pain. He was evaluated by a gastroenterologist and subsequently diagnosed with acute ulcerative proctitis, a form of UC. The surgery was postponed and treatment with oral mesalazine (1500 mg per day) was started. One month later, the patient's symptoms had remitted, and the surgery was rescheduled after consultation with the gastroenterologist. Preoperative laboratory data, including a complete blood count, C-reactive protein, total protein, and albumin levels, were all within the normal ranges. In the operating room, standard Japanese Society of Anesthesiologists (JSA) monitors were used, consisting of a pulse oximeter, electrocardiography, noninvasive blood pressure device, and a temperature monitor. Additionally, end-tidal carbon dioxide and inspired oxygen concentration were monitored. Before induction of anesthesia, dexamethasone (6.6 mg) was administered for prevention of postoperative nausea and vomiting (PONV). After a 3-minute infusion of remifentanil (0.3 μg/kg/min), anesthesia was induced by propofol (initial effect site concentration 5 μg/mL) administered via a syringe pump (TE-371, Terumo, Inc, Tokyo, Japan) with a built-in target-controlled infusion system (Diprifusor, AstraZeneca, London, UK). Rocuronium (50 mg) was then administered to facilitate nasotracheal intubation via the right nostril with a reinforced 7.0-mm endotracheal tube. Anesthesia was maintained with continuous infusions of propofol administered as a target-controlled infusion to maintain a bispectral index of 40 to 60 (~3.3 μg/mL during surgery) and remifentanil (0.2–0.4 μg/kg/min). A combination of 5 mL 2% lidocaine with 1:80,000 epinephrine and 5 mL 0.5% levobupivacaine (total dose: lidocaine 100 mg, epinephrine 0.0625 mg, levobupivacaine 25 mg) was administered via infiltration into the surgical areas prior to the surgical procedure. The operation was completed in 164 minutes, and the total anesthesia time was 235 minutes. There were no intraoperative complications. Total blood loss was 735 mL. Pentazocine (15 mg) was administered intravenously, and the PCA pump with pentazocine was started 10 minutes before the end of surgery. The patient emerged from anesthesia approximately 10 minutes after discontinuation of the propofol and remifentanil and was extubated without difficulty.

Postoperative analgesia consisting of pentazocine 90 mg in 90 mL saline (final concentration of 1 mg/mL) was delivered via the PCA pump. For prevention of PONV induced by pentazocine, droperidol (1.25 mg) was also added into the PCA bag. The PCA device was set to deliver pentazocine as a continuous infusion (1.0 mg/h) and as a bolus dose (7.5 mg) with a 15-minute lockout interval. This PCA regimen was continued for 24 hours after surgery. Acetaminophen 1000 mg was also ordered for rescue analgesia if requested by the patient.

When the patient left the operating room, his Numeric Rating Scale (NRS) pain score was 2. After arrival on the ward, oxygen was administered through a nasal cannula at a flow rate of 2 L/min. The patient was monitored to detect postoperative complications, including airway obstruction, as early as possible. Three hours after surgery, the patient complained of moderate pain (NRS 5–6), which coincided with an increase in the number of PCA demands. The PCA settings were adjusted increasing the continuous infusion rate (1.0–1.5 mg/h) and the bolus dose (7.5–10.0 mg). Thereafter, the patient's pain was gradually relieved and the NRS improved to 2 to 3 approximately 6 hours after surgery. The patient slept well during the night without any complications, such as PONV or respiratory depression.

Early the next morning (15 hours after surgery), the patient complained that his body felt rigid and that breathing became difficult soon after pushing the PCA button. His vital signs were stable at this time, and there was no appreciable airway obstruction from edema or bleeding. He was diagnosed with acute dystonia, which is an extrapyramidal symptom induced by droperidol, and the PCA pump was stopped immediately. He was then administered diazepam (5 mg) intravenously and closely observed. The patient's extrapyramidal symptoms gradually improved in the ensuing 10 minutes and virtually disappeared 2 hours after discontinuation of the PCA pump. The patient reported mild pain (NRS 4–5) after stopping the pentazocine PCA, so acetaminophen (1000 mg) was administered intravenously. The total doses of pentazocine and droperidol administered before stopping pentazocine IV-PCA were 152.8 and 2.06 mg, respectively. He resumed taking oral mesalazine on the morning after surgery. Acetaminophen (1000 mg) was administered intravenously 3 to 4 times daily for 2 days after surgery, and thereafter orally when he reported pain. Bowel motility returned on the first postoperative day without any UC exacerbations, such as diarrhea, bleeding, or abdominal pain. The patient was discharged on postoperative day 12 without any complications, and there were no findings suggestive of UC exacerbations upon endoscopic examination by a gastroenterologist.

Case 2

The patient was a 52-year-old woman (height 161.6 cm, weight 51.6 kg, BMI 19.8 kg/m^2) with diagnoses of a left mandibular dentigerous cyst and right upper and lower third molar pericoronitis who was scheduled for cystectomy and tooth extraction under general anesthesia. Her medical history was significant for fibroid surgery under general anesthesia 8 years earlier. A fecal occult blood test had been positive at the time of a medical checkup 2 years earlier, at which time she was diagnosed with incipient UC by a gastroenterologist. Treatment with oral mesalazine had been started, and the disease had been well controlled without any symptoms since that time. Preoperative laboratory data were within normal limits, physical examination was otherwise unremarkable, and the airway examination did not detect any signs of a difficult airway.

In the operating room, standard JSA monitors applied to the patient included a pulse oximeter, electrocardiography, noninvasive blood pressure device, and a temperature monitor. End-tidal carbon dioxide and inspired oxygen concentration were also monitored. Before induction of anesthesia, dexamethasone (6.6 mg) was administered for prevention of PONV. Because of the extrapyramidal symptoms observed with the prior patient, droperidol was avoided for this patient and replaced with hydroxyzine. This is because ondansetron is approved only for use in patients with cancer in Japan and is extremely costly. NSAIDs were avoided because of the patient's IBD, and combined administration of acetaminophen and bupivacaine was chosen due to long-term effectiveness.

After a 3-minute infusion of remifentanil (0.3 μg/kg/min), anesthesia was induced by propofol (initial effect site concentration 4 μg/mL) administered via a TE-371 syringe pump with the built-in target-controlled Diprifusor infusion system. Rocuronium (40 mg) was then administered to facilitate nasotracheal intubation via the right nostril with a reinforced 6.5-mm endotracheal tube. Anesthesia was maintained with continuous infusions of propofol administered as a target-controlled infusion to maintain a bispectral index of 40 to 60 (~2.6 μg/mL during surgery) and remifentanil (0.2–0.3 μg/kg/min). Ten mL 2% lidocaine with 1:160,000 epinephrine (total dose: lidocaine 200 mg, epinephrine 0.0625 mg) was administered via infiltration into the surgical areas before the surgical procedure. The operation was completed in 150 minutes, and the total anesthesia time was 225 minutes. There were no intraoperative complications. Total blood loss was 20 mL. Pentazocine (15 mg) was administered intravenously, and a PCA pump with pentazocine was started 15 minutes before the end of surgery. The patient emerged from anesthesia approximately 10 minutes after discontinuation of propofol and remifentanil and was extubated easily.

Postoperative analgesia consisting of pentazocine 90 mg in 90 mL saline (final pentazocine concentration 1 mg/mL) and hydroxyzine (50 mg) was delivered via a PCA pump. The PCA device was set to deliver pentazocine as a bolus dose (7.5 mg) with a 20-minute lockout interval. Continuous infusion of pentazocine was not utilized. This PCA regimen was continued for 24 hours after surgery. Acetaminophen (1000 mg) was available as rescue analgesia if requested by the patient.

When the patient left the operating room, the NRS pain score was 0. After arrival on the ward, oxygen was administered through a nasal cannula at a flow rate of 2 L/min and the patient was monitored for postoperative complications. She used the PCA pump 5 times in the first 24 hours after surgery and the NRS pain score was 1 to 3. There were no complications such as PONV or respiratory depression. After discontinuation of the pentazocine IV-PCA, her pain was well controlled by oral acetaminophen. The patient was discharged on postoperative day 5 without any complications, and there were no findings suggestive of UC exacerbations.

DISCUSSION

This paper has described 2 patients with UC who were managed with pentazocine via an IV-PCA without NSAIDs or additional narcotics for postoperative pain after oral and maxillofacial surgery. In case 1, the extrapyramidal symptoms likely occurred because of the use of droperidol to prevent PONV; however, the patient recovered immediately after stopping IV-PCA. Postoperative pain in both patients was well controlled by pentazocine without any UC exacerbations.

UC falls under the category of idiopathic IBD and is characterized by chronic relapsing inflammation of the colonic mucosa, which extends proximally from the rectum.[13] This chronic disease typically presents with bloody diarrhea and abdominal pain with repeated remissions and exacerbations. The overall prevalence of UC is reported to be 7.6 to 245 cases per 100,000 persons per year, and the incidence is increasing, especially in Asia, although the exact pathogenesis is unknown.[13] Most of the literature on pain management in patients with IBD has focused on chronic abdominal pain caused by exacerbations of UC or CD itself.[7,14] Therefore, there has been no established standard guideline for managing acute postoperative pain in patients with IBD undergoing noncolorectal surgery. Typically, several analgesic options for otherwise healthy patients undergoing oral and maxillofacial surgery, such as acetaminophen, NSAIDs, and/or COX-2 inhibitors, are either given alone or in combination.[3,4] Additionally, these drugs are often further combined with opioid agonists if satisfactory pain control is not achieved. Occasionally, the use of ketamine or gabapentinoids may also be considered.[4] However, in patients with IBD, these common analgesic pharmacologic strategies are not ideal. In both cases reported here, IV-PCA with pentazocine was used as the main strategy for postoperative pain management, with acetaminophen but not NSAIDs or narcotics as the secondary option.

NSAIDs exert their analgesic effect by inhibiting the production of prostaglandins induced by COX enzymes. These drugs inhibit not only the inducible form of the enzyme, namely, COX-2, but also the constitutively produced COX-1 enzyme, which helps maintain the mucosal integrity of the GI tract. Therefore, NSAIDs are likely to exacerbate IBD and are usually contraindicated in these patients; nevertheless, their use in this indication remains controversial.[9,15] For these reasons, use of selective COX-2 inhibitors may be safer in patients with IBD because of the lower risk of GI exacerbations despite some of these agents being associated with an increased risk of adverse events, including myocardial infarction and other cardiovascular events. However, the COX-2 enzyme is transiently induced in the intestinal epithelium via proinflammatory cytokines and has been shown to facilitate intestinal healing.[16] Future studies focused on examining the risk factors for exacerbations with use of NSAIDs are needed to clarify this controversial aspect of pain management in IBD.[9] On the other hand, use of acetaminophen rather than NSAIDs has been encouraged for pain management because the risk of IBD relapse following administration of acetaminophen is lower than that after NSAIDs.[17] However, acetaminophen seems to be weaker than NSAIDs in reducing postoperative pain following oral surgery.[18] It was therefore possible that the patients would need more acetaminophen after administration of pentazocine by PCA pump. Also, because acetaminophen overdose may cause acute liver failure, the use of acetaminophen as the baseline analgesic was avoided in the early postoperative period and it was used as rescue analgesia instead.

Opioids are frequently used to treat acute postoperative pain. However, there are several drawbacks concerning the use of these drugs in patients with IBD, including side effects and the potential for abuse or addiction with short- and long-term use.[19,20] Opioid-related side effects, including ileus (leading to nausea, vomiting, and constipation), fulminant colitis, toxic megacolon, and narcotic bowel syndrome are considerable risks in patients with IBD.[7,19] Mu-opioid receptors are expressed in the gut wall and play an important role in opioid-induced bowel dysfunction in humans.[21–23] Meanwhile, the relapsing chronic inflammation impacting the bowels present with IBD can easily precipitate bowel motility dysfunction.[20] Therefore, most mu-opioid receptor agonists, including morphine and fentanyl, are considered unsuitable for the management of postoperative pain in patients with IBD.[7,20] Kappa-opioid agonists, on the other hand, might be appropriate for managing postoperative pain in these patients, even though kappa-opioid receptors are also expressed in the gastrointestinal tract.[24] De Winter et al[25] suggested that activation of peripheral kappa-opioid receptors might attenuate the inhibition of gastrointestinal transit. Therefore, it was decided that a kappa-opioid agonist would be safer than a full mu-opioid receptor agonist for the management of postoperative pain in these patients with UC.

Pentazocine is a kappa-opioid receptor agonist and a partial agonist/antagonist of the mu-opioid receptor. The drug causes moderate analgesic effects and has a relatively weaker propensity to cause respiratory depression and less addiction potential than a full mu-opioid receptor agonist.[26] Pentazocine also has a rapid onset, a relatively long duration of action, and a ceiling effect in terms of respiratory depression. Therefore, it

was considered to be suitable for IV-PCA use in these cases.

The authors had previously used pentazocine for postoperative pain management in other patients undergoing oral and maxillofacial surgery. These experiences indicated the need to avoid PONV and monitor for subsequent airway obstruction. Therefore, case 1 was administered droperidol to prevent PONV during IV-PCA with pentazocine. However, when the total dose of droperidol administered by PCA reached approximately 2.0 mg, the patient developed muscle spasms affecting the face, arms, and chest that were diagnosed as probable acute dystonia. There are various treatments available for acute dystonia, including intravenous diphenhydramine, diazepam, chlorpromazine, and alimemazine.[27] Intravenous diazepam helped to resolve the muscle rigidity that occurred in this instance. Other antiemetics were considered for the next patient to avoid the side effects of droperidol. In Japan, 5-HT3 antagonists including ondansetron or palonosetron are approved for use only in the prevention and treatment of adverse effects of cancer chemotherapy and were therefore unavailable in these cases. Thus, hydroxyzine was selected for case 2 with no unpleasant side effects observed.

Unlike these 2 cases, if pentazocine IV-PCA is not available for patients with IBD after oral and maxillofacial surgery, such as those who are ambulatory or unable to follow the PCA pump instructions, alternative ways for postoperative pain management should be considered. Options include acetaminophen that may be used for baseline analgesia (maximum 1000 mg 4 times daily), and if pain persists, then a weak opioid including tramadol or codeine may be added, while closely monitoring for IBD exacerbations. Also, use of long-acting local anesthetics such as bupivacaine or ropivacaine might be considered.

CONCLUSION

IV-PCA with pentazocine may be an effective method for postoperative pain management in patients with IBD, including UC, undergoing oral and maxillofacial surgery without substantially increasing the risk of IBD exacerbations.

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