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REVIEW ARTICLE
Research

Use of Muscle Relaxants for Acute Postoperative Pain: A Practical Review

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Background: Skeletal muscle relaxants have emerged as a broad category of analgesic adjuncts, aiming to improve pain relief and reduce opioid reliance. These drugs induce muscle relaxation and reduce muscle spasms, and therefore, they are commonly used in surgical procedures involving muscle manipulation, such as abdominal surgery, breast surgery, and spine surgery. However, their analgesic efficacy and opioid-sparing effects are poorly explored.

Methods: A scoping review of literature was performed with several electronic databases. We used a search string with a sequence of text words and word variants related to central muscle relaxants, pain management, postoperative pain, and specific muscle relaxants.

Results: Review of literature shows significant heterogeneity among the studies in terms of surgical procedures, patient populations, choice of muscle relaxant, and timing and duration of administration, potentially limiting the generalizability of the findings and the ability for pooled analysis.

Conclusions: Given the lack of evidence, we recommend that the use of skeletal muscle relaxants be reserved for patients in whom an optimal multimodal analgesic technique is not adequate. Also, there may be a limited role for these drugs in patients at high risk of postoperative pain undergoing surgical procedures with expected high opioid requirements. Due to the concerns of potential adverse effects, the decision to use muscle relaxants in vulnerable populations should be made carefully, weighing the benefits against the risks. *(Plast Reconstr Surg Glob Open 2024; 12:e5938; doi: 10.1097/GOX.0000000000005938; Published online 1 July 2024.)*

INTRODUCTION

Inadequate treatment of postoperative pain continues to be a significant concern in healthcare,[1] with data suggesting that patients continue to experience moderate-to-severe pain.[2] This can delay ambulation and rehabilitation, which can delay recovery after surgery.[1] Although multimodal analgesia strategy has been recommended,[3–18] it is inappropriately applied,[19] and opioids are often administered to alleviate postoperative pain.[20] However, as a response to the opioid crisis, there has been a paradigm shift toward an opioid-averse approach to pain management, emphasizing the need for nonopioid alternatives.[21,22] Among the alternatives, skeletal muscle relaxants have emerged as a broad category of analgesic adjuncts (Table 1), aiming to reduce opioid reliance.[23] Although the precise mechanism of action is unclear, muscle relaxants depress the central nervous system, induce muscle relaxation, and reduce muscle spasms. Therefore, they are commonly used in surgical procedures involving muscle manipulation, such as abdominal surgery, breast surgery, and spine surgery.

However, the use of muscle relaxants in perioperative pain management is marked by significant knowledge gaps.[3,23] In this context, there is limited evidence on the analgesic efficacy and opioid-sparing effects of muscle relaxants as well as the optimal drug choice, dosage, and duration of therapy. Also, the efficacy and adverse effect

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balance of muscle relaxants remains largely unknown. Importantly, there is a lack of critical evaluation of available data to guide clinical decision-making, leading to a multitude of uncertainties. Consequently, healthcare professionals often prescribe these medications despite conflicting data.[23] This practical review evaluates the evidence behind the use of skeletal muscle relaxants for managing postoperative pain across all surgical procedures, including plastic surgery.

METHODS

A scoping review was performed with the help of a librarian at the University of Texas Southwestern Medical Center, Dallas, Texas. Several electronic databases (ie, Ovid Medline, Medline InProcess, Medline EPub ahead of print, Embase, and Cochrane controlled trials register published by the Cochrane Library) were searched for randomized controlled trials, retrospective and prospective observational trials, systematic reviews, and meta-analyses published from 1946 to March 2023. We used a search string with a sequence of text words and word variants related to central muscle relaxants, pain management, postoperative pain and specific muscle relaxants including baclofen, carisoprodol, chlormezanone, methocarbamol, orphenadrine, metaxalone, tizanidine, and cyclobenzaprine. In addition, the bibliography of the retrieved studies was reviewed to identify additional relevant studies. Although benzodiazepines have some skeletal muscle relaxant properties, studies assessing their use for pain management were not included because their routine use in the postoperative period is uncommon due to concerns of tolerance, dependence, and adverse effects with concomitant use of opioids.

Takeaways

Question: Skeletal muscle relaxants have emerged as a broad category of analgesic adjuncts, aiming to improve pain relief and reduce opioid reliance. However, their analgesic efficacy and opioid-sparing effects are poorly explored.

Findings: Review of literature shows significant heterogeneity among the studies in terms of surgical procedures, patient populations, choice of muscle relaxant, timing, and duration of administration, potentially limiting the generalizability of the findings, and the ability for pooled analysis.

Meaning: Given the lack of evidence, we recommend that the use of skeletal muscle relaxants be reserved for patients in whom an optimal multimodal analgesic technique is not adequate. Also, there may be a limited role for these drugs in patients at high risk of postoperative pain undergoing surgical procedures with expected high opioid requirements.

The reference list of studies retrieved from the literature search was screened (AF and AI), and the duplicate studies were removed. The remaining studies were further assessed based on title and abstract, and were removed if they did not meet the inclusion criteria of oral and intravenous muscle relaxant use in the perioperative period in the adult population. These included pain intensity scores, cumulative opioid requirements, time to first request for rescue analgesia, supplementary nonopioid analgesic use, opioid-related adverse events, and muscle relaxant-related adverse events. In addition, clinical outcome measures such as type and incidence of postoperative

Table 1. Skeletal Muscle Relaxants: Pharmacology

Generic Drug	Brand Name	Indication/Dosing	Mechanism of Action	Adverse Effect
Methocarbamol	Robaxin	Muscle spasm Oral 4.5–8 g daily IV 3 g daily	Central nervous system depression	Drowsiness, dizziness, stomach discomfort, blurred vision, black, blue, or green discoloration of urine
Orphenadrine	Disipal Norflex	Muscle spasm Oral 100 mg every 12 h; IV 60 mg every 12 h	Central nervous system depression	Dry mouth, drowsiness dizziness, lightheadedness, stomach discomfort, vomiting, constipation, difficulty urinating, blurred vision, headache
Tizanidine	Zanaflex	Muscle spasm Oral 2 mg every 6–8 h	Central nervous system depression, a2 receptor agonist	Chest pain, discomfort, fever or chills, nausea, vomiting, nervousness, pain, burning while urinating, unusual tiredness, chest pain or discomfort
Eperisone	Myonal Epry	Muscle spasm Oral 50 mg every 8–12 h	Centrally acting	Nausea, vomiting, stomach discomfort, headache, weakness, drowsiness, dizziness
Chlorzoxazone	Lorzone Parafon	Muscle spasm Oral 500 mg every 6–8 h	Central nervous system depression	Drowsiness, dizziness, lightheadedness, weakness, stomach discomfort
Cyclobenzaprine	Flexeril Amrix	Muscle spasm IR oral 5–10 mg every 8 h XR oral 15 mg once daily	Centrally acting structurally related tricyclic antidepressant	Somnolence, dry mucous membranes, dizziness, and confusion
Baclofen	Fleqsuvy Lyvispah Ozobax Lioresal	Muscle spasm Oral 5–10 mg every 8 h	Centrally acting, binds GABA-b receptor	Dizziness, drowsiness headache, muscle weakness nausea
Chlorphenesin		Muscle spasm Oral 250 mg every 8 h	Centrally acting	Sleepiness, dizziness, heartburn, stomach discomfort
Thiococlicoside		Muscle spasm Oral 8 mg every 12 h	Centrally acting	Nausea, somnolence, vasovagal reaction

complications, time to ambulation, hospital length of stay, and patient-reported outcome measures were also noted, when reported.

The following variables were extracted from each included study: (1) study characteristics, (2) interventions including the timing and frequency of muscle relaxant administration, and (3) primary and secondary outcome measures. In addition, the use of acetaminophen and nonsteroidal antiinflammatory drugs (NSAIDs) or cyclooxygenase (COX)-2-specific inhibitors in the comparator group was also recorded, because these simple analgesics are considered as basic components of an optimal multimodal analgesic strategy.[3,24] A change of more than 10 mm on the 100-mm visual analogue scale or one in the 10 points numerical rating score was defined as clinically relevant.[24]

Given the heterogeneity of the study designs, the type of muscle relaxants used, and the timing of administration, a narrative synthesis was felt to be most appropriate for this article in the form of a practical review. The purpose of this practical review is to explore and review existing evidence behind muscle relaxant use in the perioperative period, rather than a formal evaluation of the quality of studies, systematic review and/or meta-analysis. Therefore, risk of bias was not assessed.

RESULTS

The final search identified 22 studies, of which 18 studies were randomized controlled trials and four were observational trials. The study characteristics, design, interventions, pain scores, opioid consumption, use of nonopioid analgesics, and other outcome measures reported are summarized below and in the Supplemental Digital Content 1. (**See table, Supplemental Digital Content 1,** which displays the characteristics, study design, interventions, pain scores, opioid consumption, use of nonopioid analgesics, and other outcome measures reported in the included studies. **http://links.lww.com/PRSGO/D319**.)

Preoperative Administration

When comparing the efficacy of muscle relaxants in the preoperative period, the comparative literature varied based on outcomes. Talakoub et al[25] investigated the effects of a single preoperative dose of tizanidine in patients undergoing laparoscopic cholecystectomy. The study found that compared with placebo, tizanidine reduced pain scores and analgesic requirements in the first 24 hours. Also, it reduced recovery room stay; however, these differences may not be clinically meaningful. Tizanidine was associated with drowsiness, although patient satisfaction levels were higher.

A few other studies found a reduction in pain scores, of which one was conducted by Ahiskalioglu et al,[26] who found that a single preoperative dose of tizanidine before thyroidectomy along with bilateral superficial cervical plexus block had lower pain on swallowing and lower fentanyl consumption in the first 24 hours after surgery compared with the control group that did not receive either. Also, the combined use of cervical blocks and tizanidine significantly decreased postoperative cervical pain and occipital headaches. Dadmeher et al[27] also found lower pain scores and opioid use in the first 24 hours postoperatively when patients undergoing bimaxillary orthognathic surgery were divided to either receive tizanidine oral or placebo before surgery. Additionally, Aezi et al[28] evaluated analgesic effects of preoperative oral tizanidine, clonidine, and placebo in patients undergoing lumbar fusion surgery. There were no differences in pain scores over the first 24 hours, except for the second and fourth postoperative hour, although these differences were not clinically meaningful. The tizanidine and clonidine groups had lower morphine consumption, but the clinical significance of these differences can be questioned. Zeiner et al[29] found no significant differences in pain intensity and rescue opioids within the first 24 hours after cruciate ligament repair between patients who received preoperative orphenadrine and diclofenac versus diclofenac alone versus placebo.

Preoperative and/or Postoperative Administration

The vast majority of the literature was focused on administering muscle relaxants in either the preoperative or postoperative period or a combination of the two. Hidalgo et al[30] conducted a randomized study involving patients undergoing primary breast augmentation. The efficacy of preoperative and postoperative oral methocarbamol with or without intercostal nerve blocks was investigated. The results showed that methocarbamol resulted in significantly lower pain scores in the immediate postoperative period, but intercostal nerve blocks alone did not. Schneider et al[31] used methocarbamol intraoperatively and postoperatively for 7 days in patients undergoing breast augmentation. Pain scores were not reported; however, authors claimed that postoperative pain relief was superior in comparison with a historical group of patients who did not receive methocarbamol. The methocarbamol group required less opioid rescue; however, total opioid use was not reported. Bourazani et al[32] conducted a randomized controlled trial on patients undergoing breast reconstruction and showed that postoperative thiocochlicoside significantly reduced postoperative pain scores on the day of surgery and subsequent 3 days. However, an invasive surgical study conducted by Al-Yafi et al[33] on patients undergoing subpectoral breast reconstruction found that using a different muscle relaxant, postoperative cyclobenzaprine, did not have any significant reduction in pain scores or opioid usage when compared with the control group.

Some studies focused on the effects of muscle relaxants for oromaxillofacial surgery. Barroso et al[34] randomized patients undergoing third molar extraction to receive either piroxicam alone or Rheumazin, which contains a combination of piroxicam, orphenadrine citrate, dexamethasone, and cyanocobalamin. No significant difference was found in pain or swelling. Rheumazin had a lower incidence of side effects compared with the piroxicam. In contrast, Winter et al[35] evaluated the analgesic effects of orphenadrine in patients undergoing a variety of oral surgical procedures and found improved pain

scores compared with placebo. Patients were divided into four groups receiving a combination of orphenadrine and acetaminophen, each drug alone, or a placebo postoperatively and were monitored intermittently for 6 hours. The sum of pain intensity was better for the combination than the three other groups, and the two active drugs alone were also superior to placebo. Kirmeier et al[36] found no significant difference in pain or edema in the seven days postoperatively when patients received additional oral tizanidine on postoperative day 0 and postoperative day 1 in addition to the standard treatment. The only significant difference was increased ability in mouth opening for the tizanidine group in postoperative day 1 and 3, but not day 7. Santos et al[37] studied the analgesic effects of preoperative and postoperative oral cyclobenzaprine compared with placebo after oral surgery. The authors used a split-mouth design, so each participant acted as his/her own control. The investigators extracted one impacted mandibular third molar on each side of the mouth at different times. They found no significant difference between the sides of the mouth for pain, swelling, or trismus in the first 48 hours. Tomic et al[38] compared the analgesic effects of intraoperative and postoperative administration of intravenous orphenadrine and diclofenac with ibuprofen alone in patients undergoing orthognathic surgery and found no significant difference in pain intensity.

Outside oral surgical procedures, a diverse range of other surgical interventions were examined. The study by Nielsen et al,[39] which was a randomized placebo-controlled study with patients undergoing spine surgery, found no significant differences in postoperative pain during mobilization or total morphine usage when compared with placebo over the 4-hour study period. Gong et al[40] evaluated the effectiveness of eperisone in the early recovery after total knee arthroplasty by dividing patients into three groups: eperisone combined with celecoxib, celecoxib alone, and placebo. Those who received the combination of eperisone and celecoxib showed significant reduction in pain scores at rest and during movement, reduced morphine consumption, and better active range of motion, compared with the other two groups at various time periods within 14 days of surgery. Skrejborg et al[41] studied chlorzoxazone postoperatively in a placebo-controlled trial with patients undergoing total knee and hip replacement. There were no significant differences between the groups in terms of pain levels after a 5-m walk 24 hours after surgery. No differences were found in terms of opioid consumption and Oxford knee or hip scores within 7 days postoperatively or at the 12-month follow-up.

Analgesic consumption was an additional variable commonly reported by a variety of studies as well. Yazicioglu et al[42] compared tizanidine administered preoperatively and continued twice daily for a week after inguinal hernia repair with placebo. Tizanidine significantly reduced postoperative pain scores at rest and during movement, reduced analgesic consumption, and improved return to normal daily activity and quality of life. No postoperative side effects were observed; however, lower intraoperative heart rate and blood pressure values were observed. Bohl et al[43] conducted a retrospective analysis of patients undergoing anterior cervical decompression and fusion. Patients received preoperative cyclobenzaprine, acetaminophen, pregabalin, ketamine, dexamethasone, and local infiltration with bupivacaine 0.5%. Postoperatively, the multimodal analgesia group received scheduled cyclobenzaprine, tramadol, and cryotherapy (ice packs applied to back). There were no differences in the pain scores between the groups. However, the multimodal analgesia group had a lower opioid consumption and a lower rate of nausea/vomiting on postoperative days 0 and 1, as well as a shorter hospital length of stay. Desai et al[44] conducted a retrospective analysis of patients undergoing ventral and inguinal hernia repair who received postoperative methocarbamol and compared them to controls. Although inpatient opioid use was similar between groups, patients in the methocarbamol group had lower opioid use at the time of discharge with no increased need for refills. Pain scores were not reported.

Fry[45] investigated the use of single dose intravenous orphenadrine postoperatively in a randomized placebo-controlled study involving patients undergoing abdominal surgery. Orphenadrine patients had a delay in the need for rescue analgesia compared with the controls. A retrospective single center study on patients undergoing lumbar fusion, conducted by Perez et al[46] found that patients who received postoperative muscle relaxants (cyclobenzaprine and/or baclofen) had higher pain scores compared with those who did not receive any. They also discovered two-fold increase in the incidence of delirium in older patients who received postoperative muscle relaxants compared with those who did not.

DISCUSSION

The goal of this practical review is to provide readers a summary of existing research to determine the pain-relieving effectiveness and potential side effects of muscle relaxants used during the perioperative phase across a spectrum of surgical procedures, including plastic surgery. A key finding of this review is that the evidence for analgesic efficacy and/or opioid-sparing effects of skeletal muscle relaxants is inconsistent. There is significant heterogeneity among the studies in terms of surgical procedures, patient populations, choice of muscle relaxant, and timing and duration of administration, potentially limiting the generalizability of the findings. Studies involving minor surgical procedures not requiring significant opioids or muscle manipulation seem to have inappropriately used muscle relaxants. Studies evaluating single-dose administration do not provide any clinically meaningful information because of the relatively short half-life of muscle relaxants (eg, terminal half-life to be 3 hours[47]). Another noteworthy observation is that for some studies, although the differences in pain scores were statistically significantly lower in the muscle relaxant groups, they were not clinically meaningful (ie, the differences between the study group and the comparator group were less than 10 mm/100-mm scale or less than 1/10 scale[24]).

Given that muscle relaxants are generally administered to reduce opioid requirements, their use in surgical

procedures that require minimal or no opioids after surgery is questionable. However, several studies evaluating muscle relaxants were performed in surgical procedures that require minimal or no postoperative opioids.[48] For example, patients undergoing tooth extraction usually do not require postoperative opioids, as the pain can be adequately managed with acetaminophen and NSAIDs or COX-2 (cyclooxygenase-2)-specific inhibitors.[48] Similarly, patients undergoing thyroidectomy typically require 0-5 oxycodone tablets after surgery.[48] The mechanism of action for muscle relaxants helps with postoperative pain caused by muscle contractures and muscle manipulations from major procedures. It is less likely to help with other causes of postoperative pain. Boyev et al[49] performed a cohort study of 832 patients getting pancreatic resections and demonstrated that administering muscle relaxants as part of the postoperative bundle in addition to acetaminophen and NSAIDs helped decrease the inpatient opioid volume by half and the median opioid volume at discharge to 0. These findings suggest that when muscle relaxants are used appropriately in major abdominal procedures in addition to the standard nonopioid postoperative bundle, it can help reduce inpatient opioid use and increase the number of patients able to be discharged opioid free.

Another major limitation of the majority of the included studies is that acetaminophen and NSAIDs or COX-2-specific inhibitors were not administered in the comparator groups. These nonopioid analgesics are safe and inexpensive with well-documented efficacy, and therefore are considered basic analgesics.[3,24] Evidence suggests that the combination of acetaminophen and NSAIDs or COX-2-specific inhibitors provide superior pain relief compared with either drug alone.[3,24] Therefore, unless there are contraindications, a combination of acetaminophen and NSAIDs or COX-2-specific inhibitors should be administered either preoperatively or intraoperatively and continued postoperatively. Because of the lack of a basic multimodal analgesic regimen in the comparator group, the precise analgesic benefits of muscle relaxants over basic analgesics cannot be distinguished. Also, avoidance of basic multimodal analgesics might inappropriately enhance the observed efficacy and opioid-sparing of muscle relaxants.

There are concerns of potential adverse effects, including increased risks of sedation, delirium, and falls.[46] These adverse events are particularly enhanced when muscle relaxants are combined with opioids and other sedatives.[50] Combination of muscle relaxants with opioids have been shown to increase the risk of opioid overdoses when compared with opioid alone.[50] Santosa et al conducted a retrospective analysis of patients being co-prescribed opiates with muscle relaxants and benzodiazepines, and found that patients were significantly more likely to refill their opioid prescriptions even after controlling for preoperative opioid exposure.[51] Caution must be exercised when using muscle relaxants in patients at high risk of postoperative complications, including older patients (age >65 years),[52] morbidly obese patients (BMI >40 kg/m^2), those with sleep apnea, and those with significant comorbidities.

Given the lack of evidence of analgesic efficacy, including for surgical procedures involving muscle manipulation, and potential adverse effects, routine use of muscle relaxants may not be appropriate. The use of skeletal muscle relaxants should be reserved for patients in whom an optimal multimodal analgesic technique consisting of basic analgesics such as acetaminophen and nonsteroidal antiinflammatory drugs or cyclooxygenase-2-specific inhibitors combined with dexamethasone and local/regional analgesia is not adequate. Also, there may be a limited role for skeletal muscle relaxants in patients at high risk of severe postoperative pain undergoing

Table 2. Patients at High Risk of Postoperative Pain

• Presence of preoperative pain (preexisting chronic pain)
• Preoperative opioid use
• Preoperative-medication–assisted treatment (buprenorphine, methadone, naloxone)
• Substance use disorders
• Inappropriate patient expectations
• Psychological conditions [low self-esteem, severe anxiety, major depressive disorder, pain catastrophizing, or hypervigilance (ie, strong attention bias toward pain), functional pain states (eg, fibromyalgia)]

Table 3. Optimal Perioperative Multimodal Analgesic Regimen

Preoperative Interventions
• Preoperative screening and optimization of high-risk patients
• Patient and caregiver education
• Acetaminophen and COX-2-specific inhibitors, orally, unless contraindications
• Gabapentinoids (gabapentin or pregabalin): if receiving before surgery, caution in patients at risk of sedation and/or respiratory depression
• Regional analgesia techniques (procedure-specific and patient-specific)
○ Interfascial plane blocks: torso surgery (eg, thoracic, or abdominal wall and intrathoracic or intraabdominal surgery)
○ Peripheral nerve blocks: major upper extremity and lower extremity surgery
Intraoperative Interventions
• Opioid-sparing (not opioid-free anesthesia)
• Acetaminophen and NSAIDs or COX-2-specific inhibitors, unless contraindications, if not administered preoperatively
• Dexamethasone 8–10 mg, IV
• Surgical site local anesthetic infiltration and/or regional analgesic blocks, when possible
Postoperative Interventions
• Acetaminophen and NSAIDs or COX-2-specific inhibitors, scheduled
• Opioids, immediate release, preferably oxycodone, as rescue (if needed)
• Skeletal muscle relaxants, in patients undergoing surgical procedures with muscle manipulation, high pain responder, high opioid requirements, and if basic analgesics are not administered, caution in patients at risk of sedation and/or respiratory depression.
• Gabapentinoids: if already receiving before surgery, caution in patients at risk of sedation and/or respiratory depression
• Nonpharmacological interventions (procedure-specific and patient-specific)

surgical procedures with expected high opioid requirements (Table 2). Additionally, these drugs may be an option in patients in whom basic analgesics could not be used (Table 3). However, due to the concerns of potential adverse effects, the decision to use muscle relaxants in vulnerable populations should be made carefully, weighing the benefits against the risks.

Future research with larger, well-controlled studies and longer follow-up periods is needed to establish more definitive conclusions on the optimal use of muscle relaxants in perioperative pain management, including identifying best dosing schedules (ie, preoperative versus postoperative use). Also, it is necessary to explore the use of muscle relaxants in conjunction with other analgesic agents, particularly basic multimodal analgesics. Furthermore, the role of muscle relaxants in patients at high risk of postoperative pain and risk of persistent postoperative opioid use, as well as those in whom basic multimodal analgesics and/or regional analgesia could not be administered needs to be evaluated. In addition, there is a need for research in surgical procedures involving muscle manipulation such as submuscular implant-based reconstruction, muscle flaps, etc. None of the studies examined assessed patients' baseline anxiety score with a tool like the Generalized Anxiety Disorder Scale to further determine if this was contributing to the overall patient pain perception and if administration of muscle relaxants had an impact on the score, if any. This could also be an avenue for further research.

CONCLUSIONS

The decision to use muscle relaxants should be made carefully, weighing the benefits against the risks. The evidence for routine use of skeletal muscle relaxants as a component of multimodal analgesia is lacking. Also, there are concerns of potential adverse effects, particularly in vulnerable populations (eg, patients at high risk of respiratory complications). Although evidence is lacking, these medications could be used for patients in whom basic analgesics do not provide adequate pain relief or if basic analgesics cannot be administered or in patients with high opioid requirements, postoperatively. Also, there may be a role for these drugs in patients at high risk of severe pain. Further research is necessary to determine analgesic efficacy and potential adverse effects of skeletal muscle relaxants before routine use for perioperative pain management.

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