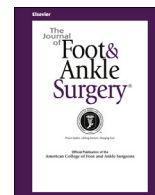




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Review Article

Gabapentin as an Adjunct to Standard Postoperative Pain Management Protocol in Lower Extremity Surgery

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ABSTRACT

Postoperative pain is a problem that plagues physicians and has since the dawn of the surgical arts. Many interventions are available and used as the standard such as preoperative local anesthetic blocks, opiates, both oral and intravenous, and nonsteroidal antiinflammatory drugs. Although the temptation often exists to increase the postoperative opiate dose, opiate abuse is an increasing problem. This abuse has fueled the search for nonopiate pain adjuncts. Gabapentinoids have been shown to both decrease postoperative pain and, secondarily, decrease opiate dependence. This is a growing field in medical research, although it is relatively lacking in the specialty of lower extremity orthopedic surgery. A PubMed query was performed for related articles, which found only 8 related to lower extremity orthopedic surgery, and of these, none addressed the foot or ankle. Studies involving chronic pain, nonorthopedic surgery, orthopedic procedures proximal to and including the hip, studies involving only pregabalin, and studies regarding cancer pain were excluded. The results from our literature review are encouraging regarding the addition of gabapentin as a regular, perioperative adjunctive pain medication because all studied reported data evaluating preoperative administration have shown a statistically significant reduction in postoperative pain and opiate consumption.

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An undesired and ubiquitous side effect of orthopedic foot and ankle surgery is postoperative pain. Postoperative pain not managed with accepted pain management protocols plagues patients and raises the question regarding other methods and modalities to manage this pain. In addition, narcotic abuse and misuse is a concerning problem in our current healthcare system because more and more patients have become addicted after surgical intervention. Thus, interest in nonopioid pain management has been increasing for physicians of all specialties.

At our institution, most patients undergoing outpatient elective foot surgeries (e.g., bunions, hammertoes, small joint arthrodesis) have been successfully treated with a preoperative local anesthetic block, short acting opioids, and the addition of interposed nonsteroidal antiinflammatory drug use postoperatively as needed. However, patients might still report unmanageable pain, especially during the first week

after surgery. Adjunctive methods for postoperative pain control have recently included gabapentin. Given that opiate misuse is an increasing problem, any opportunity to reduce the need or requirement for such is desired.

Although the mechanism of action of gabapentin is not completely understood, it is believed to bind to the 2 subunits of neural voltage-dependent calcium channels. This decreases the release of glutamate, norepinephrine, and substance P. As a consequence of taking gabapentin, the dorsal horn neuron hyperexcitability induced by tissue damage is reduced, causing a reduction in postoperative pain, hyperalgesia, and central sensitization (1,2). It is because of this preemptive mechanism that gabapentin might be a useful perioperative pain management tool. Gabapentin has also been found to be a relatively safe medication to administer in the short-term perioperative period, and the most common side effects (i.e., drowsiness, dizziness) are transient (1-4).

Gabapentin has been studied regarding its efficacy in the reduction of postoperative pain acutely and the reduction in opiate consumption postoperatively. A number of studies have reported proven success of preoperative gabapentin dosing across multiple surgical specialties (5,6), finding it to be an adjunctive option worthy of consideration. The purpose of the present study was to review the

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available data for the addition of postoperative gabapentinoid to the preoperative dose in foot and ankle orthopedic procedures.

Materials and Methods

A PubMed (available at: <http://www.ncbi.nlm.nih.gov/pubmed>) query was performed to search for investigations of perioperative gabapentin use in orthopedic procedures. A free text search of "gabapentin orthopedic surgery," "gabapentinoid orthopedic surgery," "gabapentin pharmacology," and "gabapentin surgery" were performed, and 8 articles specific to lower extremity orthopedic procedures and including 609 patients were analyzed. Our last electronic PubMed search was performed in December 2017.

Owing to the paucity of reported data available for perioperative gabapentin use in foot and ankle surgeries, all types of studies were accepted in the initial search of the articles. Further inclusion criteria were English language publication, study applied to lower extremity orthopedic surgery, and all studies involved preoperative gabapentinoid administration. During our literature search, we excluded articles addressing chronic pain, nonorthopedic procedures, orthopedic procedures proximal to and including the hip, studies only evaluating pregabalin, and reports addressing cancer pain. The articles chosen were published between August 2005 and February 2017. Ultimately, we found 8 articles that had specifically addressed the use of gabapentin in lower extremity orthopedic surgery, with none specifically addressing the foot and ankle. These were evaluated with an additional 5 supporting articles regarding the pharmacology and related applications regarding gabapentin and the perioperative period reported between April 2002 and November 2013.

Results

We reviewed 8 articles (609 patients) addressing the effect of gabapentin perioperatively (Table) in regard to lower extremity orthopedic surgery. Ten other reports were reviewed for the general use of perioperative gabapentin outside of orthopedics, its pharmacology, and the rationale behind its use as an adjunct perioperative pain medication.

A double-blind, randomized, placebo-controlled study by Clarke et al (7), studied both pre- and postoperative gabapentin use in patients undergoing total knee arthroplasty. All patients received a single 600-mg preoperative dose of gabapentin 1 to 2 hours before the

procedure. The treatment arm received 200-mg gabapentin postoperatively 3 times daily for 4 days in conjunction with celecoxib 200 mg every 12 hours for 3 days. The control group received placebo in place of gabapentin and celecoxib 200 mg every 12 hours for 3 days. Although evaluation of opiate consumption and pain levels was a secondary outcome measure, they did observe a lesser amount of postoperative pain in the gabapentin group at 18 and 24 hours, with no statistically significant difference in pain noted after the 24-hour mark.

Clarke et al (8) performed a similar study a few years before the study discussed in the previous paragraph. They evaluated the use of gabapentin both preoperatively and postoperatively in total knee arthroplasty. Clarke et al (8) divided the 36 participants into 5 small (all $n < 10$) groups, which allowed for placebo control of both preoperative and postoperative dosing with 3 different dosing regimens for the postoperative group. Because the study groups were small, the final analysis of the data combined the 5 groups into 2 groups: those who had received postoperative gabapentin and those who had received postoperative placebo. Clarke et al (8) reported a significant decrease in opiate use in the combined postoperative gabapentin group compared with the postoperative placebo group.

Ménigaux et al (9) performed a study evaluating the use of perioperative gabapentin regarding anxiety and functional recovery after arthroscopic anterior cruciate ligament repair. A total of 40 participants were equally divided between a treatment and a control arm. The treatment arm received a single 1200-mg dose of gabapentin 1 to 2 hours before surgery and the control arm received a placebo. The investigators reported a 50% decrease in pain medication consumption at 48 hours and a significant decrease in perioperative anxiety.

A triple-blind, randomized controlled trial by Mardani-Kivi et al (10) administered 600 mg of gabapentin preoperatively and reported a statistically significant decrease in pain intensity and opioid consumption after arthroscopic anterior cruciate ligament reconstruction. Postoperative pain was evaluated at 6 and 24 hours postoperatively. No statistically significant difference was found between the study and control groups regarding known the side effects

Table
Data from the 8 reviewed articles

Investigator	Procedure	Nonopiate Adjunctive Medication	Patients (Control/Trial)	Gabapentin Dosing		Significant Result
				Preoperatively	Postoperatively	
Clarke et al (7)	Total knee arthroplasty	Celecoxib, nerve block (femoral and sciatic)	76/79	600 mg, 1×, 2 h before surgery	200 mg TID for 4 days	Decrease in postoperative pain at 18 and 24 h with no significant difference after 24 h
Clarke et al (8)	Total knee arthroplasty	Celecoxib, nerve block (femoral and sciatic)	14/22	600 mg, 1×, 2 h before surgery	100 mg, 200 mg, or 300 mg TID administered for 4 days	Decrease in postoperative opiate use in the trial group No difference in pain scores
Montazeri et al (13)	Knee arthroscopy	NA	35/35	300 mg, 1×, 2 h before surgery	NA	Decrease in postoperative pain Decrease in postoperative opiate use
Panah Khahi et al (12)	ORIF of tibial fracture	NA	32/32	300 mg, 1×, 2 h before surgery	NA	Decrease in pain 2 h postoperatively
Mardani-Kivi et al (10)	Arthroscopic ACL reconstruction	NA	57/57	600 mg, 1×, 2 h before surgery	NA	Decrease in postoperative pain Decrease in postoperative opiate use
Ménigaux et al (9)	Arthroscopic ACL reconstruction	Ketoprofen	20/20	1200 mg, 1×, 1 to 2 h before surgery	NA	Decrease in preoperative anxiety Decrease in postoperative morphine consumption by 50%
Paul et al (11)	Total knee arthroplasty	Acetaminophen, ketorolac	49/52	600 mg, 1×, 2 h before surgery	200 mg every 8 h for 48 h	No statistically significant decrease in postoperative pain, opiate use, satisfaction scores, or length of hospital stay
Eloy et al (14)	Total knee arthroplasty, total hip arthroplasty, hip fracture repair	Celecoxib, bupivacaine catheter	12/17	NA	400 mg 1× on POD 0 and 400 mg 1× on POD 1	No statistically significant difference in Pittsburgh Sleep Quality Index on PODs 1 and 2; no statistically significant difference in postoperative pain scores

Abbreviations: ACL, anterior cruciate ligament; NA, not available; ORIF, open reduction and internal fixation; POD, postoperative day; TID, 3 times daily.

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