Perioperative pain management strategies among women having reproductive surgeries

Malavika Prabhu, M.D.,[a] Pietro Bortoletto, M.D.,[b] and Brian T. Bateman, M.D., M.Sc.[c,d]

[a] Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Massachusetts General Hospital; [b] Department of Obstetrics, Gynecology, and Reproductive Biology, Brigham and Women's Hospital; [c] Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital; and [d] Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts

This review presents opioid-sparing strategies for perioperative pain management among women undergoing reproductive surgeries and procedures. Recommendations are provided regarding the use of nonsteroidal anti-inflammatory drugs, acetaminophen, other adjunctive medications, and regional anesthetic blocks. Additional considerations for chronic opioid users or patients using opioid replacement or antagonist therapy are discussed. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)

Key Words: Opioids, perioperative pain management, reproductive surgery

Discuss: You can discuss this article with its authors and with other ASRM members at https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/17539-24441

Women undergoing procedures or surgeries related to infertility experience pain, which is often treated with opioid medication. This creates some important clinical considerations. For patients who are opioid naive, exposure to these addictive medications may be a trigger for persistent use. Data from reproductive procedures are limited, but recent data suggest that opioid exposure after other surgeries confers an increased risk for chronic opioid use (1, 2). For women who are taking chronic opioids or opioid replacement therapy, tolerance to opioids has the potential to make pain management more difficult. Likewise, women who have a history of an opioid use disorder may wish to avoid opioid medications, given concerns about the potential relapse. For these reasons it is important for all patients, but particularly those with a history of opioid use disorder or dependence, to optimize the treatment of pain in the perioperative period with non-opioid analgesics. In this review we present evidence-based strategies for non-opioid perioperative pain management demonstrated to improve postoperative pain scores and/or decrease consumption of opioids, and provide recommendations for implementation following common reproductive surgeries and procedures.

NON-OPIOID ANALGESICS

A variety of non-opioid analgesics are available, which can be used as part of a multimodal analgesic regimen to reduce the need for opioid analgesics. The two most commonly used classes of non-opioid analgesics are nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen. Gabapentinoids are also becoming an increasingly popular component of multimodal analgesia and are now included in many enhanced recovery after surgery protocols (3–5).

Nonsteroidal anti-inflammatory drugs inhibit cyclooxygenase (COX) enzymes to prevent the metabolism of arachidonic acid released from damaged tissue to prostaglandins, which in turn lowers the pain threshold in peripheral nociceptors (6). These medications can be administered preoperatively, intraoperatively, or postoperatively. Preoperative administration of NSAIDs may be beneficial as a preemptive analgesic. They have been demonstrated to improve pain control for many surgical procedures. Though there is a theoretical concern owing to their effect on platelet function, evidence suggests that the use of NSAIDs generally does not increase the risk for periprocedural bleeding (7, 8).

Evidence regarding preoperative NSAIDs use in reproductive surgeries or infertility-related procedures is limited. Among women having combined

Received June 1, 2017; accepted June 6, 2017.
M.P. has nothing to disclose. P.B. has nothing to disclose. B.T.B. has nothing to disclose.
M.P. and B.T.B. have received funding for research from Pacira Pharmaceuticals. B.T.B. has received funding for research from Baxalta, GSK, Pfizer, and Lilly.
Reprint requests: Brian T. Bateman, M.D., M.Sc., Brigham and Women's Hospital, Department of Medicine, Division of Pharmacoepidemiology and Pharmacoeconomics, 75 Francis Street, Boston, Massachusetts 02115 (E-mail: bbateman@partners.org).

Fertility and Sterility® Vol. ■, No. ■, ■ 2017 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2017.06.010

outpatient hysteroscopy–laparoscopy for infertility under general anesthesia, preoperative naproxen administration resulted in lower postoperative pain scores, shorter time to discharge, and less need for postoperative pain medications (9). In contrast, administration of preoperative diclofenac for outpatient hysteroscopy alone did not demonstrate improved pain scores during or after the procedure (10, 11). Although more work needs to be done to determine the exact role of preoperative NSAID administration in reproductive surgeries, it is reasonable to administer NSAIDs either preoperatively or intraoperatively for most patients given the favorable safety profile.

For postoperative patients, data suggest NSAIDs result in a 20%–40% reduction in opioid consumption over the first 24 hours after a variety of major and minor surgical procedures (12). There is no proven benefit of IV over oral NSAIDs, and no comparative efficacy data exist to drive selection of specific NSAIDs (13, 14). There are also currently no high-quality data specifically demonstrating the impact of postoperative NSAIDs on opioid consumption after reproductive surgeries. However, it is likely that the findings showing benefit in other surgical populations are relevant to these procedures.

Perioperative/periprocedural NSAIDs have traditionally been avoided during fertility treatment, given concerns about COX inhibition on pregnancy implantation (15, 16), but the importance of this has recently been questioned. In a retrospective cohort study of women undergoing oocyte retrieval for a planned fresh transfer cycle, a third of whom received postprocedure IV ketorolac, there were no differences in pregnancy rates or live birth rates, and postoperative pain scores were significantly lower among women who received ketorolac (17). No prospective or randomized, controlled trial data are available. Until better evidence accumulates it may be prudent to avoid NSAIDs in association with oocyte retrieval with a planned fresh transfer cycle.

Acetaminophen, or paracetamol, likely functions via central COX enzyme inhibition and central serotonergic activation, although the mechanism of analgesia is incompletely understood (18, 19). The addition of acetaminophen to opioid-based postoperative pain management results in a reduction in opioid consumption of 20%–40% over the first 24 hours after various major and minor surgical procedures (12, 20–23). Whether efficacy of acetaminophen differs by route of administration is controversial: although some studies suggest benefit to IV acetaminophen (24), the majority of studies have not shown any significant benefit to the administration of IV over oral acetaminophen in decreasing opioid use (25–27). There are also currently no high-quality data specifically demonstrating the impact of postoperative acetaminophen on opioid consumption after reproductive/gynecologic surgery, but it is likely that the benefits observed for other surgeries will translate.

The mechanism of action of gabapentinoids is complex and occurs along several pathways. The suspected pathway for pain modulation is via calcium channel–dependent inhibition of synaptic neurotransmitter release, which results in peripheral blocking of pain due to tissue injury (28, 29). A meta-analysis among women undergoing total abdominal hysterectomy has demonstrated decreased opioid consumption and decreased pain scores for the first 24 hours after surgery with preoperative gabapentin (30). Preoperative gabapentin or pregabalin has also been shown to significantly decrease postlaparoscopy shoulder pain in women undergoing laparoscopic gynecologic surgery (31, 32). The use of gabapentinoids should be considered in patients undergoing major reproductive/gynecologic surgeries, particularly patients at high risk for difficult-to-control postoperative pain.

No randomized trial directly compares the relative opioid-sparing effects of acetaminophen, NSAIDs, and gabapentinoids. A network meta-analysis comparing non-opioid analgesics after major surgery has demonstrated decreased opioid consumption over the first 24 hours after surgery with both acetaminophen and NSAIDs, with a mean reduction in IV morphine equivalents of 6 mg for acetaminophen and 10 mg for NSAIDs, with no statistically significant difference between these drugs (33). The combination of analgesics with different mechanisms of action results in even greater pain relief. Acetaminophen and ibuprofen co-administration yield a number needed to treat of 1.5–1.6 to effect 50% pain relief (23, 34). Taken together, the data suggest that women should be routinely treated with acetaminophen and NSAIDs, and potentially with the addition of a gabapentinoid provided no contraindication exists.

Misoprostol, used to facilitate cervical dilation, has been suggested as another adjunctive analgesic option for patients undergoing intrauterine procedures, particularly in the outpatient setting. However, a recent systematic review and meta-analysis investigating the impact of preoperative misoprostol on intraoperative pain during outpatient hysteroscopy demonstrated no clinically meaningful improvement in pain over placebo (35). Other trials comparing preoperative misoprostol with lidocaine cervical spray or NSAIDs also showed no superior benefit for pain management (11, 36, 37). A single trial that examined the preoperative administration of misoprostol well before (8–12 hours) outpatient hysteroscopy did show benefit in reducing intraoperative pain, perhaps suggesting the importance of timing of administration (38). However, given the side effect profile of a single dose of misoprostol (nausea, vomiting, diarrhea, abdominal cramping, fever (39, 40)) and the limited data suggesting benefit, this medication should probably not be used routinely for patients undergoing these procedures in the outpatient setting.

REGIONAL ANESTHETIC BLOCKS

Regional blocks with local anesthetics can serve the role of the primary intraoperative anesthetic, with or without sedation, or of adjunctive postoperative pain control. Depending on the approach (vaginal, laparoscopic, or abdominal), procedure under consideration (oocyte retrieval, hysteroscopy, dilation and curettage, hysterectomy), and patient characteristics (pain history or risks of conscious sedation or general anesthesia), regional blocks may be considered. The neuraxial approach with epidural anesthesia can be used for postoperative pain control for major open surgeries. A full review of the use of neuraxial anesthesia is out of the scope of this review, and we focus on other regional anesthetic blocks that may be useful in reproductive surgeries.