Anesthesia and analgesia for gynecological surgery

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**Purpose of review**
High-quality analgesia has been linked to improved patient satisfaction as well as improved short-term and long-term postoperative outcomes. Acute surgical pain is a modifiable risk factor for development of chronic postoperative pain, which is reported by up to 26% of gynecologic surgical patients. In other surgical populations, multimodal analgesia has shown improved pain control and decreased reliance on opioids. This review examines recent evidence for various analgesic modalities applied specifically to the gynecologic surgical population.

**Recent findings**
Nonopioid agents like acetaminophen, nonsteroidal anti-inflammatories, and gamma-aminobutyric acid analogs resulted in reduction in postoperative pain and opioid consumption. Application of regional anesthetic techniques had a favorable effect that persisted beyond the immediate recovery period. Preemptive analgesia remains unproven. The best evidence for effective combinations comes from ERAS studies that incorporated multimodal analgesia into a systemic approach geared towards early discharge.

**Summary**
Multimodal analgesia had demonstrated advantages for all types of gynecological surgeries in terms of improving postoperative pain control and minimizing opioid-related adverse effects. Multimodal analgesia includes acetaminophen, NSAIDS, and gamma-aminobutyric acid analogs combined with intraoperative nonopioid analgesics such as ketamine, regional anesthesia or intrathecal morphine. Further research should focus on determining most effective combinations and doses of multimodal analgesia.

**Keywords**
gynecologic surgery, multimodal analgesia, nonopioid analgesia, postsurgical pain

**INTRODUCTION**
Gynecological surgeries are some of the most frequent surgeries, however 4.7–26.2% of women experience chronic postoperative pain [1]. Acute pain is a modifiable risk factor for development of chronic postoperative pain and a key component to Enhanced Recovery after Surgery (ERAS) [2]. Multimodal analgesia, the administration of two or more analgesic agents or procedures (e.g. regional nerve blocks) that exert their effects along different analgesic pathways, contribute to the optimization of acute postoperative pain. Multimodal analgesia within established ERAS guidelines for gynecological surgery have demonstrated a reduction in opioid consumption, less postoperative nausea and vomiting (PONV), and earlier time to discharge, reducing healthcare costs [3,4]. This article outlines the specific multimodal techniques that may be advantageous for abdominal, laparoscopic, and vaginal gynecological surgeries with focus on these endpoints.

**SYSTEMIC ANALGESIA PHARMACOLOGY**
Common pharmacologic agents of multimodal analgesia include nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, anticonvulsant agents, lidocaine, and ketamine. Acetaminophen is a nonopioid analgesic inhibitor of N-methyl-D-aspartate (NMDA) receptors and cyclooxygenase [5]. In the central nervous system, acetaminophen modulates endogenous cannabinoids in the cyclooxygenase 2 pathway. Acetaminophen has an opioid-sparing
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KEY POINTS

- Multimodal analgesia should be considered routinely in the care of gynecologic surgical patient.
- Oral acetaminophen and NSAIDs are recommended and should be combined with regional techniques and intrathecal morphine wherever appropriate.
- Combinations of analgesic modalities have become the cornerstone of ERAS protocols in gynecology, although evidence for most effective combinations and doses is still sparse.

Effect of approximately 20% [6]. Scheduled acetaminophen regimens reduce opioid consumption compared with as-needed dosing [7]. The recommended schedule is 12–15 mg/kg, four times daily to a maximum of 3250 mg per day [8**]. Acetaminophen is well tolerated, with minimal side effects. Compounded oral agents that contain opioids generally impede the ability to deliver the daily maximum of acetaminophen and are not recommended. Oral administration of acetaminophen is suggested, as evidence does not support the need for intravenous acetaminophen because of cost. For patients who cannot tolerate oral intake, intravenous acetaminophen provided to patients at induction of anesthesia in laparoscopic hysterectomy, then regularly postoperatively, reduced opioid consumption in the first 24 h [9].

NSAIDs suppress inflammation and inhibition of the cyclooxygenase enzyme. NSAIDs are key components of multimodal analgesia with 30–50% opioid-sparing effect [6]. NSAIDs have significant side effects, like gastrointestinal, and postoperative bleeding. However, short-term use as part of a postoperative multimodal analgesic regimen reduces the incidence. Nonselective opioids like ketorolac, decreased opioid usage on the first postoperative day and reduced need for antiemetics [10]. Intravenous ketorolac 10–15 mg may be as effective as the manufacturer dose recommendation of 30 mg [11]. Cyclooxygenase-2 specific inhibitors, like celecoxib, have reduced the risk of peptic ulceration associated with NSAIDs but have an increased cardiovascular risk profile. There is a paucity of trials comparing the outcomes of selective versus nonselective NSAIDs or various nonselective NSAIDs for postoperative gynecological analgesia. Intravenous ketorolac reduces morphine consumption postoperatively after laparoscopy-assisted vaginal hysterectomy compared with placebo [12]. Ketonolac decreases opioid usage on the first postoperative day and reduces the need for antiemetic therapy [10].

Gabapentin and Pregabalin are α2-δ subunit calcium-channel ligands that reduce pain by decreasing the reuptake of glutamate, norepinephrine, and substance P. Preoperative gabapentin for abdominal hysterectomies can be effective in reducing postoperative pain, opioid consumption, and opioid-related side effects [13]. Gabapentin may decrease opioid-associated vomiting and pruritus but not without its own side effects, sedation, and dizziness [14]. Evidence suggests perioperative administration of gabapentin has no effect on postoperative pain resolution, but a modest effect on opioid cessation after surgery [15**]. Similarly, gabapentin 1200 mg for vaginal hysterectomies did not significantly alter the opioid consumption [16]. Pregabalin may not be effective in reducing opioid use up to 24 h postoperatively, following abdominal hysterectomy [17].

Ketamine is a NMDA-receptor antagonist. It disrupts nociception by binding and inhibiting NMDA channel’s excitatory glutamate receptor site. At nonanesthetic, analgesic doses, ketamine may reduce postoperative pain and opioid requirements. Low-dose ketamine (10–15 mg) has analgesic and opioid-sparing effects in the first 24 h after surgery [18]. Side effects, including hallucination, or disturbing dreams are reported but are infrequent at low doses. Evidence for the role of ketamine in gynecology surgery is limited. Grady et al. [19] suggest that ketamine does not improve functional analgesia or opioid-related side-effects after abdominal hysterectomy.

There is evidence that intravenous lidocaine is an effective analgesic adjunct in abdominal surgery, predominantly colorectal surgery. A Cochrane systematic review concludes there is evidence of small benefits in the reduction in pain, and opioid consumption and time for bowel recovery [20]. Clinically, significant reductions in opioid requirements have been demonstrated during and after abdominal surgery with intravenous lidocaine infusions. Currently, evidence for lidocaine use for abdominal hysterectomies would suggest that it neither improves functional analgesia and recovery nor reduce hospital length of stay [19,21].

Opioid analgesics are the predominate postoperative pain management tool. Oral analgesia is the preferred route postoperatively, as soon as the patient is tolerating oral intake as it is convenient, noninvasive, and cost-effective [22]. It is best to avoid intramuscular administration as this route is painful and has large variations in pharmacokinetics. Intravenous opioids, often administered with patient-controlled analgesia (PCA) pumps can restrict mobility and functional recovery. The optimal PCA setting are context-sensitive. Background continuous infusions with PCA opioids do not add any benefit to opioid-naive patients.

Opioids like morphine, hydromorphone, fentanyl, sufentanil, and remifentanil, are all used
intraoperatively. PCA infusions predominantly use morphine, hydromorphone, and fentanyl. Oral morphine, hydromorphone, and oxycodone are the most common opioids in the postoperative period. Dosage response to opioids can vary as can the susceptibility to side effects. Opioids lead or contribute to pruritus, nausea, constipation, urinary retention, respiratory depression, and delirium. The choice of opioid should be made according to pharmacological profile, that is, speed of onset, duration of action, efficacy, and side effects.

**REGIONAL ANESTHETIC TECHNIQUES**

Regional anesthetic techniques utilize anatomically targeted local anesthetics and adjuvants that interrupt afferent transmission and modulate the neuroendocrine and inflammatory response. Neuraxial techniques have been used in gynecologic surgery as primary anesthetic as well as in combination with general anesthesia and regional blocks. Both fentanyl and sufentanil improved the quality of subarachnoid block in a meta-analysis including gynecologic surgical participants [23]. Intrathecal morphine prolongs postoperative analgesia and has parenteral opioid-sparing effect [24] but doses greater than 0.2 mg may increase side effects without additional benefit [25,26]. The disadvantages of intrathecal opioids include pruritus, delayed mobilization, and urinary retention [26]. Whenever alpha-1 adrenergic agonist, clonidine, was added to subarachnoid bupivacaine and fentanyl for abdominal hysterectomy, it increased block height and duration [27]. In recent years, dexmedetomidine has emerged as a neuraxial adjuvant with important analgesic effects. Its effects are dose-dependent and include reduction in postoperative pain scores and beneficial sedation and hemodynamic profile as well as decrease in onset time and increase in duration of sensory blockade [28].

Regional block techniques used in pelvic surgery may target branches of the sacral plexus (pudendal and paracervical blocks) or the lumbar plexus and intercostal nerves [transversus abdominal plane (TAP) and quadratus lumborum blocks (QLB)]. Women who received pudendal nerve blocks for posterior colporrhaphy had lower mean pain scores for the first 24 h postoperatively and required less acetaminophen and meperidine [29]. Paracervical blocks with bupivacaine before vaginal hysterectomy reduced mean total opioid consumption for the first 24 h postoperatively and lowered the mean pain score [30]. A recent trial found that paracervical blocks for vaginal hysterectomy in combination with preemptive acetaminophen and NSAIDs reduced opioid requirements and time spent in the postanesthesia care unit [31].

TAP block is beneficial in reducing postoperative pain following abdominal surgery. In trials completed in gynecologic population, ropivacaine and bupivacaine were found to improve postoperative pain or reduce morphine consumption for up to 48 h [32,33]. Elsewhere, 0.375% bupivacaine failed to show a difference whenever compared with no TAP following laparoscopic hysterectomy [34]. A study comparing liposomal bupivacaine with plain bupivacaine in TAP blocks found liposomal preparation to significantly improve postoperative recovery following robotic-assisted hysterectomy [35]. QLB, holds promise of more extensive local anesthetic spread and possible visceral analgesia. One randomized controlled trial (RCT) found significant improvement in pain for up to 24 h with posterior QLB compared with placebo following gynecologic laparoscopy [36].

Intraperitoneal instillation of local anesthetics may decrease pain for up to 6 h following gynecologic laparoscopy [37]. A combination of bupivacaine and dexmedetomidine is superior to bupivacaine alone [38]. Continuous intraperitoneal infusion of bupivacaine postlaparoscopy shows no benefit [39]. Nebulized intraperitoneal ropivacaine either before, continuously during or at the conclusion of pneumoperitoneum has no analgesic effect [40,41]. Infiltration of local anesthetic at surgical site is a common practice with limited impact on acute postoperative pain [42].

**MULTIMODAL ANALGESIA FOR OPEN GYNECOLOGIC SURGERY**

Gabapentin may be effective at reducing postoperative pain for abdominal hysterectomy [13]. The appropriate dose, timing, and choice of patients is controversial. Systemic lidocaine does not have good evidence to suggest its routine use for this surgical cohort. Opioids should be provided on a ‘as needed’ basis as an oral preparation. If oral medication cannot be tolerated, consider opioid PCA without a background continuous infusion. Epidural analgesia is superior to intravenous PCA in reducing pain and opioid consumption in abdominal surgery [43]. The shorter length of stay after surgery in the modern era limits the effectiveness of this type of intervention [44]. Alternatively, spinal anesthesia with intrathecal morphine may facilitate early mobilization and discharge compared with epidurals [45]. Spinal anesthesia without long-acting opioids does not improve postoperative pain whenever compared with general anesthesia [46]. Wherever patients have undergone general anesthesia without neuraxial blockade, truncal nerve blocks may reduce pain and reduce postoperative morphine requirement. Continuous wound
infiltration or intraperitoneal instillation of local anesthetic has limited evidence.

**MULTIMODAL ANALGESIA FOR LAPAROSCOPIC GYNECOLOGIC SURGERY**

Same day discharge is common following laparoscopic surgery, which requires adequate analgesia with minimal PONV and ambulation within hours of anesthetic emergence. Premedication with acetaminophen and NSAIDs has been recommended for reduction of postsurgical pain [47*]. Evidence for preemptive sustained-release opioids is equivocal [48]. Preemptive pregabalin has significant opioid sparing in higher dose but also high rate of side-effects such as headache, dizziness and blurred vision, in patients undergoing laparoscopic hysterectomy [48]. Lower dose preemptive pregabalin 150 mg improved postoperative pain but had no opioid-sparing effect [49]. More recently, pregabalin 75 mg given 2h preop and repeated twice at 12h intervals improved shoulder pain and lowered analgesic consumption but did not improve surgical pain following gynecologic laparoscopy [50]. Preemptive ketamine was associated with superior analgesia and opioid sparing as compared with placebo as well as postoperative ketamine [51]. Intraoperative lidocaine infusions in gynecologic laparoscopy failed to show improved postoperative pain but did shorten time to discharge [52,53*]. Intraoperative infusion of dexmedetomidine has minimal benefit whenever compared with remifentanil and fentanyl [54].

Two trials examined effect of spinal anesthesia on postoperative analgesia in gynecologic laparoscopy demonstrating improved analgesia up to 24 h and less PONV compared with general anesthesia [55,56]. Further review of safety and benefit is required before such technique can be recommended routinely. Analgesic benefits of TAP block following gynecologic laparoscopy have been inconsistent [32,34*,35]. Intraperitoneal instillation of local anesthetic and surgical port injection analgesia is limited to the first 4–6 h postlaparoscopy [37,38,57].

**MULTIMODAL ANALGESIA FOR VAGINAL GYNECOLOGIC SURGERY**

Although evidence to guide pain management for vaginal gynecologic surgery is limited, available studies demonstrate improved analgesia whenever using nerve blocks, neuraxial anesthesia, and combinations of nonopioid-based medications. Pudendal and paracervical blocks provide advantageous multimodal strategies for vaginal gynecological surgeries [29–31]. Local anesthesia has also shown promise for urogenital prolapse surgery [58]. Whenever women received high-volume ropivacaine in site-specific posterior colporraphy and perineorrhaphy, they had significantly reduced opioid requirements and time spent in the postanesthesia care unit.

Neuraxial anesthesia is a popular technique for vaginal hysterectomies and perineal surgeries. The addition of dexmedetomidine or midazolam to 0.5% hyperbaric bupivacaine for spinal anesthesia for vaginal hysterectomies may lengthen time to first postoperative analgesic request, maximum pain scores, and consumption of postoperative analgesia [59].

An essential component of the 2015 ERAS guidelines is multimodal analgesic strategies [5]. Multimodal analgesic pain regimens for gynecological surgeries should include acetaminophen and NSAIDs in combination with gabapentin and dexamethasone. In addition to these analgesics, paracervical nerve block or intrathecal morphine should be considered for vaginal hysterectomies. Modesitt et al. [60**] implemented gynecologic ERAS protocols that resulted in a statistically significant reduction in intraoperative morphine equivalents and lower pain scores on the first postoperative day. ERAS implementation after vaginal hysterectomy has been found to reduce the median length of stay by 52% [60**]. Additionally, a study, which included preemptive multimodal analgesia and proactive intraoperative analgesia (pudendal and uterosacral nerve blocks) showed cost-efficiency savings, coupled with increased satisfaction and no rise in morbidity for the ERAS protocol [61].

**EFFECTS OF MULTIMODAL ANALGESIA ON POSTOPERATIVE NAUSEA AND VOMITING**

The general incidence of PONV is approximately 30–50%. Gynecological surgery is associated with a higher incidence of PONV and involves patients who are at high risk for this complication (female sex, nonsmoking status, and requirement for postoperative opioids) [62]. Neuraxial techniques reduces the incidence of PONV by avoiding known triggers like volatile anesthetics, neuromuscular blockade reversal, and systemic opioids [63,64]. PONV was nine times less among patients receiving regional anesthesia than those receiving general anesthesia [65]. Spinal anesthesia decreased opioid requirements in several studies involving abdominal and vaginal hysterectomies [32,33,34*]. However, only one trial noted a reduced incidence of nausea postoperatively whenever neuraxial anesthesia was used [66].
Systemic opioid administration increases the risk for PONV in a dose-dependent manner and persists as long opioids are used [67,68]. The incidence of PONV is, therefore, lower through the use of nonopioid analgesics like NSAIDs and acetaminophen [6,69]. In a systematic review, included gynecologic surgery, NSAIDs were associated with a significant reduction in opioid consumption and PONV after major surgery [69]. The number-needed-to-treat with preemptive acetaminophen to prevent an episode of vomiting was 11 [70]. It is, therefore, reasonable to use an anesthetic strategy that encompasses multimodal analgesia in the forms of NSAIDS and acetaminophen to decrease the occurrence of PONV for gynecologic surgery [69,70].

**CONCLUSION**

In summary, multimodal analgesia had demonstrated advantages for all types of gynecological surgeries by improving postoperative pain control, minimizing opioid adverse effects, and preventing PONV. Gynecologic surgery patients benefit from administration of acetaminophen, NSAID, and possibly dexamethasone and gamma-aminobutyric acid analogs. For vaginal surgery, infiltration of local anesthetic in the form of a pudendal or paracervical nerve block may be considered. Regional analgesia should be considered in specific cases. Further research should focus on determining most effective combinations and doses of multimodal analgesia.

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**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES AND RECOMMENDED READING**

Papers of particular interest, published within the annual period of review, have been highlighted as: ■ of special interest  ■ of outstanding interest

16. The latest review of gabapentin for perioperative analgesia with clinically important impact. Perioperative administration of gabapentin had no effect on postoperative pain resolution, but it had a modest effect on promoting opioid cessation after surgery.
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A well done randomized, controlled, observer-blinded study, evaluating the analgesia provided by a TAP block after elective total laparoscopic hysterectomy. TAP did not reduce morphine consumption in the first 24 h.


The newer QLB procedure is evaluated to determine the efficacy of ultrasound-guided posterior QLB in treating postoperative pain following laparoscopic gynecological surgery. The posterior QLB reduced pain in postoperative care and at rest.


In this double-blind RCT, they evaluate a perioperative lidocaine infusion to improve analgesia in women undergoing day-case laparoscopic sterilization. The postoperative pain was not significantly different between lidocaine and placebo groups. The team to meet hospital discharge criteria was significantly lower in the lidocaine group.


The evaluation of implementation of an ERAS protocol for women undergoing major gynecologic surgery. Proper implementation of ERAS protocols in gynecological surgery can improve outcomes including improved patient satisfaction and decreased hospital costs.


