Multimodal Post-Cesarean Analgesia with Spinal Morphine and Continuous Wound Infiltration of Ropivacaine Using the OnQ® Elastomeric Pump: A Dose-Ranging Study Using a High-Volume, Low-Dose Protocol

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PI: Dr. James Dolak

Abstract:
The purpose of the proposed study is aimed to determine whether continuous subfascial infusion of ropivacaine using the On-Q® elastomeric pump in combination with intrathecal (IT) preservative-free morphine (PFM) will improve post-operative cesarean section pain relative to IT PFM alone (the current standard of care). Using a double-blinded, randomized, placebo-controlled study design, 60 women undergoing their first, second or third cesarean section will be randomly assigned to one of 3 different groups receiving either saline (control, n=20) or ropivacaine (0.1% or 0.2%, experimental groups n=20 in each) subfascially via the elastomeric pump. We will enroll up to 70 subjects to achieve 60 randomized and treated subjects, to account for screen failures and/or early terminations, All participants will receive an IT dose of 200mcg of PFM as part of a standardized spinal anesthetic for their operative procedure. During closure of their abdomen, all patients will undergo placement of a multi-orifice, silver-impregnated catheter in the subfascial space. At the conclusion of the surgery, the catheter will be bolused with 8ml of one of the three test solutions, after which an On-Q® elastomeric pump (containing the same solution as initially administered through the catheter) will be attached to infuse the test solution at a rate of 8ml/hr. The infusion system will then be left in place for up to 72hr. Adjunctive pain medicines (ketorolac, morphine, ibuprofen, and oxycodone-acetaminophen) will be available for the treatment of breakthrough pain during hospitalization. The primary outcome being measured in the study is post-operative pain with movement as assessed immediately after the study bolus (baseline) and during the immediate post-operative period, when leaving the PACU (2hr), 6hr, 12hr, 24hr, 48hr, and 72hr post-op. Pain will also be evaluated by telephone at 4-6 weeks and 3mo after surgery. A visual acuity pain scale (VAPS) will be used to measure patient pain levels while hospitalized whereas pain at the 4-6 week visit and 3mo will be quantitated using a numeric pain scale (NPS). Secondary outcomes to be studied include degree of pain at rest, time to first rescue medication, time to first opioid use, amount of

inpatient non-steroidal anti-inflammatory drug (NSAID) use, amount of inpatient opioid use, incidence and severity of opioid systemic side effects, incidence and severity of local anesthetic side effects, catheter related issues, breast feeding success, maternal satisfaction, evaluation of wound healing, categorization and quantification of outpatient pain medication, and cost analysis.

Introduction and Background:

The primary hypothesis of this study is that post-cesarean section pain with movement will be significantly improved in women treated with IT PFM by the addition of continuous subfascial wound infiltration with ropivacaine. There are approximately 4 million deliveries in the United States every year; with about 30% of these deliveries being cesarean sections. This makes cesarean section one of the most common surgeries performed today. Women experience significant post-operative pain after cesarean sections. Cesarean section patients are unique among surgical patients in that they have to immediately care for their newborns after their procedure, and their infants may be affected by systemically-administered maternal pain medications if breastfeeding. Therefore, this population requires the combination of maximal pain relief with minimal sedation, while minimizing the exposure of infants to clinically-significant amounts of drugs in breast milk. This encourages further studies that will elucidate better means of accomplishing ideal post-operative pain.

Pain, both intraoperative and postoperative, has been shown to be the anesthetic outcome of greatest concern to women undergoing cesarean section with the potential side effects of pain relief being of much less concern (1). This was found to be true both in terms of absolute ranking and when using a relative value score. Pain as part of the childbirth experience may predispose the parturient to the development of post-traumatic stress disorder (2). It has also been suggested that pain after cesarean section decreases the effectiveness of breast feeding leading to more formula and pacifier use (3, 4). In addition to the obvious psychological aversion to pain by patients, it is well-known that pain can stimulate a variety of potentially detrimental physiological effects such as tachycardia, hypertension, respiratory splinting, and inactivity, which in turn can lead to

risks of myocardial infarction, aneurysmal rupture, thrombophlebitis, post-operative atelectasis and pneumonia. Poorly controlled post-surgical pain relief also influences the risk of developing chronic post-surgical pain (CPSP) (5, 6). CPSP is defined as pain of at least 2mo duration which develops after a surgical procedure, and which is not related to any other causes of pain (infection, malignancy, etc.) or to pain continuing from a pre-existing pain problem (7). The incidence of CPSP after cesarean section is believed to be between 10-12% (5, 6), meaning that as many as 168,000 women might be affected with this each year. Even more troubling is that an estimated 4% of the women undergoing cesarean section (~48,000) actually develop disabling chronic pain defined as pain > 5 on a scale from 0 to 10 (6). Recognition of the above psychological and physical attributes of pain led to the Joint Commission recommendation to treat pain as the fifth vial sign, with the stated goal for US healthcare facilities to uniformly achieve pain scores ≤ 3 out of 10 (8).

Pain after cesarean section has two well-recognized components – somatic and visceral. Somatic pain is often described as a well-localized, sharp, burning, or tearing pain. In contrast visceral pain is described as a poorly-localized, dull or cramping pain. Somatic pain has both cutaneous and deep components which are transmitted via the anterior components of the spinal nerves, whereas visceral pain is a sympathetically-mediated pain whose sensation returns via afferents from the uterus to the inferior hypogastric plexus, and hence into the sympathetic chain, ultimately arriving at the spinal cord (8). It is a well-accepted theory that multimodal pain relief helps to alleviate pain by both working on different types of pain (somatic vs visceral) and at different pain receptors leading to either additive or synergistic analgesia, while minimizing the side-effect profile of any single drug component of the analgesic cocktail (9). For instance, either systemic or neuraxial opioids are traditionally given after cesarean section to decrease post-operative pain. Unfortunately, opioids given by either of these routes have several undesired and potentially severe side-effects including pruritus, constipation, urinary retention, nausea/vomiting, sedation, and respiratory depression (10). In an effort to mitigate these troublesome issues, NSAIDs are commonly given to reduce the inflammation associated with surgical injury, thereby decreasing the inflammatory

component of the pain with a resulting opioid-sparing effect (8, 10). Additionally, NSAIDs are particularly effective against the visceral cramping pain which results from uterine involution (8).

While the combination of neuraxial opioids with systemic NSAIDs appears to provide excellent postoperative pain relief at rest during the first 24hr, a significant number of women experience pain greater than 3/10 with movement during this same period, and with both rest and movement pain at time periods greater than 24hr. These pain exacerbations primarily involve discomfort resulting from tension on the wound, often require treatment with IV or PO opioids, and appear to be due largely to cutaneous or deep somatic pain. As incisional pain can often be acutely managed with local anesthetic (LA) infiltration, interest grew in seeing if continuous local infiltration of LA alone, NSAIDs alone, or combinations of NSAIDs with LAs through a catheter inserted into the surgical wound could reduce both post-surgical pain and postoperative opioid consumption. Initial results using subcutaneous catheters were disappointing, showing at most modest reductions in opioid use, with little or no change in pain scores (11). For example, in one study comparing the subcutaneous infusion of 4ml/hr of 0.25% bupivacaine with a saline infusion control showed no difference in VAS for pain at rest, but showed a 22 mg reduction in morphine use over 24hr (12). However, a meta-analysis of a number of trials involving subsets of surgical patients showed both reductions in pain scores and opioid consumption in the obstetric/gynecologic surgery population, although only pain at rest was examined (11). Multiple studies involving cesarean section patients have shown that subfascial infusions of plain 0.2% ropivacaine (13), 0.25% levobupivacaine (14), 0.2% ropivacaine containing diclofenac (15), or 0.2 % ropivacaine with ketoprofene (16) all provide good postoperative analgesia and a reduction in opioid usage for post-operative pain. In one of these studies (16), wound infusion of identical solutions through either subfascial catheters or subcutaneous catheters was compared, and subfascial administration was shown to be clearly superior based on pain at rest and total postoperative morphine consumption. Additionally, in two of the above studies, continuous wound infusion was found to provide postoperative analgesia nearly equivalent (14) or better (13) than epidural analgesia with either LA or PFM,

respectively. In contrast to these positive studies, one negative study found that subfascial wound infusion with 5ml/hr of 0.375% ropivacaine was inferior to intrathecal PFM in terms of both pain scores and IV oxycodone use (17). Therefore, while there are both theoretical and evidential grounds to support the use of subfascial wound catheters, their absolute efficacy as sole agents for pain relief remains to be established.

To date, long-acting neuraxial opioids like PFM provide the gold standard for post-cesarean delivery analgesia whether given via the IT or epidural route, providing excellent pain relief for the first 24hr while allowing the mother to ambulate and care for her child (18, 19). However, it is clear that neuraxial opioids do not provide complete analgesia for cesarean section when used as primary agents, with more than 70% of patients requesting further analgesia (19). Even when codeine with acetaminophen is given prn, 33% of women in one study still experienced inadequate analgesia (18). Pain with movement appears to be the most poorly treated pain phenomenon using neuraxial PFM (19). Again, this points to the importance of multimodal pain control in obstetric patients. Surprisingly, while continuous wound infiltration has been examined as a primary technique for post-cesarean pain relief (13,14,15,16) and has even been compared for efficacy to epidural (13,14) and IT (17) post-cesarean analgesia, no one has tested to see if continuous wound infiltration with LAs improves the analgesia obtained from IT PFM. However, it is standard practice of some obstetricians in our institution to use the continuous wound infiltration system on every patient undergoing a cesarean section whether they have IT PFM or not. The purpose of the proposed study is to examine the hypothesis that continuous wound infusion with ropivacaine using a high-volume, low-dose protocol will significantly improve pain with movement after cesarean section in patients who have received our standard dose of IT PFM. A control group (IT PFM + saline wound infusion) will be compared to two groups receiving both IT PFM along with one of two doses of ropivacaine (experimental groups) using the OnQ® elastomeric pump for delivery of the infusions. We have purposefully used lower concentrations of ropivacaine (0.1-0.2%) along with higher volumes in recognition that the nerves to be anesthetized are of smaller diameter, and therefore require lower concentrations of LA for this effect; while ensuring a high enough volume to completely

bathe the wound at the subfascial layer. During both cesarean section under local anesthesia (20), and with transversus abdominis plane blocks for post-operative analgesia (21) - situations which involve some of the same sensory nerves blocked by continuous wound infusion - the importance of volume versus concentration of LAs has been stressed. It is expected that ropivacaine, used in conjunction with IT PFM, will provide additive or synergistic pain relief as compared to IT PFM alone, and hopefully this will lead to better breast feeding, decreased opioid use with less opioid side-effects, fewer prolonged stays secondary to pain issues, increased patient satisfaction, and ultimately to decreased hospital costs.

Objectives:

The primary outcome measured in this study is post-operative pain with movement measured both during cough and 20° straight leg raise. Pain at rest will also be evaluated. All types of pain will be measured using a visual analogue pain scale (VAPS) determined using a 100mm line with the patient making a mark on the line between no pain and worst pain ever (12). Pain scores will be collected after the bolus of study medication/placebo (zero time), at PACU discharge (2hr), 6hr, 12hr, 24hr, 48hr, and 72hr post-cesarean section. Pain at 4-6 weeks and 3mo will be quantitated over the telephone using a numerical pain scale (NPS) with 0 being no pain and 10 being the worst pain imaginable. In addition to the pain scores, pain with movement will be further evaluated qualitatively using the short-form McGill pain questionnaire (22) at all time-points in the study. This will allow us to look at pain quality (sharp, burning, etc.), as well as examining the affective components (exhausting, fearful, etc.) of the pain.

There are several secondary outcomes of this study that can be divided into rescue medication information, medication side effects, breastfeeding, wound evaluation, patient satisfaction, and cost-analysis.

Rescue medication data will be collected during the hospitalization period (0-72hr). We will note the time to dosing with the first rescue medication for breakthrough pain. After the first rescue medication is given, the patients will be eligible for further doses of IV or

PO pain medicines for continued breakthrough pain as needed (see **Study Design and Methods** section below for specifics). The time to first opioid use for pain will also be recorded whether this entails IV or PO administration. Additionally, we will quantitate narcotic use in terms of morphine equivalents given (in mg) both by post-operative day and with a cumulative total. The total dose of NSAIDs (in mg) will be recorded for each of the first three postoperative days, along with a cumulative total. We will also be measuring the proportion of patients who require opioid supplementation at 0, 2, 6, 12, 24, 48, and 72 hours post-op. We will also ask if patients are still requiring opioids and/or NSAIDs for surgical discomfort along with inquiring about the amount of each used per day at the 4-6 week and 3 month follow-up telephone calls.

As several different medications are utilized within this study, it is important to monitor side effects of the medications, and see if these profiles change under the conditions of the study. We will collect data on the incidence and severity of opioid central and/or systemic side effects – pruritus, nausea/vomiting (not associated with hypotension), somnolence, and respiratory depression. Somnolence will be graded using a published perioperative somnolence scale (23). Measurements of nausea/vomiting and pruritus will make use of previously published scales (24). Respiratory depression will be considered to be present if the respiratory rate is < 10 breaths/min. We will also make note of both the type and amount of treatment given for these opioid-related side-effects. In addition, we will collect data on the incidence and severity of ropivacaine systemic side effects – tinnitus, perioral numbness, metallic taste, and seizures – and will characterize both the type and amount of treatment required.

Breast-feeding success and safety will be monitored during this study. Breast feeding success will be measured using LATCH Scores (25) obtained in the PACU, and once per shift on the mother-baby unit for 72 hours. These will be assigned by either the labor and delivery nurses or by the nurses in the post-partum ward. We will also assess the proportion of mothers breast-feeding their infants at 24, 48, 72hr, and during their 4-6 week and 3 month follow-up phone calls. Maternal plasma and breast milk concentrations have been measured during epidural analgesia with ropivacaine (0.125%)

for labor, with the breast milk-plasma ratio being somewhere between 0.23 and 0.25 at 18-24hr (26). Surprisingly, the literature is silent regarding the concentration of ropivacaine in human breast milk after continuous wound infusion.

Both the cesarean section incision and the catheter insertion site will be evaluated. Any catheter- or infiltrate-related issues like wound infection and seroma formation will be noted. Wounds will be assessed for infection or dehiscence at 24, 48, and 72hr. At the 4-6 week and 3-month follow-up phone calls the patient will be asked about the presence of wound dysesthesia (numbness, tingling, burning, pricking, allodynia, or hyperesthesia). The patient will also be asked about the occurrence of infection, dehiscence, and keloid formation at this time.

Patient satisfaction will be monitored with a satisfaction scores (100 mm scale) at 72hr. A cost analysis will occur for the inpatient stay. Some of the costs we will look at are include those for preparation of the drugs and devices, along with monitoring/supervision costs based on nursing and physician interventions, as well as cost of days spent in the hospital (27).

Study Design and Methodology

After informed consent has been obtained, all study participants will receive spinal anesthetics based on their height to provide anesthesia for their cesarean sections as per our usual clinical practice. Patients ≥ 64 inches will get spinal anesthetics containing 12mg 0.75% bupivacaine (1.6ml), 10mcg fentanyl (0.2ml), and 200mcg PFM (0.4ml) for a total volume of 2.2ml. Patients ≤ 63 inches will receive the same spinal anesthetic as those ≥ 64 inches except that the dose of 0.75% bupivacaine be reduced to 10.5mg (1.4ml) resulting in a total volume of 2.0ml. The PFM dose of 200mcg was chosen as it is the commonly used clinical dose (28). These spinal anesthetics reliably provide anesthesia for 1.5-2hr in each patient population. The patients will have been randomly assigned to one of three study arms prior to initiation of the anesthetic using a computer generated random number list. The randomization list has already been created using a randomization free-ware packet from the internet (Random Number Generator,

stattrek.com), and is on file at the research pharmacy. The code is not known by any of the investigators. The arms are as follows: 1) a bolus dose of 8ml of normal saline followed by an infusion of 8ml/hr of normal saline using an On-Q® elastomeric pump, 2) a bolus dose of 8ml of 0.1% ropivacaine followed by an infusion of 8ml/hr of 0.1% ropivacaine using an On-Q® elastomeric pump, or 3) a bolus dose of 8ml of 0.2% ropivacaine followed by an infusion 8 ml/hr of 0.2% ropivacaine using an On-Q® elastomeric pump. The pump will be filled to its maximum capacity of 550 ml and will infuse until the total volume is delivered. The patients will undergo their cesarean sections in the usual fashion through uterine closure. The peritoneum may or may not be closed and the rectus abdominis muscles may or may not be approximated as per the usual practice of the attending obstetrician. The obstetrician will insert a 20G guide needle/introducer assembly through the skin, subcutaneous tissue and rectus fascia about 3cm above and just lateral to the incision. When the introducer is fixed in the desired location, the guide needle is removed, and a multiport, silver-impregnated catheter (6-10cm) is placed above the rectus muscle parallel to the fascial incision. The fascia is then closed above the rectus muscles, and the rest of the closure occurs as per the usual practice of the surgeon. After closure is complete, one to two drops of a topical skin adhesive (2-octyl cyanoacrylate or SurgiSeal®) will be placed on the skin at the exit site of the multiport catheter and the catheter will be further secured with adhesive surgical strips. The exit site, along with a small length of catheter will then be covered with a sterile bio-occlusive dressing. The hospital pharmacy will have delivered a 10 ml syringe filled to 8ml with the bolus test solution, along with an On-Q® elastomeric pump loaded with the same solution to the operating room prior to, or during, the cesarean section. The test solutions are all water-white in color, and will have no discerning markings to indicate whether it is saline or one of the two concentrations of ropivacaine. The preparing pharmacist will be the only person not blinded to the study. At the termination of the surgical procedure, the obstetrician will administer the 8ml bolus of test solution via the catheter using the 10ml preloaded syringe, followed by attaching and activating the elastomeric pump which will be pre-set to deliver 8ml/hr of test solution.

Ketorolac (30 mg IV) will always be given at the first request for additional pain medicine after leaving the operating room. Thereafter, the study patients will receive 30mg ketorolac q6hr prn pain for 24hr if their pain score is > 3. If their pain score remains > 3 twenty minutes after ketorolac administration, they can receive morphine 1mg IV q1hr until their pain score is ≤ 3. After 24hr, and through discharge, the study patients will receive1-2 tablets PO oxycodone-acetaminophen (5/325) q6hr for post-operative pain for pain scores > 3. Additional breakthrough pain still present 30 min after oxycodone-acetaminophen dosing will be treated with ibuprofen 600 mg PO q6hr. Again, if the pain score remains > 3 thirty min after ibuprofen dosing, IV morphine (1-2 mg q1hr) will be administered until the pain score is ≤ 3.

Each patient that ends up participating in our study will have a folder (see attached Data Collection Instrument) associated with her name. This folder will include all of the VAPS scoring sheets and the McGill pain scoring sheets obtained at the different time periods. It will also contain summary sheets for data abstracted from the medical, nursing, and pharmacy records such as uterine closure, LATCH scores, time to first rescue medication, time to first opioid use, and total opioid and NSAID use, etc. These folders will be stored in locked file cabinets in the main office of the EUHM Department of Anesthesiology where other sensitive patient information is kept securely. Data, without personal identifiers will be entered into Excel spread sheets and kept on the Emory Healthcare virtual desktop for further analysis.

Participant Selection

The study will take place at Emory University Hospital Midtown (EUHM), which cares for a mixed community- and university-based obstetric practice. Parturients will be recruited from the patient pools of both private and Emory physicians, and enrolled after appropriate consent has been obtained. The inclusion criteria for the study includes all ASA class I-III parturients at least 34 weeks pregnant, that are 18 years or older, have never had a cesarean section, have had one or two prior cesarean sections, and are undergoing scheduled or unscheduled non-emergent cesarean sections with spinal anesthesia. Exclusion criteria includes parturients who have allergies to morphine,

ketorolac, or amide local anesthetics; pregnancies less than 34wks gestational age; significant maternal cardiac, liver, or renal disease; maternal history of narcotic abuse or dependency; presence of a pre-operative fever ($\geq$ 100.4 °F); emergent cesarean sections with or with-out general anesthesia; and patients in whom valid consent is questionable (non-English speakers or mentally-impaired individuals). Study patients have the option of withdrawing from the study at any point, as the On-Q® pump infusion can be simply discontinued and the catheter removed. At such time the patient would revert to our standard pain management protocol.

Statistical Analysis

Based on a preliminary sample size calculation using an α risk of 0.05, a β risk of 0.2, and an effect size involving a 40% reduction in pain scores, we estimate that 20 patients are needed in each arm of the study. Data normality will be tested using the Kolmorgorov-Smirnov test. Normally distributed data will be presented as means ± SD, whereas non-normally distributed data will be expressed as medians with interquartile ranges. Categorical data will be reported as frequencies. VAS scores will be analyzed using two-way ANOVA for repeated measures. Non-normal data will be analyzed using the Friedman test. Categorical data will be analyzed using the X^2 test. Multiple comparisons will use a Bonferroni correction. Differences will be considered statistically significant at a $P<0.05$.

Patient Safety and Potential Benefits

There is no added discomfort of having the On-Q® device placed, as it is inserted during surgery under spinal anesthesia. There is also minimal to no discomfort upon removal of the catheter which is simply pulled out when the infusion is completed, if the patient withdraws from the study, or if the patient is discharged from the hospital. An adhesive bandage is placed over the insertion site and left in place for 12-24hr after catheter removal. Control patients who end up getting the normal saline infusions will be receive the current standard of care for pain relief at our institution (PFM and adjunctive medications).

All medications utilized in this study are currently employed on the labor and delivery and postpartum wards at EUHM. The spinal anesthetics described earlier constitute our standard of care for the provision of intraoperative anesthesia for cesarean section. The treatment of post-operative pain with IV ketorolac, and further with IV morphine for unremitting pain, represents our usual standard during the first 24hrs after cesarean delivery. Pain relief on the second and third postsurgical days is commonly provided by our obstetricians using oxycodone-acetaminophen (5/325) and ibuprofen, with IV morphine being occasionally used in refractory cases.

Several of our obstetricians routinely place the OnQ® pain system post-cesarean delivery, and administer 0.5% bupivacaine at 5 ml/hr through a subfascial catheter. In this study, we propose changing the LA infused from 0.5% bupivacaine at 5 ml/hr to either 0.1% or 0.2% ropivacaine, at 8 ml/hr. This change should actually enhance patient safety as not only does this represent a reduction in LA dose/hr (from 25mg/hr with bupivacaine to either 8 or 16mg/hr with ropivacaine, respectively), but also constitutes a change from a relatively cardiotoxic LA (bupivacaine) to one considered significantly less so (ropivacaine) (29). Ropivacaine is widely used in obstetric anesthesia for labor epidurals, and in fact, 0.2% ropivacaine at 8-12ml/hr forms our standard labor epidural infusion at EUHM. Finally, it should be noted that the highest daily ropivacaine dose utilized (day 1 which includes the hourly infusion plus an 8ml bolus (which works out to either 200mg or 400 mg for the two infusions) in this study is well below the maximum recommended daily dose of 800mg (30).

Additionally, patients in the study will be immediately unblinded via phone call to the pharmacy in the three following situations: a) if they experience any 2 of 4 minor LA toxicities (perioral numbness, metallic taste in mouth, tinnitus, or light-headedness); b) any signs of severe systemic toxicity (seizures, arrhythmia, obtundation, cardiac arrest); or allergic reactions which appear by timing as due to LA administration (hives, angioedema, anaphylaxis). Minor toxicities will be treated by simply stopping the infusion and watching the patient for 6hr (approximately 3 half-times in circulation - product insert). Major toxicities will be treated by stopping the infusions and providing

appropriate supportive or resuscitative care. It is felt that major toxicity is very unlikely considering the drug utilized, the drug dosage, the use of a clinically-approved delivery device, and the restrictions on recruiting patients with LA allergies.

The OnQ® elastomeric pump and silver-impregnated catheter are FDA-approved devices for the treatment of post-surgical pain after all types of surgery including cesarean section. Theoretically, it could be argued that there is a small risk of skin or wound infection due to the presence of a tunneled percutaneous catheter for three days. This risk will be mitigated in three ways. First, sterile technique will be used throughout the procedure and the patients will be given antibiotic prophylaxis before the cesarean section. Second, the silver-impregnated catheter has inherent antimicrobial properties which prevent formation of a bacterial microfilm with subsequent catheter colonization; and also elutes silver directly into the implantation site where it may have direct antimicrobial activity (31). Finally, LAs themselves have intrinsic bacteriostatic and/or bactericidal properties against a wide range of pathogenic bacteria, and thereby continuous wound infusion with these agents might create an unfavorable milieu for infection (32).

There are possible benefits of being enrolled in the study. If our hypothesis is correct, both acute postoperative pain (at rest and with movement) and chronic postsurgical pain will be reduced in patients that receive the ropivacaine infusions. These patients would likely experience a reduction in the use of opioids and other adjunctive pain medicines. This could lead to a reduction in the incidence and treatment of medication-related side-effects. The reduction in pain, as well as a decrease in medication use, might result in more successful and safer breastfeeding. Pain and side-effect reduction might also lead to the need for fewer nursing interventions, along with a potential decrease in the length of stay after a cesarean section. If these goals are met, this truly multimodal technique of postoperative pain control might also decrease the cost of these patients' hospitalization.

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