



## Brief Report

# A Multimodal Approach for Opioid-Free Analgesia after Cesarean Section using Surgical Site Infiltration with Liposomal Bupivacaine

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### Abstract

**Background:** Opioid-related adverse events and chronic opioid use drive demand for effective opioid-minimizing regimens after cesarean section. Wound infiltration with local anesthetics reduces opioid consumption in this setting. Surgical site infiltration with Liposomal Bupivacaine (LB), a prolonged-release formulation of bupivacaine HCl, is a new pain management technique amenable to opioid-sparing, multimodal care pathways for cesarean section. Proper infiltration technique is key to optimizing reduction in opioid consumption and recovery enhancement.

**Technique:** After adequate hemostasis of the subcutaneous space, patients receive 266 mg (20 mL) LB expanded to 40 to 60 mL with saline via twenty to thirty (depending on incision size) 2-mL subfascial injections 1 cm apart circumferentially underneath the reapproximated fascial incision, including the lateral aspects. An enhanced recovery after surgery protocol, including spinal anesthesia, acetaminophen and nonsteroidal anti-inflammatory drugs, is applied.

**Experience:** Local infiltration of LB as part of a multimodal post-surgical pain management approach can provide effective pain control with no opioid use. The three consecutive patients described achieved early ambulation, resumption of oral intake and voiding; actively participated in maternal care; and reported high satisfaction during the peri-partum course.

**Conclusion:** Meticulous technique with LB within an enhanced recovery protocol provided a pathway to opioid-free cesarean section.

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### Introduction

An opioid-free cesarean section, with well-controlled pain, is important for return of function and maternal care for newborns, as well as for prevention of chronic pain [1]. Neuraxial techniques such as epidural, spinal, or combined spinal-epidural anesthesia are generally recommended for most cesarean deliveries, with the choice tailored to patient factors such as anesthetic, fetal and obstetric risk; individual preferences; and progress of labor [2]. The effect of opioids on breastfeeding is important to consider when selecting postcesarean section analgesics [1]. Opioids pass into breast milk and have been known to cause severe central nervous system depression, which can lead to infant mortality [3]. Moreover, cesarean section can be viewed as a gateway to opioid addiction as the primary driver of first exposure to prescription opioids [4]. Patients and especially women, are often overprescribed opioids after surgery, including cesarean section and unused medications pose substantial risk for diversion [5]. Thus, there is a need for opioid-sparing and even opioid-free, approaches for postcesarean pain management.

The ability to provide effective postsurgical analgesia with reduced or eliminated opioid consumption favors use of multimodal pain management approaches [6]. Multimodal pain management options for cesarean delivery include nonsteroidal anti-inflammatory drugs and acetaminophen; neuraxial anesthesia techniques such as epidural with or without opioids and intrathecal opioids with oral or parenteral opioids for rescue; and regional anesthesia techniques such as surgical site infiltration with local anesthetics and Transversus Abdominis Plane (TAP) block [6]. Wound infiltration with a local anesthetic has been demonstrated to provide effective analgesia after cesarean section with a low rate of side effects [7].

Liposomal Bupivacaine (LB; EXPAREL<sup>®</sup>, bupivacaine liposome injectable suspension; Pacira Pharmaceuticals, Inc., Parsippany, NJ) is a prolonged-release formulation of bupivacaine HCl indicated for single-dose infiltration into the surgical site to produce postsurgical analgesia. LB has been demonstrated to provide postsurgical analgesia for up to 72 hours and reduce opioid consumption, with some patients remaining opioid-free postsurgery [8]. Although a recent retrospective observational study reported significant reduction in postsurgical opioid consumption following wound infiltration with LB for cesarean section, data are limited [9]. Evidence in other surgical settings indicates that meticulous infiltration technique is fundamental to optimizing patient outcomes with LB. This article presents the author's technique and initial experiences with wound infiltration of LB in cesarean section; three cases are described to exemplify outcomes.

### Dr. Chudacoff's multi modal cesarean section pain management protocol

#### Description of Patient Care

##### Pre-op

Patients were counseled extensively in the clinic during prenatal checks regarding multi modal opioid free pain management, especially the type of discomfort expected (pain scale) and post operative

milestones. Patients counseled that expectation would be no greater than 5/10.

#### **Intra-op personal modifications of routine cesarean section:**

- The perineum is entered bluntly and, after checking to make sure there are no adhesions of bowel to the anterior abdominal wall, the peritoneum is stretched
- A large Alexis wound protector retractor (Applied Medical, Rancho Santa Margarita, CA) is placed into the abdomen
- Without externalizing the uterus the endometrial cavity is swept clean of remnant membranes and blood clots using a dry lap tape
- The hysterotomy is then reapproximated with a running locking suture of 0 Monocryl suture (Ethicon, Somerville, NJ), with hemostasis of the incision noted
- The colic gutters are swept clean of amniotic fluid and blood with moist lap tapes
- The rectus muscle is reapproximated using a running suture of 3-0 chromic gut, (Ethicon, Somerville, NJ), without incorporating the peritoneum
- The rectus muscle the rectus fascia is closed with a running suture of 0 Vicryl suture (Ethicon, Somerville, NJ)
- After confirming hemostasis of the subcutaneous space a mixture of 20 mg of Exparel mixed with an additional 20 ml of saline, is injected subfascially. Using a four 10 ml syringes and a 22-gauge needles 2 ml of the LB/saline mixture are injected under the reapproximated fascia, 1 cm apart and taking care to inject the lateral 'corners' of the closed fascia incision. The plunger is withdrawn prior to each injection to prevent intravenous injection
- Scarpa's fascia is reapproximated with a running suture of 3-0 chromic gut
- The skin is closed with 4-0 Monocryl (Ethicon, Somerville, NJ) and the incision is covered with Tegaderm (3M Medical, St. Paul, MN)
- The patient receives 30 mg IV ketorolac either at the end of the case in the OR or in the PACU immediately following surgery

#### **Post-op**

- Patient is given ice chips when out of bed to a chair
- Patient is given coffee, tea or coke (caffeine) and the urinary catheter is removed when they walk out of the room and to the nurse's station
- Once they tolerate the coffee, tea or coke patient is allowed a regular, unrestricted diet

The patient that received general anesthesia was prepped and draped, and the Foley catheter was placed, before intubation. Spinal anesthesia patients were prepped and draped after spinal anesthesia. All patients received preoperative antibiotics.

### **Three Case Descriptions**

Patient 1 was a 24-year-old gravida 2, para 1, had a previous cesarean delivery requiring a 4-day hospital stay and 24 hours of bed rest immediately after surgery. She also stated she had significant postpartum depression and was therefore apprehensive about a repeat

c section. She was admitted to labor and delivery at 36 weeks, 5 days gestation with regular, painful uterine contractions and cervical change. She was not a candidate for spinal anesthesia secondary to severe scoliosis. She underwent a repeat cesarean section, under general anesthesia, having declined a trial of labor after cesarean section. Postoperatively, she rated her maximum pain as 5/10, complaining mostly of uterine cramping. This pain was relieved after she began walking and after she voided. She tolerated oral pain medication well 1 hour after surgery, ambulated 2 hours after surgery, while voiding and tolerating solids within 4 hours after surgery. At 2- and 6-week follow-ups, she observed that compared with her previous cesarean section she had a more pleasant and less painful postoperative course, including earlier ambulation and no evidence of postpartum depression. Nurses observed that the baby was more awake and feed better than patients with routine opioid postoperative pain management.

Patient 2 was a 20-year-old gravida 1 at 39 weeks estimated gestational age, measured large for dates at term and, after discussion, elected to have a primary cesarean section using the multimodal pain management protocol including local infiltration of LB. She was treated with the multi modal, opioid free pain management protocol, including 1 gram of acetaminophen 12 hours and one hour preoperatively. Postoperatively, she rated her maximum pain as 3/10, which she described as uterine cramping. She tolerated oral pain medication well 3 hours after surgery. The patient was ambulating and tolerated liquids within 3.5 hours after surgery, voided 4.5 hours after surgery and tolerated solid foods within 6 hours after surgery. At her 1-week postoperative visit, she reported no significant pain. At 2, 4 and 6 weeks post operative she reported being pain free, doing well and bonding with her child.

Patient 3 was a 23-year-old gravida 2, para 1 at 37 weeks estimated gestational age, elected to have a primary cesarean section with local infiltration of LB because she had a medio-lateral episiotomy with her previous vaginal delivery, which caused her significant dyspareunia. Her sister had experienced a favorable postpartum course after a primary cesarean section with LB, with no pain after the delivery. The patient presented to labor and delivery with regular, painful uterine contractions and mild cervical change. Her maximum postoperative pain was 4/10, which she described as cramping. She tolerated oral pain medication 3 hours after surgery. Postoperatively she was ambulating, voiding and tolerating oral fluids within 4.5 hours after surgery. She tolerated solids within 6 hours after surgery. At her 3-week postoperative visit, she reported being well and required no pain medication other than ibuprofen and acetaminophen (Table 1).

### **Discussion**

Effective and elective opioid-sparing approaches to postsurgical pain management after cesarean section are essential to optimize recovery, support early breastfeeding, enhance maternal-infant bonding and minimize risks for chronic opioid use and medication diversion. In the author's experience, wound infiltration with LB using meticulous techniques as part of a multimodal pain management protocol was a successful approach, enabling opioid-free cesarean section. The three patients included here reported postsurgical pain scores of  $\leq 5$  out of 10; were able to ambulate, void and tolerate liquids and solids within 6 hours postsurgery; and reported overall satisfaction with this pain management approach. Moreover, they did not report common opioid-related adverse events.

Pre-operative	Intra-Operative	Post-operative	Discharge
<ul style="list-style-type: none"> <li>Patient education - Managing pain expectation and goal of opioid free:                             <ul style="list-style-type: none"> <li>Goal is pain of less than 5/10 on a scale of 1-10</li> </ul> </li> <li>Acetaminophen 1gm PO 12 and 1 hour pre-surgery</li> </ul>	<ul style="list-style-type: none"> <li>Spinal or Epidural with anesthetic only</li> <li>Local (subfascial) Infiltration intraoperative after fascia closure: LB 266mg/ 20ml in 20ml NS 0.9% Total - 40ml; 22 gauge needle</li> <li>Ketorolac 30mg IV at end of case or in PACU</li> </ul>	<ul style="list-style-type: none"> <li>Alternating every 3 hours, scheduled: 1) ibuprofen 600mg po q6h; 2) acetaminophen 1gm po q6h</li> <li>Ice chips when out of bed and to a chair</li> <li>Coffee, Tea, or Coke with first ambulation past nurse's station</li> <li>Catheter removed when walks past nurse's station</li> <li>Regular diet after tolerating po fluids</li> <li>Opioids are not written prn. Nurses must call MD to initiate opioid use</li> </ul>	Same as postoperative for 72h, scheduled, longer as needed

**The Pain Scale**

0 - Pain free.

**Mild Pain** - Nagging, annoying, but doesn't really interfere with daily living activities.

- 1 - Pain is very mild, barely noticeable. Most of the time you don't think about it.
- 2 - Minor pain. Annoying and may have occasional stronger twinges.
- 3 - Pain is noticeable and distracting, however, you can get used to it and adapt.

**Moderate Pain** – Interferes significantly with daily living activities.

- 4 - Moderate pain. If you are deeply involved in an activity, it can be ignored for a period of time, but is still distracting.
- 5 - Moderately strong pain. It can't be ignored for more than a few minutes, but with effort you still can manage to work or participate in some social activities.
- 6 - Moderately strong pain that interferes with normal daily activities. Difficulty concentrating.

**Severe Pain** - Disabling; unable to perform daily living activities

- 7 - Severe pain that dominates your senses and significantly limits your ability to perform normal daily activities or maintain social relationships. Interferes with sleep.
- 8 - Intense pain. Physical activity is severely limited. Conversing requires great effort.
- 9 - Excruciating pain. Unable to converse. Crying out and/or moaning uncontrollably.
- 10 - Unspeaking pain. Bedridden and possibly delirious. Very few people will ever experience this level of pain.

Characteristic	Patient 1	Patient 2	Patient 3
Age, y	24	20	23
Gravidity	2	1	2
Parity	1	0	1
Vaginal	0	-	1
Cesarean	1	-	0
Gestational age at admission	36 wk, 5 d	39 wk*	37 wk*
Scheduled (Y/N)	Y	Y	Y
Presentation	Cephalic	Cephalic	Cephalic
Dense adhesive tissue (Y/N)	N	N	N
Comorbid disorders (Y/N)			
Opioid use disorder	N	N	N
Drug use/abuse disorder	N	N	N
Chronic pain disorder	N	N	N
Depression	Y	N	N

**Table 1:** Patient Demographics and Clinical Characteristics.

\*Estimated gestational age.

Wound infiltration with LB has demonstrated effectiveness in improving postsurgical pain and decreasing opioid consumption after various surgical procedures [8]. For cesarean section, wound

infiltration has demonstrated similar effectiveness as TAP block with regard to postsurgical analgesia and opioid consumption [7]. Data regarding LB in cesarean section are limited, but findings from a retrospective study demonstrated a 36% reduction in opioid consumption postcesarean in patients receiving local infiltration of LB at the site of their Pfannenstiel incisions [9]. However, meticulous infiltration techniques have proven necessary to optimize outcomes with LB and these techniques are still evolving in different surgical settings. The techniques presented here, which use multiple small-volume injections placed subfascially along the reapproximated fascial incision, were designed to account for the lesser spread of LB compared with bupivacaine HCl. These techniques provide a basis for further refinement and testing in a clinical trial.

The current findings suggest that a multimodal approach incorporating wound infiltration with LB can support opioid-free cesarean section. This is an important finding as opioid-free regimens remove the risks of opioid-related adverse events and mitigate the risk of chronic opioid use and abuse. As more than one third of the approximately 4 million annual US births are performed via cesarean section, opioid-free cesarean section would result in 1.2 million fewer opioid exposures and a similar reduction in the amount of prescription medication stored at home [10].

The small number of patients limits the current findings. Moreover, the patients presented here received spinal anesthesia only; it will be critical to collect broader experience in women receiving epidural or combined spinal-epidural block. The lack of any comparator represents a further limitation. Although these data are preliminary, they may help to define best practice for infiltration techniques that

can be assessed in future clinical trials. To this end, a study has been initiated to compare 30 patients prospectively treated using this approach with a retrospective cohort of 50 patients who received conventional opioid-based pain management utilizing intrathecal opioids. Wound infiltration with LB as part of a multimodal approach to postsurgical pain management after cesarean section was successful in the three patients presented. These patients reported adequate pain control, rapid recovery and overall satisfaction. The anesthesia providers noted the absence of pruritus and welcomed that they no longer needed to monitor patients for 24 hours after spinal opioids. These promising results warrant further study in clinical trials.

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