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Postpartum Analgesia

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OBJECTIVES

1. Review the pain physiology of post-cesarean and post-vaginal delivery acute pain.
2. Review the central axial and systemic options available for management of post-cesarean pain.
3. Review management options to treat post-vaginal perineal pain.

I. ACUTE PAIN IN THE POSTPARTUM PERIOD

The pain arising following a cesarean delivery or vaginal delivery is predictable based upon the site of trauma and pathways sending afferent signals to the central nervous system. The tissue trauma of delivery triggers a complex modulation of afferent and efferent pathways in the spinal cord and brain, which results in the perception of pain. For a woman following a cesarean delivery, the afferent signals arise from both visceral and somatic trauma. Visceral trauma to the uterus are transmitted via the T10 – L1 distribution of the sympathetic nerves and peritoneal innervation through the celiac plexus. The pain arising from this source of trauma is the poorly localized, episodic pain situated in the periumbilical area and associated with loss of appetite or nausea, and vomiting. The somatic trauma, involving incisions to the lower abdominal skin, fascia, and abdominal musculature, is dermatomal in distribution. As well, respiratory muscle function accentuates the very localized, sharp and stabbing pain stretching from the T8 – L1 distribution. The duration of post-cesarean pain is individual, however is significant during the first two weeks post-surgery, and noticeable for a further 2 – 4 weeks. There are also a small proportion of cesarean delivery patients who must also contend with the additional pain related to a failed vaginal delivery.

Vaginal deliveries primarily follow with a shorter course of primarily somatic pain arising from the stretch and tearing of the perineal skin. This pain is transmitted along afferent pathways of the pudendal nerve (via S2 – S4) and persists for 2 – 4 weeks on average depending upon the degree of trauma. From research in our own institution, we recognized that initial perineal pain is significant for all women regardless of the degree of perineal trauma(). In the first days after delivery this pain interferes with most women's ability to sit, urinate, walk or sleep. However, most women after vaginal delivery are reluctant to use prescribed pharmaceutical therapies, and rely on non-pharmaceutical options, such as perineal washes, ice packs and seat cushions.

II. POST-CESAREAN PAIN MANAGEMENT

Post-cesarean pain therapy was originally managed by obstetricians who ordered intermittent intramuscular opioids. However, this regime relied upon patients requesting pain relief and nurses administering it in a timely fashion. Studies have demonstrated that nurses tend to underestimate pain and analgesic requirements(). With anesthesiologists' knowledge of pharmacological pain therapies, our specialty was an obvious manager of post-cesarean pain relief. Thus, in the early 1980's anesthesiologists began their involvement using central axial and systemic narcotics(3-5).

The goals for anesthetic-managed post cesarean pain management include:

- Lowest pain scores at rest and movement
- Greatest patient satisfaction
- Lowest incidence of side effects
- Minimal neonatal effect
- Economically feasible

With these goals in mind, the current standard of care in North America for post-cesarean analgesia is one of the following options for the parturient:

Table I. Comparison of central axial narcotics.

Drug	Dose	Onset (min)	Peak effect (min)	Duration (hrs)
Epidural:				
Morphine	2 - 4 mg	45 - 60	60 - 120	12 - 24
Fentanyl	50 - 100 μg	5	20	2 - 3
Sufentanyl	25 - 50 μg	5	15 - 20	2 - 4
Hydromorphone	0.4 - 0.75 μg	15	45 - 60	10 - 20
Meperidine	50 mg	15	30	4 - 6
Intrathecal:				
Morphine	01 - 0.25 mg	30	60	12 - 24
Fentanyl	10 - 20 μg	5	12 - 3	
Sufentanyl	5 - 10 μg	5	10	2 - 4
Meperidine	10 mg	10	15	4 - 5

1. Single dose central axial opiates
2. Patient-controlled epidural analgesia (PCEA)
3. Patient controlled intravenous analgesia (PCIVA)
4. Multimodal analgesia strategy including one of the above with systemic non-narcotic analgesics

SINGLE DOSE CENTRAL AXIAL OPIATES

Single dose spinal/epidural opiate was the original analgesic technique used by anesthesiologists for post-cesarean analgesia. Morphine, hydromorphone, fentanyl, sufentanil and meperidine are the most commonly administered central axial agents. The choice of agent depends upon the desired onset of action, and duration of action. **Morphine and hydromorphone are hydrophilic agents** and thus have longer intervals to onset of action; epidural morphine reaches peak CSF levels between 60 – 90 minutes while spinal morphine's time to peak CSF levels are slightly faster at 45 – 60 minutes. However, morphine and hydromorphone's duration of analgesia after epidural or spinal administration are the reason for selection – please refer to table 1 for comparative times. These agents provide a reasonable duration to allow for conversion to oral analgesics, and thus avoid the necessity of intravenous or intramuscular agents. This is particularly true if morphine or hydromorphone are combined with other analgesic agents. (please refer to multimodal analgesia). The ideal doses for epidural or spinal morphine has been evaluated by numerous authors and appears to be: 2.0 – 2.5 mg epidural morphine and 0.1 – 0.15 mg spinal morphine[6-8]. Larger doses do not improve the quality of analgesia or increase the duration of effect, but primarily increase the incidence of side effects (Table I).

The lipo**philic narcotics, fentanyl, sufentanyl and meperidine have pre**dominantly been administered in the epidural or spinal space to improve intraoperative anesthesia. Although these agents have a much faster onset of action, their short duration of effect limits their use as the sole agents for post-cesarean analgesia. Their duration of effect is usually limited to less than four hours post-surgery, a time when the patient may not tolerate orally administered analgesics and will have to receive intramuscular, subcutaneous or intravenous agents. Using these agents alone for post-cesarean analgesia may be useful in delivery settings that cannot monitor patients for respiratory depression on the postpartum wards. Using lipophilic narcotics with a longer acting narcotic,such as morphine, could be recommended if the cesarean local anesthetic agent is short-acting. Women can have breakthroughs of pain in the early post-operative period if the local anesthetic effect wears off before the epidural or spinal morphine effect has begun. This is especially true for agents such as chloprocaine or lidocaine.

At Mount Sinai Hospital, in Toronto, Ontario, Canada we deliver over 7,000 women per year, and our current cesarean delivery rate is 37%. Most women (99.2%) have cesarean deliveries under regional anesthesia, and receive epidural/spinal morphine as the cornerstone of their postpartum analgesia. However, the women also receive simultaneous analgesics including non-steroidal antiinflammatories and acetaminophen. These agents are given around the clock for 24 hours under anaesthesia orders, and an additional systemic narcotic is available for breakthrough pain in the first 24 hours. After 24 hours the analgesic routine is carried on by the obstetricians who use a regime of oral narcotics, antiinflammatories and acetaminophen.

SIDE EFFECTS OF SINGLE DOSE CENTRAL AXIAL OPIATES

The most common side effects of epidural or spinal opiates are pruritus and nausea/vomiting. The incidence of these effects varies from study to study depending upon the definition of positivie outcome. If women are required to volunteer presence of the side effect or requires the administration of treatment

therapy, the incidence is less than if asked directly by investigators. **Pruritus** - Pruritus, the most common effect occurs in approximately 40 – 80% of women receiving central axial opiates for cesarean delivery analgesia. The incidence is often still occuring with ultra-low doses of morphine and hydromorphone, and can be segmental in distribution especially with lipophilic agents. The incidence of pruritus has fallen with reductions in epidural morphine doses from 4 or 5 mg down to 2 – 3 mg, and spinal doses of 0.5 mg to 0.15 mg. Treatment of pruritus relies initially with reassurance for the patient that it is not an allergic phenomenon and that it is expected. However, 10 – 20% of parturients with pruritus will request treatment and it is primarily based upon narcotic antagonist therapy (naloxone infusions, nalbuphine intermittent administration, naltrexone single dose therapy), antihistamines (although it is not a histamine mediated occurence) and more unusual therapies including ondansetron, propofol. The usual therapy administered in our institution is as follows:

1. nalbuphine 5 mg IV q1h prn
2. diphenhydramine 12.5 – 25 mg IV q3h prn
3. naloxone 0.8 mg added to 1000 ml IV solution to infuse at 75 – 125 ml/hr.

Nausea/vomiting – Nausea and vomiting are less common than pruritus, but arguably are more distressing for a new mother. Again, reduction in doses of central axial opiates has reduced the incidence, but it still occurs in current low doses. Usually anti-emetic therapy is successful in stopping or reducing symptoms. Our own clinical experience has incorporated multi-modal therapy for the vomiting parturient. Symptoms typically do not present until analgesic effects of the opiate occur, and therefore initial recovery room nausea and vomiting should still be considered due to maternal hypotension until proven otherwise. Recommended therapies include:

1. anti-histaminics (Gravol 12.5 – 25 mg IV q3h prn)
2. anti-serotoninergics (Granisetron 1 mg IV q12h; Ondansetron 4 mg IV q6h)
3. anti-cholinergics (Metocloperamide 1.25 – 2.5 mg IV q4h prn)
4. anti-dopaminergics (Stemetil)

Therapies including steroid agents (Decadron) have not been investigated in this population, however propofol has again been demonstrated to have some benefit. The use of propofol demands careful presence for excessive maternal sedation in the setting of a full stomach.

Urinary retention - This uncommon occurence is difficult to quantify following cesarean delivery because indwelling catheters are often left in post-operatively for 12 – 24 hours. However, in the initial use of large dose epidural/spinal morphine, urinary retention was identified and necessitated the continuation of catheters from the operating room until 12 – 24 hours postpartum. The incidence of inability to urinate requiring catheterization was reported as 57% when 4 - 5 mg of epidural morphine was given[9].

Respiratory depression – The incidence of this rare, but serious event is less than reported in non-obstetric patients, likely due to the smaller doses and the hyperventilation physiology of pregnancy. Modern incidence reporting of this event has also demonstrated a reduction in the incidence, likely coinciding with doses being reduced. In 1990[10], the incidence of respiratory depression amongst women given central axial opioids was 0.2% (12/4,880), and in 1998[11] was reported as 0.06% (3/5,000). This particular side effect, although rare has been the greatest factor in preventing all patients from receiving single dose opioids following cesarean delivery under regional anesthesia. Postpartum units caring for these patients must have clear guidelines for monitoring, resuscitation orders in the event of significant respiratory depression or arrest, and timely access to medical providers capable of acute respiratory assistance. All opiates given in the spinal or epidural space have the potential to produce excessive sedation leading up to respiratory arrest. Typically the respiratory depression can occur early after administration of narcotics (early-onset respiratory depression) related to intravascular absorption of the agent and effect on the CNS. Or respiratory depression can occur later during the analgesic phase of the agent (delayed respiratory depression). Depending upon the type of opiate, and the space where the agent is administered, the period of risk can be reasonably predicted.

Lipophilic narcotics given in the epidural space have quick uptake into the systemic circulation and cause early-onset respiratory depression due to supraspinal intravenous effects. This effect can appear within 30 minutes of administration of the narcotic and therefore, the patient should be carefully monitored for the first 2 hours after fentanyl, sufentanil or meperidine epidural administration. Early-onset respiratory depression does not occur with spinal administered lipophilic narcotics, as intravenous levels are neglible. However the sedation effect can occur after onset of peak effect until the end of the period of expected analgesia (first 2 – 4 hours).

Hydrophilic agents, such as morphine or hydromorphone can cause early-onset respiratory depression, if given into the epidural space, and delayed respiratory depression 6 – 12 hours after administration. (6 – 8 hours after spinal administration; 9 – 12 hours after epidural administration). These patients are often in recovery room still when acute respiratory depression occurs, but are on the postpartum floor when delayed events occur. For this reason most institutions have implemented programs incorporating pre-printed order sheets with clear instructions for monitoring and nursing policies in place for recognition and management of respiratory depression.

Monitoring to predict and prevent respiratory depression of epidural or spinal narcotic has been unsuccessful in identifying a simple cost-efficient technique. If resources are available, pulse oximetry appears to identify the serious respiratory depression associated with hypoxemia. However the standard of care in monitoring in North America has been hourly assessment of respiratory rate and level of sedation. If nurses have a procedure for identifying the somnolent, shallow and infrequently breathing parturient and contacting medical personnel who can quickly evaluate and treat these patients, serious morbidity can be avoided. Current standard of care in our institution includes hourly monitoring of maternal respiratory rate and level of sedation for the first 24 hours after hydrophilic opiate administration. A copy of our institutions pre-printed order sheet is included.

PATIENT-CONTROLLED EPIDURAL ANALGESIA (PCEA)

This particular mode of analgesia is viewed as the "cadillac" of post cesarean analgesic techniques in our institution. Its evaluation in the literature is primarily in comparison to intravenous or intramuscular narcotics, for which it's advantages, include greater patient satisfaction, improved analgesia, and reduction in total narcotic doses required, and decreased sedation[12]. The disadvantages of this technique are primarily cost, including increased nursing surveillance of the pump's correct functioning every hour, and cost of the PCEA pump. It's comparison to single-dose epidural or spinal narcotics, such as morphine, has been reported in only three studies[13-15]. These studies evaluated epidural meperidine or fentanyl bolus-only PCEA to epidural morphine. Their conclusions indicate that pain relief is similar with all these agents, and that meperidine and fentanyl can reduce maternal pruritus, but have a higher cost involved. The use of local anesthetics with narcotics in PCEA may prevent expected maternal ambulation in the post-cesarean period, and in one study was not felt to be better than PCEA with fentanyl alone[16]. Amongst those with significant medical co-morbidities requiring prolonged stay in labor and delivery or intensive care post-cesarean we will continue our labor PCEA solution utilizing both infusion and bolus options. (bupivicaine 0.0625% with fentanyl 2 μg/ml or sufentanil 0.05 μg/ml).

PAIN CONTROLLED INTRAVENOUS ANALGESIA (PCIVA)

Patient controlled PCIVA has found its use in our obstetric unit for parturients who receive general anesthesia for cesarean delivery. This particular mode of analgesia has reasonable analgesia, although better at rest than during movement, and requires less narcotic and greater satisfaction compared to nurse-administered IV narcotics. The disadavantages are the cost of the PCA pump and increased nursing surveillance of the patient and pump's function. Medications which have been used for post-cesarean PCIVA include (Table II).

Table II.

Drug	Bolus dose	Lockout Interval (min)
Meperidine	5 – 15 mg	5 – 1 0
Fentanyl	25 – 50 μg	5
Hydromorphine	0.1 – 0.4 mg	10 - 15
Morphine	0.5 – 2.0 mg	10 - 15

All studies evaluating post-cesarean patients have used the bolus-only modality, withholding the infusion option to reduce the potential for respiratory depression. However, like all PCA modalities, the bolus dose is typically small and requires surveillance and dose-adjustment to ensure adequate analgesia.

MULTIMODAL ANALGESIA

Probably the greatest improvement in postpartum analgesia care second to central axial opiates has been the recognition of alternative analgesic receptors which can be stimulated in conjunction with opioid receptors to provide superior analgesia. The most commonly administered supplemental agents include systemically administered nonsteroidal antiinflammatories (NSAID) and acetaminophen. Using these two agents has been shown to reduce opioid requirements and together have additive analgesic effects[17,18]. These agents are approved by national pediatric associations for use during breastfeeding[19]. The recommended agents for use are in the following table, and should be commenced in the early postoperative period and given routinely for the first three days (Table III).

Table III.

Drug	Dose	Scheduled dosing
Ketorolac	30 mg IV load; 15 mg IV/IM subsequent doses	Every 6 hours
Diclofenac	75 – 100 mg IM or 100 mg per rectum load; 50 – 75 mg po subsequent doses	Every 8 hours
Naprosyn	500 mg po or per rectum load and subsequent doses	Every 8 – 12 hours
Acetaminophen	1 gm po or per rectum load; 1 gm subsequent doses	Every 6 hours

The potential complications of the NSAID agents are rare but significant and include gastric irritation; prostaglandin-mediated renal insufficiency; and bleeding diathesis. The potential toxicity with acetaminophen use is the development of liver damage when doses exceed 4 gm/day.

Additional receptors mediating analgesia can be modulated with the systemic use of such agents as ketamine (NMDA antagonist) and clonidine/desmedetomidine (alpha-2 agonist). Although these agents are rarely used in the routine post-cesarean analgesia setting, they may provide significant analgesia for complex pain scenarios, including multiple narcotic allergies or chronic pain syndromes in-conjunction with acute post-operative pain. These agents have predictable side effects including hypertension & tachycardia (ketamine), hypotension and sedation (alpha-2 agonists) but may be useful in selected settings. The most effective method for post-operative ketamine administration has been with IV infusions. Alpha-2 agonists are only available for oral administration in Canada, and the dosage would be 50 – 100 μg q12 h.

III. POST-VAGINAL DELIVERY ANALGESIA

At Mount Sinai Hospital 63% of our 7000 deliveries are vaginal, and a majority of the women have epidural analgesia for the pain during labor. Anesthesia has been actively involved in reducing the discomfort of labor, however we have taken a limited role in managing acute postpartum perineal pain in this population. We examined the scope of acute perineal pain (that occuring in the first 2 days of hospitalization after delivery) and identified primiparous women, women with operative vaginal deliveries, women with increased perineal trauma at increased risk and severity for this pain[20]. However, even women with intact perineum had a 75% incidence of acute perineal pain, and 40% of this group the pain interfered with more than one activity (sitting, urinating, walking, or sleeping).

The management of perineal pain is often overseen by the delivering physician, and appears to be dependent upon local nursing staff practice. Patients in our institution were previously left with self-managed pharmaceutical packages including acetaminophen and non-steroidal inflammatory (typically ibuprofen). The patients would frequently not ingest these medications, and would rarely request the prescribed oral narcotic, typically 30 – 60 mg codeine combined with acetaminophen 10 mg/kg. Some physical therapies have also been utilized including perineal ice packs, perineal wash bottles, sitz baths. However, the overall organization for pain management in hospitals or in the weeks postpartum is not well described in medical or nursing literature. The delivering mother can often be left to her own care until the first postpartum health checkup at 6 weeks.

Previous studies evaluating epidural administered analgesia for postpartum perineal pains are limited. Niv and colleagues studied the augmentation of bupivacaine analgesia in labor by epidural morphine[21]. The authors noted the incidental benefit of prolonged freedom from pain after episiotomy in the group that had short-acting, labor epidural narcotics. Although this was not a primary outcome of the study, it did indicate potential usefulness of epidural morphine for postpartum perineal pain. Another study, a randomized double-blind comparison of epidural fentanyl/bupivacaine or sufentanil/bupivacaine in 60 laboring women reported the incidence of 24 hour postpartum symptoms[22]. This study showed that approximately 50% of the parturients in each group reported perineal pain in the first 24 hours. In a similar study , the authors examined spontaneous delivery rates and maternal satisfaction associated with labor epidural analgesia[23]. The incidence of perineal pain was high in both groups following a comfortable and satisfactory labor period with an epidural. The overall incidence of postpartum perineal pain was between 43%-53%. These studies indicate that the addition of fentanyl or sufentanil while effective for the relief of the pain of labor is not adequate for the control of postpartum perineal pain. This is not surprising due to the limited duration of effect of narcotics used in labor epidural analgesia. Fentanyl or sufentanil are the two most commonly used narcotics and their analgesic effect lasts only 2-4 hours. Although the authors did not set out to study postpartum perineal pain, the studies do show the magnitude of postnatal perineal pain and lack of effective postpartum pain relief with labor epidural analgesia.

One agent, which has proven of benefit to women following caesarean delivery and is considered for women who have epidural analgesia for labor is a single administration of epidural morphine. Studies to date have shown conflicting results in the success of a single bolus of epidural morphine given to alleviate post vaginal delivery perineal pain. Ascanio et al evaluated the extent and treatment of perineal pain after vaginal delivery in a randomized, placebo controlled clinical trial using a single dose epidural morphine[24]. Twenty women were enrolled in this study, with 10 women receiving a single dose of epidural morphine (2 mg) prior to removal of the epidural catheter. The results indicated that those receiving epidural morphine had superior pain relief for perineal discomfort in patients with or without episiotomy. The findings of the study were limited as results were based upon twenty patients and mean VAS pain score difference may have been statistically significant but not clinically significant. Niv and colleagues evaluated the timing of the administration of epidural morphine[25]. The hypothesis was that the injection of the epidural morphine before the onset of pain could substantially lessen post-episiotomy pain. All women received 2 mg of epidural morphine. The

patients were randomized to receiving it either early or late following delivery. They showed that epidural morphine pretreatment was superior to the administration of epidural morphine after the onset of pain for the control of post-episiotomy pain. Nunlee et al in a randomized placebo-controlled clinical trial using single 2 mg dose epidural morphine failed to demonstrate a difference in women's perineal pain scores following vaginal delivery[26]. However the study was flawed by an unequal distribution of primiparous patients between groups, with more primiparous in the morphine group than the control group. Primiparous women tend to have a greater degree of perineal trauma.

In 2002, our institution embarked on a definitive randomized placebo-controlled trial to evaluate a single dose of epidural morphine, given after vaginal delivery in the prevention of perineal pain[27]. 228 women of all perineal trauma types were followed in the study after receiving 2.5 mg epidural morphine or saline placebo within one hour of delivery. Both groups of women received supplemental scheduled analgesics, including acetaminophen 15 mg/kg every 6 hours, and naprosyn 500 mg every 12 hours. Women receiving placebo were 4.5 times more likely to request additional analgesics in the first 24 hours and asked for analgesics sooner than women receiving morphine. The benefit of morphine was not limited to primiparous women, nor just women with more severe perineal trauma. Inconjunction with systemic non-narcotic analgesics, a single dose of epidural morphine appears to be benefit all women with epidurals who have a vaginal delivery. However, the discomfort in this area persists for weeks following delivery, and women must be instructed on physical measures, such as sitz baths, and pharmaceutical agents when discharged home. Further work in this area is required to help empower women outside of the acute health care setting (Table IV).

Table IV.

Outcome	Morphine group (N = 113)	Saline group (N = 115)	p value
# women additional analgesic postpartum	8 (7%)	37 (32%)	0.000
VAS @ time of extra analgesic (sd)	4.6 (2.6)	5.2 (2.1)	0.50
Incidence of:			
Pruritus	13/108	16/109	0.099
Nausea/vomit	10/107	5/109	0.19
Urinary retention	20/109	11/111	0.08

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