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Chapter

Perioperative Analgesia in Caesarean Section: What's New?

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Abstract

Caesarean section is associated with moderate to severe postoperative pain during the first 24 hours after surgery. Inadequate pain management can influence recovery, maternal psychological well-being and breastfeeding. In the search of alternatives to minimize the use of systemic opioids, new recommendations have been made to implement protocols to improve recovery after caesarean section, with multimodal analgesia, new suggestions for neuraxial techniques, regional analgesia with ultrasound-guided fascial plane blocks and non-pharmacological approaches. Some of the interventions, such as epidural or spinal blocks, although effective, carry a significant risk of complications (for example post-puncture headache). In their place, newer alternatives such as interventions guided by ultrasound are safe and effective for relieving pain in this common clinical context. The goal of this chapter is to provide clinicians with up-to-date evidence for optimal pain management after elective caesarean section.

Keywords: Caesarean section analgesia, pain after caesarean

1. Introduction

Caesarean section is the most performed surgical procedure in the world. This procedure is associated with moderate to severe postoperative pain during the first 24 hours after surgery. Inadequate pain management can influence recovery, maternal psychological well-being and breastfeeding. A core principle of successful postoperative analgesia is implementation of multimodal analgesia, and the caesarean section is no exception to the rule. The most effective and evidence-based intervention for effective postoperative analgesia for caesarean section is the use of neuraxial techniques such as epidural block, subarachnoid block or combined techniques, where morphine has played a fundamental role in analgesia in this surgery combined with non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen [1]. However, there are multiple factors that may cause a patient to experience discomfort or pain during caesarean section, some of which are preventable and must certainly be

Preoperative	Intraoperative	Postoperative	Surgical technique
<ul style="list-style-type: none"> • Intrathecal (IT) long-acting opioid morphine 50–100 µg or IT diamorphine (up to 300 µg) (Grade A). • Epidural morphine 1–3 mg or diamorphine up to 1–3 mg may be used as an alternative, for example, when an epidural catheter is used as part of a combined spinal-epidural technique (Grade A) 	<ul style="list-style-type: none"> • Intravenous (IV) paracetamol if not administered pre-operatively (Grade A) • IV NSAIDs (Grade A) • IV dexamethasone (Grade A) • If IT morphine is not used, local anaesthetic wound infiltration (single-shot) or continuous wound infusion and/or regional analgesia techniques [fascial plane blocks such as transversus abdominis plane blocks and quadratus lumborum (QL) blocks] (Grade A) 	<ul style="list-style-type: none"> • Oral or IV paracetamol (Grade A) • Oral or IV NSAIDs (Grade A) • Opioid for rescue or when other recommended strategies are not possible (e.g., contra-indications to regional anaesthesia) (Grade D) • Analgesic adjuncts include transcutaneous electrical nerve stimulation (TENS) (Grade A) 	<ul style="list-style-type: none"> • Joel-Cohen incision (Grade A) • Non-closure of peritoneum (Grade A)

Adapted from Roofthoof et al. [2].

Table 1.

Overall recommendations for pain management in patients undergoing planned caesarean section.

managed. Therefore, knowing the updates on postoperative pain management in caesarean section gives us tools that allow us to manage pain in specific scenarios and individually. The most recent guidelines for the management of specific postoperative pain in caesarean section have been published by the Prospect Group [2], and their recommendations have been summarized in **Table 1**.

2. Multimodal analgesia

2.1 Acetaminophen

Acetaminophen is one of the most prescribed analgesics worldwide, it has an excellent safety profile and relatively few adverse effects. Its action mechanism for inhibiting acute postoperative pain has not been elucidated completely, however, it is believed to inhibit the cyclooxygenase (COX) enzyme and modulate the receptors Transient Receptor Potential Vanilloid 1 (TRPV1) and Cannabinoid 1 (CB1) in the midbrain, medulla and spinal cord which are mediators of pain modulation. It is usually administered via oral or IV routes, there is no difference in area under the curve and $t_{1/2}$ between both routes, thereby being effective for analgesia in both presentations [3]. Recent guidelines establish that acetaminophen should be administered preoperatively (most easily oral), intraoperatively and should be continued in the postoperative period [4]. Established doses are 1000 mg every 6–8 hours, with a maximum established dose of 4000 mg per 24 hours [5].

2.2 Nonsteroidal anti-inflammatory drugs

NSAIDs are analgesic, antipyretic and anti-inflammatory drugs that inhibit the COX pathway of prostaglandin production [6]. Specifically, prostaglandin E2 and

F2a result in the sensitization of nociceptive nerve fibres to painful stimuli following tissue injury, NSAIDs cause a reduction in their synthesis and therefore analgesia [7]. There are no clear differences in analgesic efficacy between equipotent doses of different NSAIDs, the most used are ketorolac (IV) and ibuprofen (oral). These should be started in the intraoperative period (after delivery) and continued in the postoperative period. Their use in this patient population is well established, a meta-analysis by Zeng et al. [8] demonstrated that the perioperative use of NSAIDs in caesarean delivery patients resulted in significantly lower pain scores, less opioid consumption and less drowsiness/sedation.

2.3 Dexamethasone

Dexamethasone is a corticosteroid that has potent inhibitory effects on local inflammatory mediators and multiple pain pathways. It is a well-established anti-emetic and is recommended in guidelines as prophylaxis for postoperative nausea and vomiting [9]. Recent evidence highlighted by a meta-analysis (that included multiple randomized control trials analysing patients having caesarean sections) reported a significant reduction in 24-hour morphine consumption and prolongation of time to first analgesic request with intraoperative dexamethasone use as part of a multi-modal analgesic regimen [10]. Dexamethasone does increase blood glucose but the clinical significance is small, caution should be exercised in patients with glucose intolerance or diabetes, and the risk for other adverse events after surgery is minimal [11]. The general recommendation is a single dose of 8–10 mg intraoperatively, higher doses have not been proven to be of added benefit [2].

2.4 Neuraxial analgesia

Neuraxial techniques are considered the cornerstone of pain management after caesarean section, since the relief reported by the patients compared to other techniques is superior. Kaufner et al. [12] compared three strategies of postoperative analgesia after caesarean section in 199 women who were randomized into three groups: the IT group, the epidural group and the patient-controlled epidural analgesia (PCEA) group. They reported analgesia less effective with PCEA (continuous infusion and epidural bolus controlled by the patient-PCEA of ropivacaine 0.1% bolus and sufentanil 0.5 mg/ml) compared with 3 mg epidural morphine and 0.1 mg spinal morphine in terms of pain relief. IT morphine had a better analgesic-sparing effect than epidural morphine. In this study, low dose and concentration of local anaesthetic in the PCEA group might explain this difference, and more evidence would be necessary to conclude.

However, recently in a systematic review [13] that included 54 randomized controlled trials (RCT) (3497 patients), the prevalence of inadequate neuraxial anaesthesia for elective caesarean section was 14.6% (95% CI 13.3–15.9%). The prevalence of conversion to general anaesthesia was 0.06% (95% CI 0.0–0.2%). Spinal/combined spinal-epidural anaesthesia was associated with a lower overall prevalence of inadequate neuraxial anaesthesia than epidural anaesthesia (10.2% vs. 30.3%, respectively) (95% CI 9.0–11.4% and 26.5–34.5%).

When the combined epidural-spinal block without morphine is selected as an anaesthetic strategy, it is always important to consider that the epidural may be insufficient for analgesia. Further management strategies are needed to optimize the treatment when inadequate or insufficient epidural analgesia occurs [1]. Pain after

caesarean section under neuraxial anaesthesia represents a challenging clinical situation, where the anaesthesiologist will need to make swift decisions. It is important to explain to the woman possible rescue modalities if the neuraxial block is providing sub-optimal analgesia. Attention must be paid when the patient reports pain and an immediate change of plan must be made. A sensitivity test with pinprick and/or cold pressure should be performed during continuous anaesthetic local infusion. In case of insufficient analgesia (e.g. patched analgesia) the addition of epidural morphine or an opioid should be the first consideration. If the catheter does not work, the analgesic strategy may be the use of IV opioids or ultrasound-guided regional techniques [14].

Seki et al. [15] in 66 RCTs comprising 4400 patients undergoing caesarean section, compared with placebo, IT opioids (fentanyl, sufentanil and morphine) significantly prolonged the analgesia duration by 96, 96 and 190 minutes, respectively (mean difference). Although morphine ranked first, the efficacy of opioids was similar. Except for diamorphine, all opioids were associated with significant increases in the incidence of pruritus. Sufentanil and morphine were associated with increases in the incidence of respiratory depression. However, the use of IT or epidural morphine has been shown in several investigations to significantly optimize postoperative pain scores. Recently, the recommended dose of IT morphine has been reduced to 100 µg or lower doses resulting in adequate analgesia with fewer side effects [2, 16, 17]. Sharawi et al. [18] reported the safety of IT morphine for caesarean section with low incidence of respiratory depression, however, caution is especially required when IT morphine is used in morbidly obese patients. It is important to consider that morphine presents specific side effects (pruritus, nausea and/or vomiting) that may require specific monitoring, prophylaxis or interventions [19, 20]. The NICE guidelines have recommended IT diamorphine as an alternative to IT morphine. The dose spinal is 300 µg, and the epidural dose is 2–3 mg [2, 18, 21].

2.5 Regional blocks

2.5.1 Transverse abdominal plane block

The transverse abdominal plane (TAP) block involves injection of local anaesthetic into the fascia between the internal oblique muscle and transversus abdominis muscle, blocking the afferents of thoracolumbar nerves originating from the T6 to L1 spinal roots that run through the same fascia and innervate the anterolateral abdominal wall [22]. The safest and most efficient method of performing the TAP block is by real-time ultrasound guidance. A major disadvantage of the TAP block is that it doesn't provide visceral analgesia [23]. It is recommended as an analgesia adjunct of multimodal analgesia for patients having caesarean section and not receiving neuraxial morphine for any reason (e.g. general anaesthesia) [2]. The previous recommendation is based on information obtained from a recent meta-analysis, Champaneria et al. [24] state that TAP blocks significantly reduce pain and postoperative morphine consumption at rest both when compared with placebo or no TAP blocks, however, this significance is lost when compared to IT morphine or given in co-administration. Contrary to this, a recent network meta-analysis by Ryu et al. [25] concluded that combined IT morphine in conjunction with ilioinguinal–iliohypogastric nerve and anterior transversus abdominis plane block was the most effective post-caesarean analgesic strategy with lower rest pain at 6 hours and cumulative 24-hour morphine consumption. Additionally, other effective options for effective analgesia were IT morphine, ilioinguinal–iliohypogastric nerve block with IT morphine, lateral TAP block, and

single shot or continuous wound infiltration (CWI). Ng et al. [26] analysed in a meta-analysis the difference between high-dose or low-dose local anaesthetic (bupivacaine equivalents >50 or ≤ 50 mg per block side, respectively) and demonstrated no difference in postoperative opioid consumption or pain scores after caesarean delivery. It is recommended to use low-dose local anaesthetic preparations for TAP blocks because of a lack of evidence of more effective analgesia with higher doses and to diminish the risk of local anaesthetic toxicity in this vulnerable patient population.

2.5.2 *Quadratus lumborum block*

The QL block involves the injection of local anaesthetic into one of three fascial planes adjacent to the QL muscle (anterior, middle or posterior layers) which comprise part of the thoracolumbar fascia (TLF). The action mechanism of this block is believed to be through blockade of nociceptive and sympathetic neurons that traverse the TLF and by a possible spread to the paravertebral space with somatic nerve and sympathetic trunk blockade [27, 28]. It is believed to provide somatic and visceral analgesia, usually between T7 and L1 dermatomes.

The QL block appears to be effective for postoperative analgesia after caesarean section. A recent meta-analysis de Tan et al. [29] found that in postoperative caesarean section, QL block reduced 24-hour opioid consumption (mean difference -10.64 mg morphine equivalents; -16.01 to -5.27), reduced dynamic pain at 6 hours and static pain and opioid consumption at 6 and 12 hours compared to controls.

Verma et al. compared the analgesic efficacy of QL block and TAP block after caesarean section. Their main findings were time for rescue analgesic requirement was significantly prolonged in patients with QL block (68.77 ± 1.74 hours) compared to patient with TAP block (13.3 ± 1.21 hours). The QL block group had significantly less analgesic demand ($P < 0.001$) at 2, 4, 6, 12, 24, 36, 48 and 72 hours postoperatively [30]. A more recent RCT compared the efficacy of ultrasound-guided TAP block and QL block on postoperative pain after caesarean section. The results favoured the efficacy of QL block with 15% of patients with QL block and 77% of patients with TAP block requiring rescue analgesia ($P < 0.001$). Significant differences in pain scores at 6, 8, 10, 12, 16 and 20 hours postoperatively, by 24 hours postoperatively the difference ceased to be statistically significant. Time to rescue analgesia in QL group was 1353 minutes (± 224.07) and TAP group was 915 minutes (± 391.62) ($P < 0.001$) [31]. Although evidence appeared promising that the QL block is more effective than the TAP block for postoperative pain after caesarean section, a recent meta-analysis found that QL block and TAP block were equivalent and superior in their analgesic efficacy relative to inactive control for up to 48 hours and that QL block was not associated with a reduction in 24-hour IV morphine equivalent consumption when compared with TAP block [32]. Recent guidelines recommend QL block as an option as part of a multi-modal analgesic strategy if IT morphine is not used [2].

2.5.3 *Continuous wound infiltration*

CWI is an analgesic technique that uses a multiorifice catheter placed at the surgical site and connected to an elastomeric infusion pump that delivers a constant, fixed-rate infusion of medications (usually local anaesthetics) to surrounding cutaneous nerves. For caesarean delivery, catheter placement is either between rectus fascia and subcutaneous tissue or deep into the fascia [23]. Many RCTs have demonstrated the benefit of this technique for postoperative analgesia. A recent randomized controlled

double-blind study of 69 patients concluded that morphine consumption was significantly lower in the infusion group ($21.52 \text{ mg} \pm 21.56$) compared to the placebo group ($29.57 \text{ mg} \pm 22.38$; 95% CI $[-18.8 \text{ to } 2.76]$; P -value = 0.047). No significant differences were observed in pain evaluated by visual analogue scale (VAS), except for pain at mobilization 6 hours after surgery (ropivacaine vs. placebo: 3.90 ± 2.66 vs. 5.36 ± 2.55 ; P -value = 0.030) [33]. Recent guidelines recommend CWI as an option as part of a multi-modal analgesic strategy if IT morphine is not used [2].

2.5.4 Erector spinae plane block

The erector spinae plane (ESP) block involves injection of local anaesthetic into the fascial plane of the TLF at the transverse process of the vertebrae [34]. The action mechanism is believed to be the spread of local anaesthetic through connective tissue and ligaments towards the costotransverse foramen and having a direct effect on the ventral and dorsal nerve roots of the spinal nerves corresponding to different thoracic segments. Another theory is blockade of communicating rami and the sympathetic chain to produce visceral analgesia [35].

Considering the probable visceral analgesia provided by the ESP block, it may have potential use in obstetric patients for postoperative analgesic management. In comparison with IT morphine for analgesia after elective caesarean delivery under spinal anaesthesia in an RCT [36], ESP block delayed the time to first analgesic request (4.93 ± 0.82 hours in the ITM group and 12 ± 2.81 hours in the ESP group) and significantly lowered tramadol consumption (101.7 ± 25.67 mg in IT morphine group, 44 ± 16.71 mg in ESP block group). This study also found significantly reduced VAS scores in the postoperative period (0–24 hours), however, the average reduction was 0.25 units which should not be considered clinically significant.

A recent meta-analysis [37] reported that there was no statistical difference in pain in the first 24 hours of the postoperative period when comparing ESP block to other interfascial blocks and IT morphine. However, ESP block showed a lower consumption of tramadol (mean difference = -47.66 ; 95% CI -77.24 to -18.08 ; $I^2 = 59\%$; very low certainty) and longer blockade duration (mean difference = 6.97 ; 95% CI 6.30 – 7.65 ; $I^2 = 58\%$; very low certainty), although the quality of evidence of these outcomes was very low.

A recent RCT [38] compared ESP block before induction of general anaesthesia for caesarean delivery versus conventional management with an IV analgesic regimen in the postoperative period. The ESP block group required less patient-controlled IV analgesia boluses ($P < 0.001$), had lower VAS scores and higher Bruggeman comfort scale scores at 2- and 6-hours postoperative intervals ($P < 0.05$), with no difference at 12 and 24 hours postoperative periods. The ESP block group also required less propofol and remifentanyl ($P < 0.001$), had significantly shorter emergence time ($P = 0.003$) and less incidence of postoperative nausea and vomiting ($P = 0.014$). Recent guidelines recommend ESP block as an option as part of a multi-modal analgesic strategy if IT morphine is not used [2].

2.5.5 Ilioinguinal and iliohypogastric blocks

The ilioinguinal–iliohypogastric block has been shown to reduce postoperative opioid requirements after caesarean section; however, they apparently don't have benefits in postoperative analgesia compared with IT morphine [39–41]. Recently, Staker et al. [42] conducted a prospective, triple-blind, placebo-controlled randomized

study of 100 women undergoing elective caesarean section. All women had spinal anaesthesia with hyperbaric bupivacaine, 15 µg fentanyl and 150 µg morphine, as well as 100 mg diclofenac and 1.5 g paracetamol rectally. Women were randomly allocated to receive the ilioinguinal–transversus abdominis plane block or a sham block at the end of surgery. The primary outcome was the difference in fentanyl patient-controlled analgesia (PCA) dose at 24 hours. Secondary outcomes included postoperative pain scores, adverse effects and maternal satisfaction. The cumulative mean (95%CI) fentanyl dose at 24 hours was 71.9 (55.6–92.7) µg in the ilioinguinal–transversus abdominis group compared with 179.1 (138.5–231.4) µg in the control group ($P < 0.001$). VAS scores averaged across time-points were 1.9 (1.5–2.3) millimetres (mm) vs. 5.0 (4.3–5.9) mm ($P = 0.006$) at rest and 4.7 (4.1–5.5) mm vs. 11.3 (9.9–13.0) mm ($P = 0.001$) on movement, respectively. Post-hoc analysis showed that the ilioinguinal–transversus abdominis group was less likely to use ≥ 1000 µg fentanyl compared with the control group (2% vs. 16%; $P = 0.016$). There were no differences in opioid-related side effects or maternal satisfaction with analgesia. The addition of the ilioinguinal–transversus abdominis plane block provides superior analgesia to usual multimodal analgesic regimen. More studies are needed to verify these data.

In the experience of the main author, after 48 hours of surgery, shortly before the discharge of the patient undergoing caesarean section (Pfannenstiel-type surgical wound), to complement oral analgesia at home, a bilateral ilioinguinal and iliohypogastric block is placed under ultrasound guidance, with 10 ml of 7.5% ropivacaine, this analgesic strategy achieves comfortable ambulation, low pain scores and analgesic savings.

2.6 Systemic opioids

When neuraxial analgesia or regional blocks for analgesia are not an option, oral or IV multi-modal analgesia strategy for postoperative pain management after caesarean delivery is implemented, a large percentage of patients will require systemic opioids. Oral or IV opioids should be used for rescue analgesia only, at the lowest effective dose and for the shortest duration possible. Oral opioids should be preferred over IV presentations if patients tolerate oral intake. A classic RCT [43] compared oral versus IV opioid strategy after caesarean delivery, demonstrating that oral opioid analgesia with oxycodone-paracetamol may offer superior pain control with less pain at 6 and 24 hours after the procedure ($P = 0.04$ and $P = 0.004$, respectively) and with fewer side-effects compared to morphine PCA. A practice advisory from the American College of Obstetricians and Gynecologists [44] advised that breastfeeding mothers should not receive codeine or tramadol based on evidence that the use of these medications in CYP2D6 ultra-metabolizers can result in excessive amounts of morphine in maternal breast milk with potential for neonatal overdose and respiratory depression. Instead, patients should receive oral oxycodone or hydromorphone. No individual drug has proven to be superior in terms of analgesia or side-effect profile when compared with any other opioid [2]. Due to considerations of continuous breastfeeding, in case of requirement of IV opioids for postoperative analgesia, morphine is the recommended choice based on reliable clinical effects and proven safety [21, 44]. Offer oral morphine sulphate to women. If the patient cannot take oral medication (for example, because of nausea or vomiting), offer IV morphine. Consider IV PCA using morphine for women who have had a general anaesthetic for caesarean birth. If IV PCA is not acceptable to the woman, or the pain is less severe, consider oral morphine sulphate [21].

2.7 Non-pharmacological interventions

TENS is a non-invasive peripheral stimulation technique used to relieve pain. Some publications have shown a beneficial effect of TENS as a treatment or as a rescue strategy, in addition to the fact that patients report more satisfaction with its use [45, 46].

Surgical strategies that have been shown to reduce pain scores are the Joel-Cohen incision and non-closure of the peritoneum [47–49].

On the other hand, music therapy has been shown to reduce the physiological and cognitive responses of anxiety in patients undergoing caesarean section [50].

3. Conclusions

Providing adequate analgesia after a caesarean section confers advantages in the mother-child relationship. The combination of NSAIDs, paracetamol and neuraxial techniques with IT morphine or diamorphine is considered the cornerstone of analgesic management. However, new regional ultrasound-guided techniques have now emerged, such as TAP block, QL block, ESP block, ilioinguinal and iliohypogastric among others, which in a multimodal context also favour adequate pain relief. The use of opioids is reserved as analgesic rescue in combination with the previously mentioned techniques or for those patients who are not candidates for neuraxial or regional techniques, where the minimum effective doses of opioids are recommended. Finally, the use of non-pharmacological strategies is not yet widespread in hospitals, although some techniques such as music and tens seem to be effective.

Conflict of interest

The authors declare no conflict of interest.

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