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REVIEW ARTICLE

Local anaesthetic techniques for post-caesarean delivery analgesia

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ABSTRACT
In this narrative review we summarise pertinent data from published studies investigating the use of local anaesthetic techniques as adjuncts for managing post-caesarean delivery pain.
Based on currently available evidence, ultrasound-guided transversus abdominis plane (TAP), quadratus lumborum (QL) and ilioinguinal and iliohypogastric (ILIH) blocks are preferable to landmark techniques. When intrathecal morphine is used for caesarean delivery analgesia, TAP blocks do not confer any additional benefit. In the absence of intrathecal morphine, TAP blocks have been shown to reduce pain scores and opioid consumption in the first 24 h postoperatively. In the absence of intrathecal morphine, single-dose local anaesthetic wound infiltration also results in a moderate reduction in opioid consumption postoperatively. If a wound catheter is to be incorporated into a multimodal analgesic regimen, a position below the fascia and a continuous infusion of low-concentration local anaesthetic solutions should be considered. Intraperitoneal local anaesthetic instillation may be of benefit in patients who undergo peritoneal closure but larger studies are still needed. Quadratus lumborum and ILIH blocks show promising results but the data are limited, so recommendations for routine use cannot be made.
In summary, evidence supports the use of local anaesthetic techniques for post-caesarean delivery pain but additional research is required to determine the optimum dosing regimens, and the potential role of liposomal local anaesthetics. Further studies are required to compare techniques and determine their role in conjunction with low-dose long-acting neuraxial opioids.

Keywords: Anaesthetic, local; Post-caesarean delivery; Analgesia

Introduction

Caesarean delivery and postoperative pain

Caesarean delivery (CD) is the most commonly performed operation in the United States (U.S.).[1] Women undergoing this procedure typically have postoperative pain[2] and may require opioid analgesics in hospital and upon discharge.[3] Reduced postoperative pain and opioid consumption following CD improves recovery, aids early mobilisation, improves ability to care for the neonate, and can expedite hospital discharge. Many institutions within the United Kingdom (U.K.) and U.S. are implementing "enhanced recovery after surgery" protocols. Optimising analgesic regimens is a crucial aspect of these pathways and may be a cost-effective way of improving postoperative outcomes and patient satisfaction.

Current analgesic methods for elective caesarean delivery

Intrathecal diamorphine and morphine, as part of multimodal regimens, are currently regarded as the gold standard for analgesia following elective CD in the U.K. and U.S. respectively.[4] Analgesic benefits of utilising higher opioid doses must be weighed against the subsequent increased incidence of undesirable side-effects, such as nausea, vomiting and pruritus, which increase in a dose-dependent manner (using contemporary doses these occur in up to 22%, 15% and 60% of women respectively[5–7]). Current guidance advocates combination therapy with long-acting intrathecal morphine (ITM) (or diamorphine),[4] scheduled paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs), reserving opioids for break-through pain.[8]

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Role of adjunctive local anaesthetic techniques

While multimodal analgesia remains the core approach to managing post-CD pain, this regimen may not be suitable for all parturients and managing post-CD pain remains a challenge. Consequently, over the past two decades there has been interest in exploring the use of local anaesthetic (LA) techniques as adjunctive strategies for preventing and treating post-CD pain. This approach has been further enhanced by the increased popularity of ultrasound (US) guidance, which improves success rates when compared to traditional landmark and nerve stimulator techniques.[9] More recently, elucidating which patients experience improved outcomes as a result of regional anaesthesia was highlighted as one of the research priorities outlined by the James Lind Alliance.[10] An advantage of performing postoperative regional nerve blocks such as transversus abdominis plane (TAP), quadratus lumborum (QL) or ilio-inguinal and iliohypogastric (ILIH) blocks, is that the residual neuraxial blockade following CD renders the procedure painless to patients. In this review we discuss the literature surrounding a variety of LA techniques that can be incorporated into modern obstetric anaesthesia practice to help minimise post-CD pain.

Transversus abdominis plane block

Techniques

The TAP block was first described by Rafi in 2001.[11] The technique involves infiltrating LA into the neurofascial plane between the internal oblique and the transversus abdominis muscles[12] (Fig. 1), thereby blocking the neural afferents to the anterior abdominal wall (T7-L1) to provide analgesia.[13] Blockade of these nerves reduces somatic pain but not visceral pain associated with CD. Correct needle placement using a landmark technique, in the non-obstetric population, has been shown to occur in fewer than 25% of cases when ultrasonography is subsequently used for verification[14] and there are also reports of injury to underlying structures.[15] Consequently, the landmark technique has been superseded by US-guidance. Several methods for performing US-guided TAP blocks have been described in the literature: these include the anterior subcostal, lateral

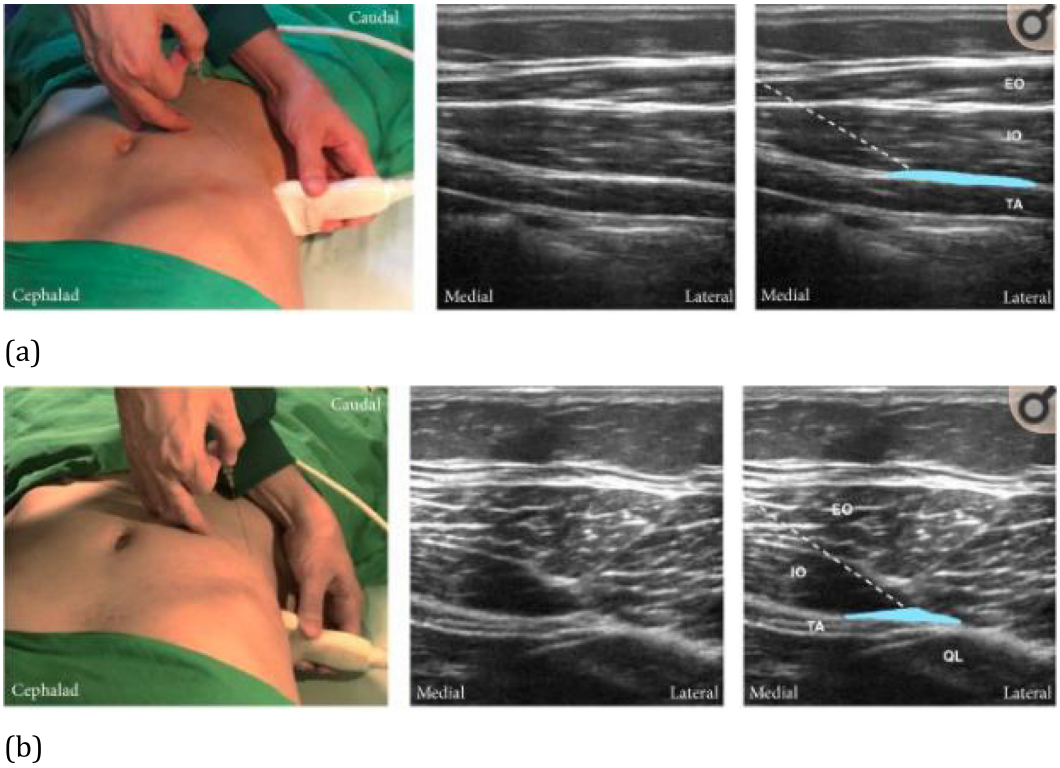

Fig. 1 Commonly described approaches for performing TAP blocks (Images courtesy of Tsai et al.).[116] (a) Lateral approach TAP block showing probe position and needle trajectory. Corresponding US images displaying the muscle layers and local anaesthetic disposition between the internal oblique and transversus abdominis muscles. (b) Posterior approach TAP block showing probe position and needle trajectory. Corresponding US images displaying the muscle layers and injection point at the posterior junction of the abdominal muscles and the anterolateral border of the QL muscle. White dashed line: needle trajectory. Light blue area: the deposition site of local anaesthetic. TAP: transversus abdominis plane; IO: internal oblique; EO: external oblique; QL: quadratus lumborum; US: ultrasound. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article)

(mid-axillary) and posterior approaches. Cadaveric and contrast studies show that LA spread varies depending on the technique used and that this may impact analgesic outcomes. Both lateral[16–18] and posterior[19] approaches for performing US-guided TAP blocks have been described to treat post-CD pain (Fig. 1a and b), however most studies using US have evaluated the lateral approach. To date, there is only one randomised controlled trial directly comparing the analgesic outcomes between lateral and posterior US-guided TAP blocks in this setting.[19] The authors of this study reported that the posterior approach was associated with lower pain scores up to 24 h postoperatively, lower opioid consumption up to 36 h postoperatively and improved patient satisfaction.[19] Similar findings have been reported in a meta-analysis comparing lateral and posterior TAP blocks for transverse incision lower abdominal surgeries.[20] The improved analgesia achieved with the posterior approach may be attributed to improved posterior spread of LA, with some involvement of the paravertebral space between T4 and L1, as demonstrated in a magnetic resonance imaging (MRI) study.[21]

Obstetricians have also developed their own technique for administering TAP blocks under direct visualization of the intra-abdominal structures.[22] To date, the only study directly comparing the surgical and the anaesthetic US-guided TAP block for post CD pain was a randomised controlled trial by Narasimhulu et al.[23] Surgically administered TAP blocks took significantly less time to perform yet provided comparable post CD analgesia.

Current evidence suggests that an US-guided posterior TAP block is the most appropriate method for treating CD pain. However, research investigating the impact of block technique (lateral vs posterior approach) on analgesic outcomes following CD is lacking. Similarly, more research comparing surgical and US-guided TAP blocks is also required. Future work should focus on exploring these concepts further, especially with regards to outcomes such as nausea and vomiting, mobilisation and patient satisfaction, all of which are important for enhanced recovery protocols. Finally, research evaluating the role of TAP catheters for post CD pain is warranted as published trials thus far have only investigated single-dose techniques. The use of TAP catheters for post CD pain has been described in a case series of three women who all received ITM.[24] This initial series is encouraging, with reports of minimal postoperative opioid requirements and a possible reduction in neuropathic pain symptoms. Nevertheless, a randomised controlled trial evaluating the analgesic benefit of TAP catheters is still needed.

Analgesia: TAP block in the presence of ITM

Several meta-analyses have consistently reported that when ITM is used for CD, TAP blocks do not offer any additional analgesic benefit.[25–27] Studies investigating the role of TAP blocks in the presence of ITM have used a minimum dose of 100 μg morphine spinally. It would be of interest if future studies investigated the potential to enhance analgesia and reduce opioid-related side effects by combining lower doses of ITM with TAP blocks.[27] Studies are also needed to explore the use of TAP blocks using long-acting liposomal preparations of LA that supersede the duration of ITM. There are no published randomised controlled trials to date investigating the use of these LA preparations.

Analgesia: TAP block in the absence of ITM

Using TAP blocks for post CD pain in the absence of ITM reduces resting and dynamic visual analogue scale (VAS) pain scores in the first 24 postoperative hours,[28–32] however beyond this time frame the effects are less clear.[29,31] In patients who undergo CD with general anaesthesia or neuraxial anaesthesia without a long-acting opioid, TAP blocks reduce opioid consumption at 24 h[25–27] and 48 h[29,31] as well as increasing time to first analgesia request.[16,28,31,33] On average, TAP blocks have been shown to reduce intravenous morphine requirement by 20–24 mg in the first 24 h after CD among patients not receiving ITM.[25–27] This reduction in opioid consumption does not necessarily correspond with a reduction in opioid-related side effects: the evidence is conflicting. Several studies investigating TAP blocks in women not receiving ITM have reported no difference in the incidence or severity of nausea and vomiting, and no reduction in anti-emetic use,[30,31,34] while other studies have found contrasting results.[16,32,35] Similarly, while some investigators have found a reduced incidence of sedation with TAP blocks in patients not receiving ITM,[30,31] others have failed to support this conclusion.[16,32,34] In the absence of ITM, when compared with no block or placebo, TAP blocks do not reduce the incidence of pruritus,[16,30,32] but overall have been shown to increase maternal satisfaction.[16,34,35] The discrepancies in findings regarding opioid-related side effects may be due to variations in study design, study population, choice of LA and LA dose.

Analgesia: TAP block compared with ITM

Several studies have investigated the analgesic efficacy of TAP blocks versus ITM for post-CD pain.[36–39] Intrathecal morphine provides superior analgesia to TAP blocks, with reduced pain scores up to 24 h post CD and reduced opioid consumption.[36–39] However, this analgesic benefit comes at the expense of increased opioid-related side effects such as nausea and vomiting[36–38] and pruritus.[36,37] There is no significant difference in the incidence of sedation when ITM is compared to TAP blocks for CD pain.[37–39]

The analgesic efficacy of TAP blocks for post-CD pain has been studied extensively but data are limited to healthy parturients who are typically undergoing elective CD. There is a paucity of data investigating the analgesic efficacy of TAP blocks in parturients with chronic opioid use, on treatment for opioid abuse, or in those who experience severe breakthrough pain. Further work evaluating if TAP blocks could prove advantageous in these patients is still needed.

Adjuncts for TAP block

Adjuncts to LA can augment neuraxial and peripheral nerve blockade. In women having CD under general anaesthesia the addition of 10 μg sufentanil to TAP block reduced opioid consumption over 24 h,[40] yet studies investigating the addition of fentanyl to a TAP block have failed to show any analgesic benefit.[41,42]

Singh et al. showed that the addition of 1 μg/kg clonidine to TAP blocks in parturients undergoing CD without ITM increased the time to first analgesia request, and also reduced the need for rescue pain relief.[43] However, Bollag et al. found that adding 75 μg clonidine to TAP blocks in the presence of ITM did not reduce early or chronic pain reported by patients after CD.[17] The results of these two studies highlight the superior analgesia provided by ITM and suggest that any benefit from adding clonidine to TAP blocks may only be evident in the absence of ITM.

The addition of 8 mg dexamethasone[44] or 0.5 μg/kg dexmedetomidine[45] to TAP blocks for CD have both been found to have analgesic benefits by increasing the time to first analgesia request while reducing postoperative opioid requirements and pain scores. Based on current evidence, further work exploring the safety profile of adjuncts is required before routine use can be recommended.

Choice of local anaesthetic, dose and volume

The use of bupivacaine, levobupivacaine and ropivacaine for TAP blocks following CD has been investigated. During pregnancy, there is an increased sensitivity to LA that increases the likelihood of LA systemic toxicity (LAST).[46] There are several case reports of tonic-clonic seizures, attributed to LAST, in obstetric patients following TAP blocks for CD.[47,48] Ng et al. conducted a meta-analysis comparing the analgesic benefits of high- and low-dose LA for TAP blocks after CD.[49] This group found that there was no difference in analgesia or opioid-sparing effect when using >50 mg bupivacaine equivalents per side compared to ≤50 mg bupivacaine per side. In the meta-analysis, the LA dose varied between the high-dose and low-dose groups because of differences in the LA concentration, rather than the LA volume, administered. Consequently, this study was unable to evaluate the effect of volume on TAP block efficacy. Another review reported that a volume of 12 mL LA per block side (total bupivacaine equivalent dose 60 mg) was sufficient for analgesia and that higher doses did not provide any opioid-sparing effect.[50] Thus, the evidence would support using lower doses of LA (≤50 mg bupivacaine equivalents per block side) for TAP blocks following CD, as these provide adequate analgesia while limiting the risk of LAST.

Quadratus lumborum block

The quadratus lumborum block (QLB) involves a more posterior approach than the TAP block and deposits LA between the quadratus lumborum and psoas muscles. An US-guided approach (termed QLB 1) was first described at the European Society of Regional Anesthesia annual meeting in 2007.[51] In magnetic resonance imaging (MRI) studies involving the administration of a LA-contrast mixture in male volunteers via the QLB 1 approach, spread of LA into the epidural and paravertebral spaces, extending from the sixth to tenth thoracic vertebrae, was demonstrated.[21] Since then several variants of the US-guided QLB have been described (QLB 1, QLB 2, QLB 3/TQLB), with no consensus on nomenclature.[52,53] Fig. 2 summarises the three common approaches to QLB depending on needle placement. The QLB 1 and QLB 2 approaches are accessible when the patient is in the supine position and have been studied in obstetrics.[54–56] Reports of lower limb weakness associated with these blocks may limit early mobilisation.[57] The transmuscular (TQLB/QLB 3) technique involves use of a posterior needle approach (in either the lateral or sitting positions).[58] This approach has demonstrated greater spread of LA when compared to TAP blocks in adults and children postoperatively.[58] There is greater cranial spread of LA into the thoracic paravertebral space and the thoracolumbar fascia and an extensive network of sympathetic nerve fibres in this plane has been demonstrated in 3-D modelling of cadaveric specimens.[55,59] This approach theoretically provides improved analgesia compared to TAP blocks[21,54] and decreased motor blockade compared to QLB 1 and QLB 2, but requires randomised trials to clarify this.[60]

There are four randomised controlled clinical trials evaluating QLB in the obstetric setting (Table 1). Three of these demonstrate the efficacy of QLB after CD compared with a control group (no block[61] or a sham block[54,56]). QLB 1 or QLB 2 were administered along with short-acting intrathecal opioids (fentanyl[54,61] or sufentanil[56]) after elective CD. There was a reduction in postoperative morphine usage at 6 h (2 mg vs 7 mg) and 12 h (8 mg vs 14 mg) but not at 24 or 48 h.[54] These results are similar to findings by Mieszkowski et al. who found reduced mean cumulative morphine usage in a QLB 1 group compared with a non-intervention group 48 h after CD (16 mg vs 42 mg).[61] Only one randomised trial has compared QLB 2 to

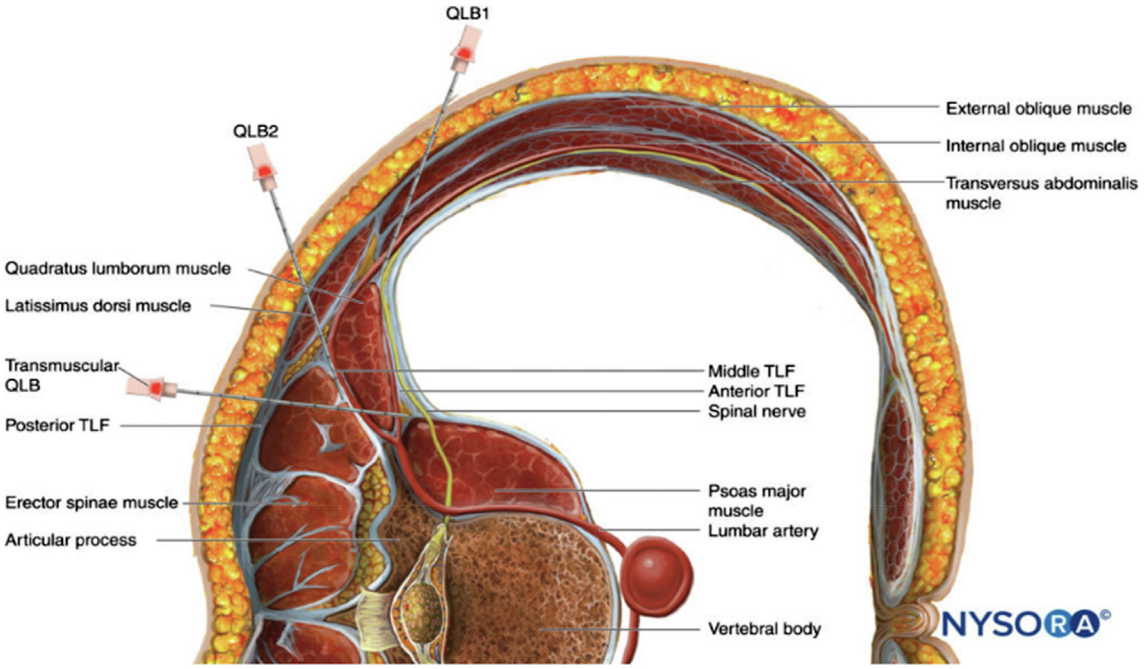

Fig. 2 Diagram showing needle approaches for quadratus lumborum block 1, 2 and 3[117]

TAP block. In this study QLB 2 was associated with superior analgesia and reduced cumulative median morphine doses compared with TAP block at 12 h (5 mg vs 8 mg), 24 h (6.0 mg vs 13.5 mg) and 48 h (9.0 mg vs 17.5 mg) but not at 4 or 6 h after CD.[55] However, it should be noted that none of these studies included long-acting neuraxial opioids in the control groups, which is now considered standard practice. The TQLB/QLB 3 thus far remains underexplored in obstetric practice, although there are three obstetric trials aiming to evaluate this technique currently registered with clinicaltrials.gov.

The relative merits of the different approaches of QLB are yet to be formally validated following CD and further research is required to optimise dosing strategies and evaluate the risks (for example, severe hypotension has been reported when QLB 2 was combined with general anaesthesia).[62] Due to the sparse evidence and few outcome-based studies it is still too early to draw conclusions regarding the role of QLB, especially in comparison to neuraxial morphine or diamorphine. The possible effects of LA dispersion through the paravertebral space via single dose or catheter-based techniques in obstetric patients also warrant further investigation.

Ilio-inguinal and iliohypogastric nerve blocks

The ilio-inguinal (ILI) and iliohypogastric (IH) nerves originate from the first lumbar spinal root (L1). The ILI and IH nerves pierce the transversus abdominis and the internal oblique muscle to lie between the internal and external oblique muscles. Further branches then pierce the external oblique muscle to provide cutaneous sensation. The IH nerve supplies cutaneous sensation to the inguinal region and the ILI nerve supplies sensation to the skin over the superior medial aspect of the thigh. Therefore combined ILI and IH (combined ILIH) nerve blocks provide anterior abdominal wall analgesia after CD, specifically in the dermatomal distribution supplied by L1 where the Pfannenstiel incision lies.[63] Studies have compared bilateral ILI nerve blocks to a control group that received no block, after CD under GA, and assessed pain scores and opioid consumption postoperatively.[64–66] Patients receiving ILI blocks reported reduced pain scores and opioid consumption.[64–66] In one study, patients undergoing CD under GA had reduced papaveretum requirements (four hours postoperatively) in the ILI nerve block group compared to controls at eight hours (6.2 vs 13.3 mg) and 12 h (3.8 vs 13.9 mg) but not at 24 h postoperatively.[64] These findings are in contrast to the results reported by Bunting and McConachie, who demonstrated extended analgesia at 24 h after CD. Participants received a cumulative papaveretum dose of 16.75 vs 51.5 mg in the ILI and control groups respectively.[65] Due to these contradictory results, no conclusion regarding the duration of analgesia can be made, other than pain scores and opioid consumption are reduced for at least eight hours after CD under GA. Isolated ILI nerve block usage has been largely superseded by the combined ILIH nerve block technique because both nerves are accessible without a significantly greater procedure time, difficulty or requirement for additional expertise.

Table 1 Summary of randomised controlled trials evaluating quadratus lumborum block for post-caesarean delivery pain

Study author Year Country	No. patients studied	Group comparison	Anaesthetic technique	Primary outcome	Main findings/Quantitative opioid reduction at 24 h
Blanco[54] 2015 UAE	25 25	Group 1 – QLB 2 0.125% bupivacaine 0.2 mL/kg total Group 2 – QLB 2 0.9% saline 0.2 mL/kg total	Spinal with hyperbaric bupivacaine 15 mg and fentanyl 20 μg	Total number of PCA morphine demands and actual doses delivered at 1, 2, 4, 6, 12, 24 and 48 h after surgery	QLB 2 group utilised less morphine at 6 and 12 h (but not at 24 and 48 h) and had fewer morphine demands at 6, 12, 24 and 48 h
Blanco[55] 2016 UAE	38 38	Group 1 – QLB 2 0.125% bupivacaine 0.4 mL/kg total Group 2 – TAP block 0.125% bupivacaine 0.4 mL/kg total	Spinal with hyperbaric bupivacaine 15 mg and fentanyl 20 μg	Total PCA morphine consumption at 1, 2, 4, 6, 12, 24 and 48 h after surgery	QLB 2 (with LA) had reduced morphine consumption at 12, 24 (6.0 [4–15.25] vs 13.5 [7.5–22.0] mg; P=0.015) and 48 h
Mieszkowski[61] 2018 Poland	30 30	Group 1 – QLB 1 0.375% ropivacaine 48 mL total Group 2 – Control group (no intervention)	Spinal with hyperbaric bupivacaine 12.5 mg and fentanyl 20 μg	Total morphine consumption in the first 48 h after surgery	QLB 1 had reduced mean cumulative morphine consumption at 24 h (36.6 mg vs 21.89 mg; P=0.0001), 48 h (16.36 mg vs 41.77 mg; P=0.0000)
Krohg[56] 2018 Norway	20 20	Group 1 – QLB 1 0.2% ropivacaine 0.8 mL/kg total Group 2 – QLB 1 0.9% saline 0.8 mL/kg total	Spinal with isobaric bupivacaine 10 mg and sufentanil 4 μg	Total PCA ketobemidone consumption in the first 24 h after surgery	QLB 1 (with LA) had lower cumulative ketobemidone consumption at at 24 h compared with control group (ratio of mean = 0.60; 95%CI 0.37 to 0.97; P=0.04)

Ultrasonography was used in all studies for needle placement. QLB: quadratus lumborum block; PCA: patient-controlled analgesia; TAP: transversus abdominis plane; LA: local anaesthetic; UAE: United Arab Emirates; Values are median [IQR]: interquartile range; CI: confidence interval.

This is in addition to the potential for improved analgesia by combining techniques. No studies following CD have compared ILI to IH; ILI to ILIH; or IH to ILIH blocks.

Similar to the TAP block, combined ILIH nerve blocks provide somatic analgesia but limited effect on visceral pain. Combined ILIH peripheral nerve blocks, administered as one or more injections, have been demonstrated to provide effective analgesia after CD in studies where women did not receive ITM.[65,67–70] These studies compared combined ILIH nerve blocks to control groups that either received no nerve block or a sham block (with 0.9% saline). Only one randomised controlled trial demonstrated no difference in 24 h postoperative opioid consumption between combined ILIH and a control group when ITM was not administered.[71] Inconsistency amongst results may be attributable to the block technique, which involved a single injection using a landmark technique[64,65] rather than an US-guided[72] or a landmark multilevel technique.[67–69,73]

ILIH block versus TAP block

There is also conflicting evidence when combined ILIH nerve blocks are compared to TAP blocks. Kiran et al. demonstrated a significantly greater mean cumulative 24 h tramadol consumption (63 mg vs 27 mg) in the combined ILIH group when compared to TAP blocks, but no difference in time to first request for analgesia or postoperative pain scores between groups.[74] In contrast, in a non-randomised prospective trial by Ahemed et al. combined ILIH nerve blocks were associated with reduced 24-h cumulative tramadol consumption (37.25 mg vs 52.45 mg) and prolonged time to first analgesic request (14.09 h vs 10.71 h) compared to TAP blocks after elective CD.[75] In both studies there were no significant differences in pain scores between groups at any time points. Due to heterogeneity in terms of LA dosing, volumes administered and postoperative analgesic regimens, direct comparison between these two studies is not possible. Generalisability is also limited due to ethnic and cultural variations among the study populations and differences in block techniques (such as use of US-guidance and site of injection). It has been demonstrated that the point where the ILI nerve enters the TAP and perforates the internal oblique muscle is subject to significant anatomic variability,[76] and hence LAs do not always spread to the ILIH. It is thought that the L1 dermatome is spared 50% of the time after a posterior TAP block.[77] Due to the paucity of evidence, a recommendation about which technique (combined ILIH or TAP block) is superior cannot be made; and further research is required to determine the optimum technique and dose of LA.

No studies have compared combined ILIH blocks with long-acting neuraxial opioids in conjunction with a multimodal analgesic regimen. Several obstetric randomised controlled trials have studied combined ILIH blocks in the absence of multimodal analgesic regimens.[66–68,71] Table 2 summarizes randomised controlled trials in women receiving at least one form of non-opioid analgesia regularly in the postoperative period.[69,72,73,78] All but one of the four studies demonstrated improvement in postoperative pain scores or reduced total opioid consumption when combined ILIH nerve block was compared to control.[72]

An article by Staker et al. is unique in that it is the only published randomised trial comparing combined ILIH nerve and TAP block (I-TAP) to a control group receiving a non-invasive "simulated block."[78] Both groups received ITM and a standardised multimodal analgesic regimen consisting of regular doses of paracetamol and ibuprofen. Women who received the I-TAP had lower 24-h cumulative fentanyl patient-controlled analgesia (PCA) usage compared to women who received standard therapy (71.9 μg vs 179.1 μg) and significantly reduced static and dynamic VAS (0–100 mm) pain scores (2.8 mm vs 4.7 mm and 10.9 mm vs 15.3 mm respectively at 24 h). This combination of ILIH and TAP blocks has also been described in a case series of four patients who had relative contraindications to general and/or neuraxial anaesthesia.[79] All patients underwent successful CD with no intra-operatively complications and "reported little or no pain during the dissection of skin, muscle, and peritoneal layers." It should however be noted that at the time of delivery (and presumably time of maximum visceral stimulation), small doses of ketamine and propofol were administered to augment patient comfort. The current evidence, though limited, suggests that a combination of truncal peripheral nerve blockade has an opioid-sparing effect in women who deliver by CD, especially in those who cannot receive long-acting neuraxial opioid, multimodal analgesia or who experience breakthrough pain.[70,80]

Wound infiltration

Pre-operative analgesia

Wound infiltration with LA is a simple method of providing somatic analgesia for post CD pain. Previous research has postulated that pre-incisional LA infiltration prevents transmission of noxious stimuli from the site of injury to the central nervous system, thereby reducing postoperative pain. However, pre-operative LA wound infiltration for CD has not been shown to reduce postoperative pain scores or analgesia requirements when compared to LA administered at wound closure.[81–83]

Table 2 Obstetric randomised controlled trials evaluating combined ILIH nerve blocks with use of a multimodal analgesic regimen

Study Author Year Country	Ultrasound guided/ landmark technique	No. of patients studied	Group comparison Drug Volume	Anaesthetic technique and dose Postoperative multimodal analgesic regimen	Primary outcome	Result/Quantitative opioid reduction at 24 h
Bell[69] 2002 USA	Multilevel landmark	31	Group 1 Bilateral ILIH NB 0.5% bupivacaine with 1:200 000 epinephrine 24 mL in total	Spinal hyperbaric bupivacaine 12.5 mg or epidural lidocaine 400 mg and epinephrine 5 μg/mL	24 h PCA morphine consumption after surgery	Combined ILIH with LA reduced morphine consumption at 24 h (48 mg; (27) vs 67 (28) mg; P=0.0063)
		28	Group 2 Bilateral ILIH NB 0.9% saline 24 mL in total	All patients received regular oral naproxen 500 mg every 12 h		
Wolfson[73] 2012 USA	Multilevel landmark	17	Group 1 – Bilateral ILIH NB 0.5% bupivacaine 24 mL in total	Spinal bupivacaine* 12 mg and fentanyl 10 μg and morphine 200 μg	Resting VAS (0–100) pain score at 24 h after surgery	Combined ILIH with LA reduced VAS pain scores (0–100) at 24 h (median, 15 [10–30] vs 40 [10–50] mm; P=0.04)
		17	Group 2 – Bilateral ILIH NB 0.9% saline 24 mL in total	All patients received IV ketorolac 30 mg on first request followed by as required oral acetaminophen 1000 mg/ oxycodone 5 mg		
Vallejo[72] 2012 USA	Ultrasound guided	17	Group 1 – Bilateral ILIH NB 0.5% bupivacaine 20 mL in total	Spinal hyperbaric bupivacaine 12 mg and fentanyl 10–20 μg and morphine 150–200 μg	Pain VRS at 8, 16, 24, 32, 40, 48 h after surgery	No difference in pain scores at any time points
		16	Group 2 – Unilateral ILIH NB 0.5% bupivacaine 10 mL and 0.9% saline 10 mL on the other side	All patients received regular IV ketorolac 30 mg every 6 h for first 24 h postoperatively followed by oral analgesic regimen based on patient preference		
		17	Group 3 – Bilateral ILIH NB 0.9% saline 20 mL in total			
Staker[78] 2018 Australia	Landmark	50	Group 1 – Bilateral ILIH and TAP block, 0.33% ropivacaine 60 mL in total	Spinal hyperbaric bupivacaine 8.5–13.5 mg and fentanyl 15 μg and morphine 150 μg	24 h cumulative PCA fentanyl consumption after surgery	Combined ILIH had reduced cumulative fentanyl consumption at 24 h (71.9 [95%CI 55.6 to 92.7] vs 179.1 [95%CI 138.5 to 231.4] μg; P <0.001)
		50	Group 2 – Sham block simulated but without invasive procedure	All patients received regular oral 1 g acetaminophen four times a day and 50 mg diclofenac three times a day postoperatively		

ILIH; ilioinguinal–iliohypogastric; NB: nerve block; VAS: visual analogue scale; IQR: interquartile range; VRS: verbal rating scale; IV: intravenous; *: baricity not stated; LA: local anaesthetic; PCA: patient-controlled analgesia. Values are presented as mean (SD) and median [IQR] unless stated otherwise.

Single dose infiltration

A meta-analysis showed that single-dose wound infiltration is unlikely to be of benefit in women undergoing CD in the presence ITM, but may be useful in those patients requiring GA or where ITM has been omitted.[83] The benefit is most likely to be evident for women undergoing CD under GA as the effect of single-dose wound infiltration is unlikely to extend beyond the effect of the neuraxial anaesthetic.[8] Single-dose wound infiltration with LA has been shown to reduce intravenous morphine requirement by approximately 9 mg in the first 24 h after CD in patients not receiving ITM.[83] However, this moderate reduction in opioid consumption has not been shown to reduce opioid-related side effects such as nausea, vomiting and pruritus.[83,84]

Studies investigating the effects of single-dose wound infiltration for CD exhibit heterogeneity in terms of LAs, volumes and concentrations. Larsen et al. addressed this by investigating the effect of wound infiltration using 125 mL 0.2% ropivacaine compared with 50 mL 0.5% ropivacaine on post CD pain.[85] Although these investigators found a statistically significant reduction in 24-h opioid consumption in the higher concentration group, they concluded that any clinical benefit was likely to be minimal.

More recently, there has been an interest in liposomal bupivacaine, which is a new agent that releases LA over 48–72 h. The proposed advantage of using such an agent is that the analgesic effects of these LAs should continue after 24 h when the analgesic benefit of ITM has receded. Prabhu et al. investigated the analgesic effect of wound infiltration with 266 mg liposomal bupivacaine in parturients who received long-acting neuraxial opioids as part of their multimodal analgesia regimen for CD.[86] The results of this study showed no difference in postoperative pain scores at 24, 48 and 72 h when compared with equal volumes of placebo. Furthermore, there was no difference in opioid consumption or patient satisfaction amongst the study participants. To date, this is the only published randomised controlled trial to have investigated liposomal bupivacaine for post CD pain and further research in this area is warranted.

There are several randomised controlled trials that have compared single-dose TAP block with single-dose wound infiltration, however the results of these studies are conflicting. Some studies have reported that TAP blocks reduce postoperative pain scores, increase time to first analgesia and reduce postoperative opioid requirement compared with wound infiltration,[87,88] while others have found differences between the two techniques to be equivocal.[89,90] Differences in results may be attributed to heterogeneity amongst the studies in terms of study design and type, dose and concentration of LA administered.

Catheter-based techniques

Single dose wound infiltration with LA has a finite duration of action whereas extended delivery of LA to the wound site, using catheter-based techniques, has been shown to reduce opioid requirement and pain scores post CD compared to placebo.[91–97] Table 3 summarises the randomised controlled studies that have investigated wound infiltration using catheter-based techniques and LA alone for post-CD pain. There are no randomised trials directly comparing the efficacy of a catheter-based technique with single-dose wound infiltration for post-CD pain. Indirect comparison based on meta-analysis found no difference in post CD pain scores or opioid consumption when catheter-based techniques were compared with single-dose infiltration.[83] However, the authors recommended interpretation of this finding with caution due to the wide confidence intervals of their results.

Wound infiltration using a catheter-based technique can be delivered by continuous infusion or intermittent bolus. Indirect comparison of the two methods suggests that continuous infusion improves pain scores at rest over the first 24 h when compared with intermittent bolus, but not pain scores on movement.[83] Current research suggests that wound catheters positioned below the fascia provide better analgesia when compared with catheters above the fascia, resulting in improved pain scores and a 10.7 mg (15.7 mg vs 26.4 mg) mean reduction in intravenous morphine requirement at 48 h.[83,98] Despite the numerous studies investigating the use of wound catheters for post CD pain, the optimal dose and infusion rate are yet to be determined. Intermittent wound infiltration with higher concentration ropivacaine (0.2%) was not found to improve analgesia when compared to a lower concentration (0.1%) following abdominal hysterectomy via a Pfannenstiel incision.[99] Based on recent literature, if a wound catheter is to be incorporated into a multimodal analgesia regimen, it should be positioned below the fascia and a continuous infusion of low concentration LA should be considered.

There are few studies that have compared continuous wound infiltration to long-acting neuraxial opioids for post CD pain and the results are conflicting. Two studies have compared ITM to continuous wound infiltration, with ITM appearing to provide superior analgesia with reduced opioid consumption at 12 h[100] and an increased time to first analgesia.[97] In contrast, continuous wound infiltration using ropivacaine 0.2% at 5 mL/h was found to improve 24- and 48-h pain scores while reducing opioid-related side effects when compared with 2 mg epidural morphine administered 12 hourly for two days.[101]

There are two randomised controlled trials that have compared single-dose TAP block to wound infiltration

Table 3 Randomised controlled trials investigating wound infiltration using catheter-based techniques for post-caesarean delivery pain

Author Year Country	Methods							
	Anaesthetic Drug/Dose	ITM	Catheter position	Intervention		Control	Postoperative analgesia regimen	Study duration (h)
				LA used	LA delivery rate			
Eldaba[91] 2013 Egypt	Spinal 10 mg hyperbaric bupivacaine	–	Above fascia	0.25% bupivacaine	5 mL/h	0.9% saline at same rate	Ketorolac 30 mg IV TDS, morphine PCA IV, paracetamol 500 mg IV PRN	24
Fredman[92] 2000 Sweden	Spinal 8–10 mg hyperbaric bupivacaine	–	Above fascia	0.2% ropivacaine	10 mL bolus PCA, max dose 1 bolus/h	Sterile water at same rate	Dipyrone 1 g PO, then dipyrone 1 g PO prn. If VAS >4, then morphine 2 mg IV q10 min until VAS <3	24
Givens[93] 2002 USA	Epidural LA details not stated	Not stated	Above fascia	0.25% bupivacaine	20 mL initially, then 4 mL/h	0.9% saline at same rate	Morphine PCA IV	48
Jolly[94] 2015 France	Spinal 10 mg hyperbaric bupivacaine + 5 μg sufentanil	–	Below fascia	0.25% levobupivacaine and 0.125% levobupivacaine	20 mL initially (0.25%) followed by 5 mL/h (0.125%)	No treatment	Celecoxib 400 mg PO, followed by 200 mg BD, paracetamol 1 g PO QDS for 3 days, nefopam 20 mg PO QDS for 24 h and morphine PCA IV	72
Lalmand[97] 2017 Belgium	Spinal 10 mg hyperbaric bupivacaine + 5 μg sufentanil	–	Below fascia	0.2% ropivacaine	15 mL initially, then 10 mL/h	0.9% saline at same rate	Paracetamol 1 g (route not specified) QDS, diclofenac 75 mg (route not specified) BD and morphine PCA IV	30
Lavand' homme[95] 2007 Belgium	Spinal 7.2–8 mg hyperbaric bupivacaine + 1.8–2 μg sufentanil	–	Above fascia	0.2% ropivacaine	5 mL/h	0.9% saline at same rate	Diclofenac 75 mg IV BD and morphine PCA IV Paracetamol 1 g (route not specified) for rescue	48
Mecklem[96] 1995 Australia	Spinal 10–13.75 mg hyperbaric bupivacaine	–	Below fascia	0.25% bupivacaine	20 mL initially, followed by 7 doses (each 20 mL) 6 hourly	0.9% saline at same rate	Morphine IV PCA	44
Kainu[100] 2012 Finland	CSE 10 mg isobaric bupivacaine + fentanyl 15 μg	–	Below fascia	0.375% ropivacaine	5 mL/h	0.9% saline at same rate	Ketoprofen 100 mg PO TDS and oxycodone PCA IV	48
Reinikainen[103] 2014 Finland	Spinal 10–13 mg hyperbaric bupivacaine 10–11 mg 0.5% levobupivacaine	–	Above fascia	0.75% ropivacaine	10 mL initially, then 2 mL/h for 48 h	0.9% saline at same rate	Paracetamol 1 g PO TDS, ibuprofen 600 mg PO TDS. If VAS >3 0.1 mg/kg IM oxycodone. If VAS >7, 0.05 mg/kg oxycodone IV	48

Author Year Country	Outcomes					
	Opioid consumption	Pain scores	N + V	Pruritus	Sedation	Satisfaction
Eldaba[91] 2013 Egypt	Significantly reduced IV morphine at 24 h in the LA group 25 ± 7.3 mg vs 40 ± 12.3 mg P <0.0001	Significantly reduced at 4, 12, 24 h in the intervention group	No difference	–	Significantly higher in the control group	–
Fredman[92] 2000 Sweden	Significantly reduced IV morphine requirement over first 6 h in LA group 2 ± 3 mg vs 10 ± 5 mg P <0.01	Significantly reduced VAS at rest and coughing at 3, 4, 5, 6 h	No difference in nausea	–	No difference	Significantly higher in the LA group
Givens[93] 2002 USA	Cumulative IV morphine requirement significantly reduced at 12, 24, 48 h in the LA group 24 h results: 46.8 ± 23.6 mg vs 78.9 ± 28.5 mg P <0.01	No difference	–	–	–	–
Jolly[94] 2015 France	Significantly reduced IV morphine requirement in first 24 h in LA group 19.8 mg vs 13.1 mg P <0.02 (SD not provided)	Significantly reduced VAS at rest at 4, 8, 36, 48, 72 h in LA group	No difference	No difference	No difference	No difference
Lalmand[97] 2017 Belgium	Significantly reduced IV morphine requirement over first 30 h in LA group 8 [4.5–19 mg] vs 20.5 [10–30.5 mg] P <0.01	–	No difference	No difference	–	–
Lavand' homme[95] 2007 Belgium	No difference	Reduced at 12 h in the intervention group, but no difference at 24 and 48 h	–	–	–	–
Mecklem[96] 1995 Australia	Cumulative IV morphine requirement significantly reduced over 44 h in LA group. Significantly reduced during 0–4 and 24–36 h epochs in LA group 24 h results: 57.2 mg vs 45.6 mg P <0.05 44 h results: 84.2 mg vs 63.3 mg P <0.001 (SD not provided)	Significantly reduced during 18–24 h epoch in LA group No difference at any other time	Nausea reduced in LA group No difference in vomiting over 24 h	No difference	Significantly reduced in LA group at 4–8 h No difference at any other time	–
Kainu[100] 2012 Finland	No difference	No difference	No difference in nausea	No difference	No difference	No difference
Reinikainen[103] 2014 Finland	No difference	No difference	No difference in nausea	–	–	No difference

LA: Local anaesthetic; CSE: combined spinal-epidural; ITM: intrathecal morphine; VAS: visual analogue scale; PCA: patient-controlled analgesia; IV: intravenous; PO: oral; OD: once daily; BD: twice daily; TDS: three times daily; QDS: four times daily; PRN: as required; q10 min: every 10 minutes. Opioid consumption data presented as mean ± SD or median [IQR].

with a continuous infusion, in the absence of a long acting neuraxial opioid.[48,102] Despite the two studies using different LA and infusion rates, both reported no differences in postoperative pain scores or opioid consumption. Further studies directly comparing TAP blocks and wound infiltration using catheter techniques are needed.

Studies investigating wound infiltration with catheter techniques have repeatedly reported increased leakage of fluid from the wound, requiring recurrent dressing changes that may impact on patient satisfaction.[93,100,103] Other complications of catheter-based techniques include wound haematoma[100] and wound infection.[93] Extra consideration should therefore be given when using wound infusions in high-risk parturients such as those with obesity or diabetes mellitus. There are no adequately powered prospective studies investigating the complications associated with wound catheters and further work investigating the safety profile would be of interest.

Adjuncts for wound infiltration

The use of non-steroidal anti-inflammatory drugs (NSAIDs) for wound infiltration following CD has been suggested and initial research has shown promising results. Lavand'homme et al. found that wound infiltration with diclofenac reduced post-CD pain scores and opioid consumption compared to the same dose administered systemically for 48 h.[95] Carvalho et al. also found that the addition of ketorolac, but not hydromorphone, to continuous LA wound infiltration was associated with lower levels of inflammatory mediators (IL-10 and IL-6) in wound exudate, in addition to reduced pain scores and analgesic use after CD.[104] The authors proposed that in addition to likely systemic effects, NSAIDs modulate local inflammation to reduce pain.

Single-dose wound infiltration with tramadol has been shown to reduce opioid consumption and pain scores in the first 24 h when compared to single dose wound infiltration with LA or placebo.[105,106] The addition of magnesium sulphate to LA for wound infiltration used either as a single dose or for continuous infusion has also been found to decrease pain scores and analgesic requirement post CD.[91,107] Similarly, using dexmedetomidine as an adjunct to LA wound infiltration appears to improve analgesia when compared to LA alone.[108] In contrast, the addition of ketamine to LA for wound infiltration at CD under neuraxial anaesthesia does not seem to confer any advantage in terms of postoperative opioid consumption or patient satisfaction.[109] Research into the use of adjuncts for wound infiltration remains in the early stages and further work is needed before routine use can be recommended.

Intraperitoneal instillation

Intra-operative analgesia

Intraperitoneal instillation of analgesic drugs is a quick and simple technique that requires little skill to perform but there is limited research regarding management of CD pain. Despite an early case series reporting successful surgical anaesthesia for CD when intraperitoneal instillation was used in conjunction with local field block with 100 mg 1% procaine, the technique gained little popularity.[110] More recently, Werntz et al. reported a case series describing the use of intraperitoneal instillation with 3% chloroprocaine as a rescue technique for intra-operative pain in women having CD under neuraxial anaesthesia.[111] In this case series of 32 women, an average of 11.8 mg/kg chloroprocaine was used to treat intra-operative pain: 53% of patients reported a significant improvement in pain scores and no patients requiring conversion to GA. Although results from this case series suggest that intraperitoneal instillation may be a useful treatment for managing intraoperative CD pain, randomised controlled trials evaluating this technique are needed before it can be incorporated into standard practice.

Postoperative analgesia

The use of intraperitoneal LA instillation has been reported to be an effective method of postoperative multimodal analgesia for a variety of abdominal surgical procedures. A study investigating intraperitoneal instillation for CD found that using 20 mL 2% lidocaine with epinephrine reduced early postoperative pain scores at two hours but did not affect 24-h pain scores or postoperative opioid requirement.[112] However, in this study some women underwent peritoneal closure as part of their surgical technique. Subgroup analysis showed that intraperitoneal instillation with LA reduced pain scores on movement at 24 h in patients with peritoneal closure whereas no significant differences in pain scores were demonstrated for patients without peritoneum closure. Shahin and Osman investigated the effect of intraperitoneal instillation with LA in women undergoing CD with parietal peritoneal closure and reported the technique reduced postoperative pain scores, opioid consumption and opioid-related side effects when compared to placebo.[113]

In women undergoing CD under GA in whom intraperitoneal instillation was used in conjunction with LA wound infiltration (maximum dose 225 mg ropivacaine), early and late pain scores were reduced and pethidine requirement lowered by 44 mg at 48 h postoperatively.[114] Using this combined technique of LA intraperitoneal instillation and local wound infiltration, plasma ropivacaine levels were below toxic levels for up to 24 h, with peak levels achieved at 30 minutes following the procedure.[115] Little work has been

conducted evaluating the pharmacokinetics of LAs after intraperitoneal instillation and further research investigating this is required to determine the optimum LA dose for balancing safety with efficacy.

There has been renewed interest in exploring intraperitoneal instillation of LA as a technique to minimise post-CD pain but research is insufficient. This approach may be of benefit in patients who undergo peritoneal closure but better evidence is needed. Research comparing intraperitoneal instillation to more popular LA techniques such as TAP block and wound infiltration, in the absence of ITM, is also required before these techniques are incorporated into standard practice.

Conclusion

There is mounting evidence supporting the use of LA techniques as adjuncts for post-CD analgesia. The TAP block is the most studied technique and as such has the largest body of evidence supporting its routine use in the absence of ITM. If a TAP block is to be administered, an US-guided posterior approach with <50 mg bupivacaine per side should be used. Studies investigating other US-guided techniques such as the ILIH and QLB show promise in providing post-CD analgesia but due to the sparse evidence and limited number of outcome-based studies, it is still too early to draw firm conclusions regarding their role. In the absence of expertise and equipment, single-dose wound infiltration may be a feasible and useful option in achieving a moderate reduction in postoperative opioid consumption.

While there are studies exploring the role of TAP blocks, QLB, ILIH blocks, peritoneal and wound infiltration, further research is required to determine the optimum drug and adjunct-dosing strategies and the potential role of liposomal preparations. This research should also focus on comparing the efficacy of various LA techniques for post CD analgesia, as well as combining these techniques with low-dose long-acting neuraxial opioids.

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The authors have no conflicts of interest to declare.

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