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REVIEW ARTICLE

Transversus abdominis plane block versus local anaesthetic wound infiltration for analgesia after caesarean section

A systematic review and meta-analysis with trial sequential analysis

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BACKGROUND Transversus abdominis plane (TAP) block and local anaesthetic wound infiltration are used to relieve pain after caesarean section.

OBJECTIVES To determine whether TAP block or local anaesthetic wound infiltration is the better analgesic option after caesarean section.

DESIGN Systematic review and meta-analysis with trial sequential analysis.

DATA SOURCES MEDLINE, Embase, Cochrane Central Register of Controlled Clinical Trials, Web of Science up to June 2020.

ELIGIBILITY CRITERIA We retrieved randomised controlled trials comparing TAP block with wound infiltration after caesarean section. Primary outcome was pain score during rest (analogue scale, 0 to 10) at 2 h postoperatively, analysed according to the TAP block technique (ultrasound-guided/landmark-guided), anaesthetic strategy (spinal/general), intrathecal fentanyl (yes/no) and multimodal analgesia (yes/no). Secondary pain-related outcomes included pain scores during rest at 12 and 24 h, and total intravenous morphine consumption at 2, 12 and 24 h. We sought rates of block complications, including postoperative infection, haematoma, visceral injury and local anaesthetic systemic toxicity.

RESULTS Seven trials, totalling 475 patients, were identified. There was no difference in pain score during rest at 2 h between groups. Subgroup analyses revealed no differences related to TAP block technique ($P = 0.64$), anaesthetic strategy ($P = 0.53$), administration of intrathecal fentanyl ($P = 0.59$) or presence of multimodal analgesia ($P = 0.57$). Pain score during rest at 12 h and intravenous morphine consumption at 2 and 12 h were identical in both groups. Data were insufficient to compare block complications. Overall quality of evidence was moderate.

CONCLUSION There is moderate level evidence that TAP block and wound infiltration provide similar postoperative analgesia after caesarean section.

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Introduction

The number of caesarean sections is increasing worldwide, and postoperative pain remains a significant problem.[1] Regional anaesthetic techniques in this population have been shown to reduce postoperative opioid consumption, improve patient comfort, and support early ambulation and breast feeding.[1] These are some of the reasons why the PROSPECT (PROcedure SPECific postoperative pain managemenT) group, a group of experts in anaesthesiology and surgery, recommends a fascial plane block, such as transversus abdominis plane (TAP) block or wound infiltration to relieve postoperative pain in the absence of intrathecal opioid.[2] The TAP block

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consists of injecting local anaesthetic in the plane between the internal oblique and the transversus abdominis muscles in order to anaesthetise the sensory nerves supplying the anterior abdominal wall,[3] whereas wound infiltration is the direct injection of local anaesthetic into the area of the wound.

Several meta-analyses have summarised evidence that both TAP block[4–6] and wound infiltration[7,8] provide effective analgesia after caesarean section when compared with placebo. In addition, a recently published systematic review compared TAP block with wound infiltration for postoperative analgesia following caesarean delivery.[9] However, the authors of that publication included trials with continuous infusions of local anaesthetic, a technical strategy that is infrequently employed in common practice. Furthermore, that report did not include a trial sequential analysis, which prevents a conclusion as to whether firm evidence was reached by the review.[10] As the use of a continuous local anaesthetic infusion to the TAP block requires significant postoperative resources and ongoing patient monitoring, this approach is incompatible with fast-track surgery or early mobilisation. We, therefore, decided to undertake an updated systematic review and meta-analysis with a focus on the single-injection technique. We also include a trial sequential analysis to determine whether TAP block provides superior analgesia when compared with wound infiltration after caesarean section.

Methods

This investigation was conducted following the recommended process from the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA) statement[11] and was prospectively registered through the International Prospective Register of Systematic Reviews (registration number CRD42020208046).

The following electronic sources were queried for the period prior to 17 June 2020: MEDLINE, Embase, Cochrane Central Register of Controlled Clinical Trials and Web of Science. The population search terms applied were: caesarean OR caesarean section. The output from this search was combined with the terms Block OR Transversus abdominis OR TAP OR Local anaesthesia OR Wound infiltration. Population limits were then applied including Clinical trials OR Random allocation OR Therapeutic use. The following words were searched as keywords: Caesar*, Incisi*, Operation*, Operative*, Surger*, Surgical*, Perioperati*, Pain*, Nociception*, Analges*, Anesthe*, Anaesthe*, Transversus abdominis plane block, Transvers*, Infiltration*. Deduplication of the retrieved records was done manually. In addition, Google Scholar was queried for any remaining relevant publications. Furthermore, authors who had unpublished clinical trials registered on clinicaltrials.gov were contacted. Details of this literature search are provided in Supplementary Document 1, http://links.lww.com/EJA/A574.

Search results were independently screened by two authors (S.G. and E.A.) using the title and the abstract. Only randomised controlled trials on humans were included, without language restriction. The full texts of potentially eligible articles were subsequently evaluated for inclusion. Discrepancies were resolved by discussion until consensus was reached or, if needed, involvement of the third author (K.R.K.). Finally, after compiling the results of the above search, the authors independently reviewed the references from all included trials for any applicable articles that were not captured by the described approach.

Population

The meta-analysis addressed patients undergoing caesarean section under regional or general anaesthesia.

Intervention and comparator

Only trials that investigated pain outcomes and compared single-injection TAP block with single-injection wound infiltration were included in this meta-analysis.

Outcomes

Defined outcomes were extracted from each article following the routine approach previously described in meta-analyses on acute postoperative pain.[12–14] The primary outcome was the pain score during rest 2 h postoperatively. Secondary pain-related outcomes included: pain scores during rest at 12 and 24 h postoperatively; pain scores during movement at 2, 12 and 24 h postoperatively; total intravenous morphine consumption at 2, 12 and 24 h postoperatively; and the rate of postoperative nausea and vomiting within the first 24 h postoperatively. Other secondary outcomes sought were the rates of haematoma, postoperative infection, visceral injury and local anaesthetic systemic toxicity. We also aimed to capture hospital resource-related outcomes including hospital length of stay and procedure-related time.

Trial characteristics

Extracted trial characteristics included the strategy for TAP block guidance; timing of TAP block and wound infiltration relative to the surgery; concentration and volume of local anaesthetic administered; anaesthetic strategy and postoperative analgesic regimen.

Rating of the studies

The Cochrane Collaboration's Risk of Bias Tool[15] was applied to each randomised trial in order to evaluate the methodological quality. Two authors (S.G. and E.A.) independently reviewed and scored the items from this tool for each trial. A third author (K.R.K.) adjudicated disagreements during the initial assessment.

Data extraction

The texts, tables or images from the included trials were assessed to extract the number of participants, number of events, means, standard deviations, standard error of means and 95% confidence intervals (CI). In the event that an included trial did not indicate the sample size or failed to describe the results as a mean and standard deviation or standard error of the mean and 95% CI, we attempted to contact the corresponding author twice via e-mail. We requested access to the missing data or alternatively to the complete dataset and if we were unable to obtain these additional elements, we employed the median and interquartile range as approximations of the mean and standard deviation, by estimating the mean as equivalent to the median and the standard deviation as the interquartile range divided by 1.35 or the range divided by 4.[15] All opioids were converted to equianalgesic i.v. morphine doses (i.v. morphine 10 mg = oral morphine 30 mg = i.v. tramadol 100 mg = i.v. pethidine 75 mg = i.v. fentanyl 100 μg = i.v. nalbuphine 10 mg = oral hydrocodone 30 mg = oral codeine 165 mg).[16] For pain scores reported by a 11-point verbal, visual or numerical rating scale, we converted the results to a 0 to 10 analogue scale for the purpose of statistical evaluation. Finally, the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group system[17] was used to evaluate the quality of evidence for each reported outcome.

Statistical analysis

All meta-analyses were conducted using the Review Manager software (RevMan version 5.3.5; Copenhagen, The Nordic Cochrane Centre, The Cochrane Collaboration 2014). For continuous data, this software estimates the weighted mean differences, and similarly the risk ratio for categorical data between groups, with an overall estimate of the pooled effect. In the event that two or more included trials presented an outcome, we conducted a meta-analysis. We set predetermined limits for low (25 to 49%), moderate (50 to 74%) and high (≥ 75%) heterogeneity based on the calculated I^2 coefficient.[18] A random effects model was employed when heterogeneity was found to be moderate or high; otherwise, a fixed effects model was applied.[19]

In an attempt to account for potential contributors to heterogeneity, we performed subgroup analyses for our primary outcome according to the TAP block technique (ultrasound-guided vs. landmark-guided), the anaesthetic strategy (spinal vs. general anaesthesia), the administration or not of intrathecal fentanyl for spinal anaesthesia and the presence or absence of multimodal analgesic therapy. The risk of publication bias associated with the primary outcome was estimated by drawing a funnel plot of the mean difference standard error of rest pain score at 2 h postoperatively (*y*-axis) as a function of the mean difference of rest pain score at 2 h postoperatively (*x*-axis)[20] and confirmed with Duval and Tweedie's trim and fill test.[21] This assessment was performed using Comprehensive Meta-analysis Version 2 software (Biostat, Englewood, New Jersey, USA). Finally, trial sequential analysis was performed on the primary outcome to confirm whether firm evidence was reached or not (TSA software version 0.9.5.10 Beta; Copenhagen Trial Unit, Center for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark).

We present results as the mean difference or relative risk (RR) with 95% CI and a two-sided value less than 0.05 was deemed to be significant.

Results

Of the 1123 trials identified from the literature search, seven met the inclusion criteria,[22–28] accounting for a total of 475 patients. Figure 1 shows the PRISMA flow diagram of literature search results and Fig. 2 summarises the risk of bias of the different trials.

Trial characteristics

Table 1 shows the trial characteristics. All caesarean sections were performed under spinal anaesthesia, except for two studies in which general anaesthesia was used.[22,26] Hyperbaric bupivacaine was administered for all spinal anaesthetics, which was given in one study[27] with fentanyl 15 μg and in two studies[24,28] with fentanyl 20 μg. In none of the trials was a long-acting opioid, such as morphine injected into the intrathecal space.

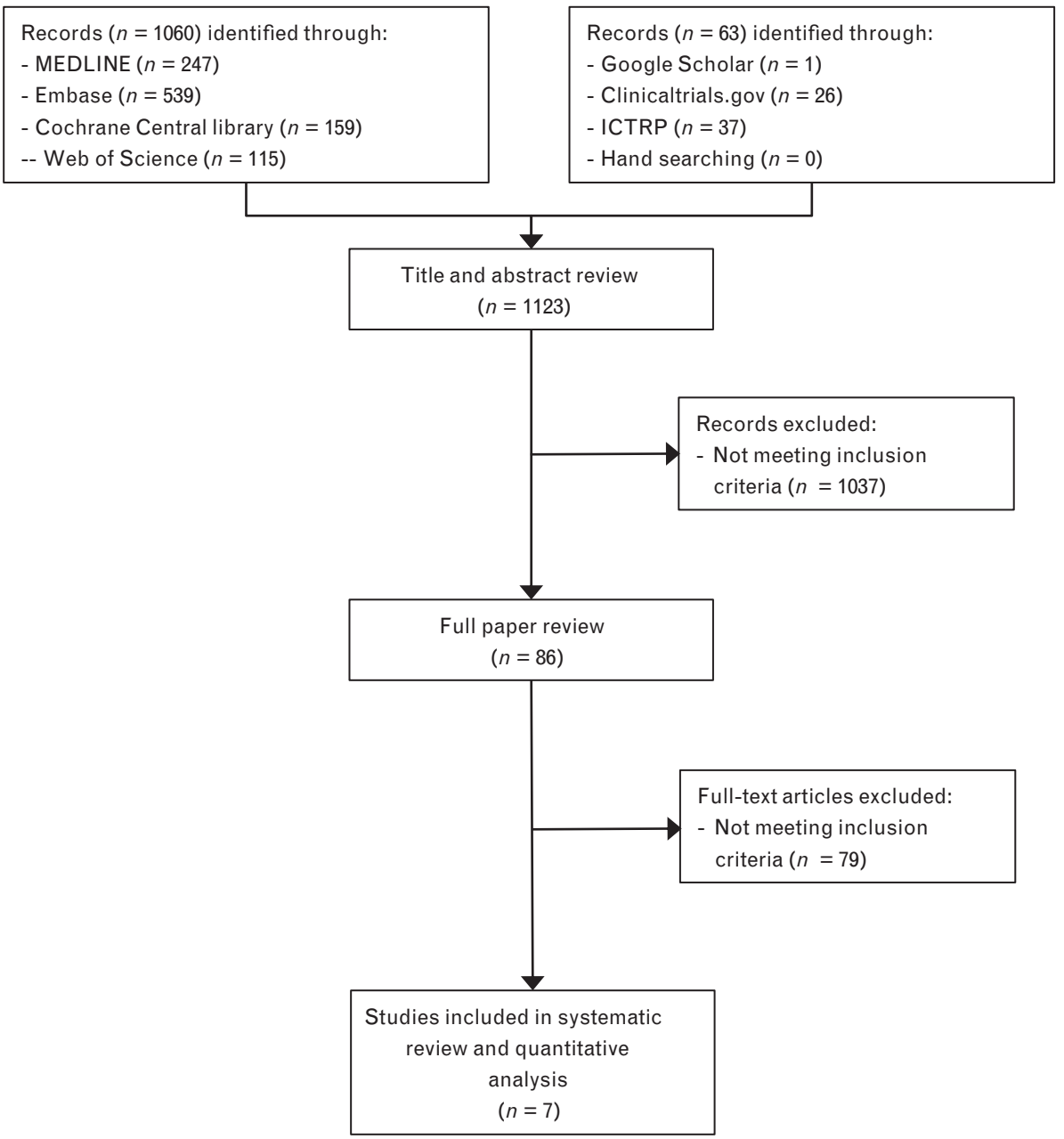
Primary outcome

On the basis of six trials, the mean ± SD pain score during rest at 2 h postoperatively was not significantly different between TAP block and wound infiltration [mean difference (95% CI), −1.0 (−2.2 to 0.2), $I^2 = 88\%$, $P = 0.09$], without subgroup differences according to the anaesthetic strategy (general vs. spinal anaesthesia, $P = 0.53$) (Fig. 3). Other subgroup analyses did not reveal any additional difference between TAP block guidance technique (ultrasound- vs. landmark-guidance, $P = 0.64$), the administration or not of intrathecal fentanyl ($P = 0.59$) or the prescription or not of multimodal analgesia ($P = 0.57$). The trial sequential analysis indicated that firm evidence was not reached regarding the contribution of TAP block to decreased rest pain score at 2 h postoperatively (Fig. 4). There was no risk of publication bias for the primary outcome according to the funnel plot (Fig. 5). This was confirmed with the Duval and Tweedie's trim and fill test. This test calculated the combined studies point estimate to be −0.52 (95% CI, −1.12 to 0.08) with a random effects model, and using trim and fill, these values were unchanged, suggesting that no studies are missing from the included trials.

Secondary outcomes

Table 2 shows the secondary pain-related outcomes that were inconsistently improved in favour of the TAP block. On the basis of three trials,[23,25,27] the rate of postoperative

Fig. 1 PRISMA flow diagram showing literature search results.



ICTRP, International Clinical Trials Registry Platform (from World Health Organisation).

nausea and vomiting was similar between groups, with a risk ratio (95% CI) of 0.8 (0.4 to 1.6, $I^2 = 0\%$, $P = 0.52$). No studies reported complications, such as postoperative infection, visceral injury or local anaesthetic systemic toxicity. One trial[26] reported the incidence of postoperative haematoma, and there was none. No studies reported duration of hospital stay.

Quality of evidence

According to the GRADE system, the quality of evidence was moderate for both the primary and secondary outcomes (Supplementary Table 1, http://links.lww.com/EJA/A575).

Discussion

This systematic review and meta-analysis explored the analgesic efficacy of TAP block compared with wound infiltration in patients undergoing caesarean section. On the basis of seven randomised controlled trials including a total of 475 patients, we demonstrated that both techniques provided similar postoperative analgesia. Indeed, there were no significant differences between groups in

Fig. 2 Cochrane collaboration risk of bias summary: evaluation of bias risk items for each included study.

Green circle, low risk of bias; red circle, high risk of bias; yellow circle, unclear risk of bias.

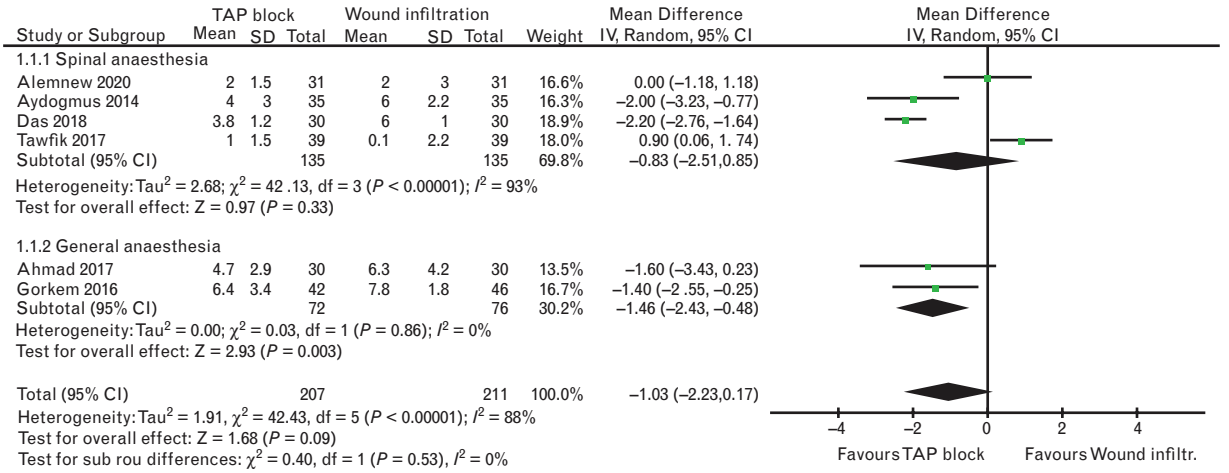
pain scores during rest, i.v. morphine-equivalent consumption at 2 and 12 h postoperatively or pain scores during movement at 12 and 24 h postoperatively. The lower pain score during rest and consumption of i.v. morphine at 24 h postoperatively is suspected to represent a type I error. We believe this to be the case, given the lack of impact seen earlier in the patients' recovery and the likelihood that local anaesthetic analgesia had worn off by this time. Likewise, the reduced pain score during rest at 2 h postoperatively with TAP block when patients are under general anaesthesia might also represent a type I error, as this subgroup included only two trials, and as there was no subgroup difference with patients under spinal anaesthesia. Additional studies including patients scheduled for caesarean section under

Table 1 Trial characteristics

Reference	Group (*n*)	TAP block technique	Timing		Local anaesthetic injected		Anaesthetic strategy	Postoperative analgesia
			TAP block	Wound infiltration	TAP block (total dose)	Surgical infiltration		
Ahmad[22]	TAP block (30) Wound infiltration (30)	Landmark	Not specified	End of surgery	Bupivacaine 0.25%, 0.6 ml kg^{-1}	Bupivacaine 0.25%, 0.6 ml kg^{-1}	General anaesthesia	i.v. tramadol
Alemnew and Lemma[23]	TAP block (31) Wound infiltration (31)	Not specified	End of surgery	End of surgery	Bupivacaine 0.25%, 40 ml	Bupivacaine 0.25%, 15 ml	Spinal anaesthesia	i.v. tramadol, i.v. diclofenac
Aydogmus *et al.*[24]	TAP block (35) Wound infiltration (35)	Ultrasound	End of surgery	End of surgery	Levobupivacaine 0.25%, 40 ml	Levobupivacaine 0.25%, 40 ml	Spinal anaesthesia	i.m. diclofenac, i.v. tramadol
Das *et al.*[25]	TAP block (30) Wound infiltration (30)	Ultrasound	End of surgery	End of surgery	Ropivacaine 0.5%, 40 ml	Ropivacaine 0.5%, 40 ml	Spinal anaesthesia	i.v. diclofenac, i.v. tramadol
Görkem *et al.*[26]	TAP block (42) Wound infiltration (46)	Ultrasound	End of surgery	End of surgery	Bupivacaine 0.25%, 40 ml	Bupivacaine 0.25%, 20 ml	General anaesthesia	i.m. diclofenac, i.m. pethidine
Tawfik *et al.*[27]	TAP block (39) Wound infiltration (39)	Ultrasound	End of surgery	End of surgery	Bupivacaine 0.25%, 40 ml	Bupivacaine 0.25%, 30 ml	Spinal anaesthesia	i.v. PCA of fentanyl, i.v. ketorolac, oral paracetamol
Telnes *et al.*[28]	TAP block (28) Wound infiltration (29)	Ultrasound	End of surgery	End of surgery	Bupivacaine 0.25% + epinephrine 5 μg ml^{-1}, 40 ml	Bupivacaine 0.25% + epinephrine 5 μg ml^{-1}, 20 ml	Spinal anaesthesia	i.v. PCA of morphine, oral paracetamol, oral diclofenac

PCA, patient-controlled analgesia.

Fig. 3 Pain score during rest at 2 h postoperatively in patients undergoing caesarean section with TAP block vs. wound infiltration, according to the anaesthetic strategy.

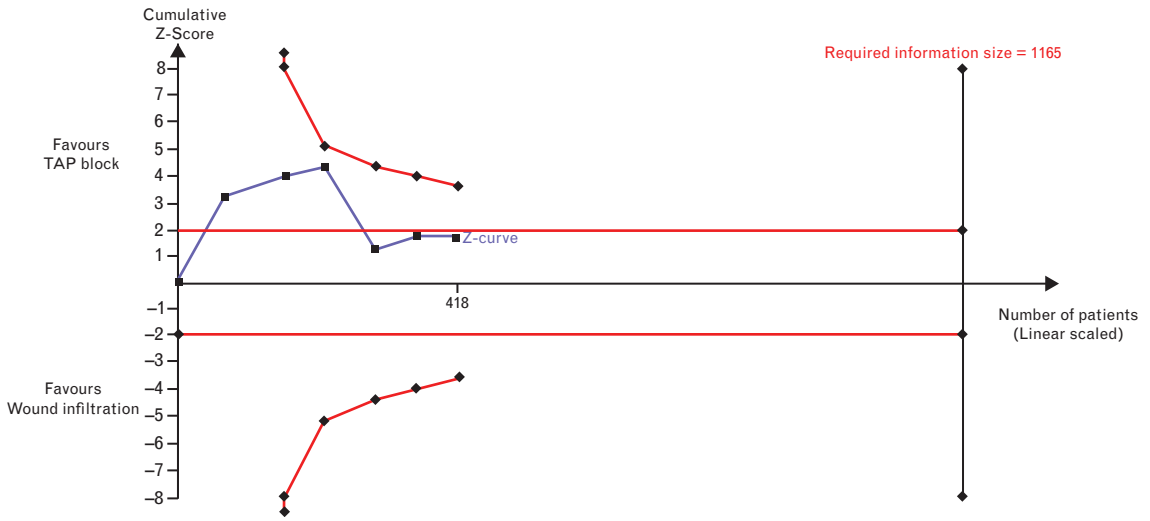


general anaesthesia are necessary before establishing evidence, even if we acknowledge that would not represent the standard of care.

More broadly, the trial sequential analysis revealed that the threshold for firm evidence is not reached by the existing literature and that more randomised controlled trials are needed, totalling an additional 747 patients, before these conclusions could be said to meet that level of reliability.

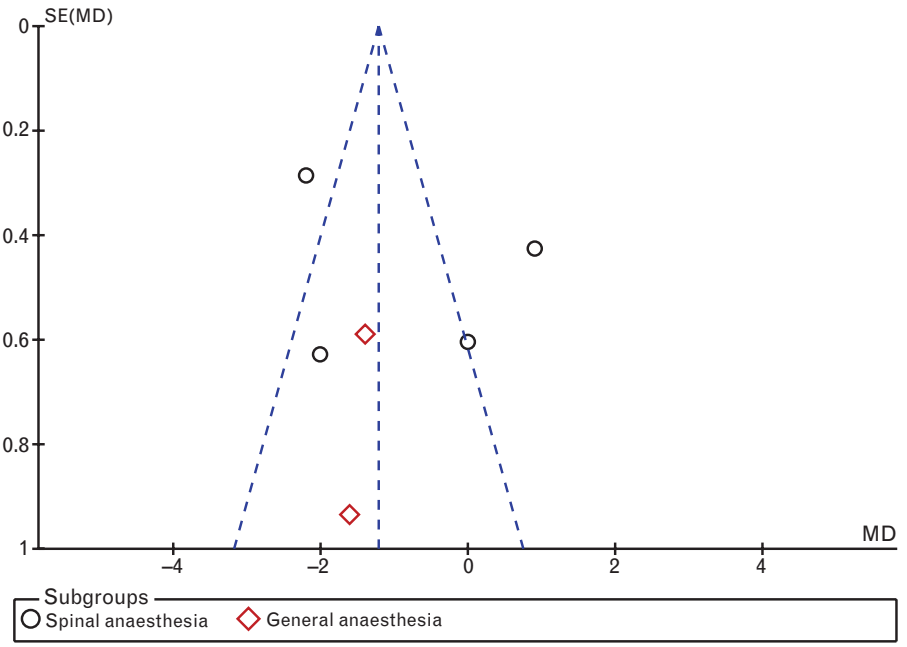
Our results suggest the interpretation that a diversity of analgesic options are available when caring for patients undergoing caesarean section. Indeed, the skills and qualifications of the attending physicians may appropriately permit either a TAP block or wound infiltration to be offered as part of a multimodal analgesic treatment. As past comparisons with placebo suggest, either technique contributes to pain reduction, improved patient comfort and reduced opioid consumption in the long-term.[29] Our results strengthen the recommendations of the PROSPECT group that specify that either a fascial plane block or wound infiltration should be performed to relieve postoperative pain in the absence of intrathecal morphine.[2] Following what was most frequently administered by

Fig. 4 Trial sequential analysis for pain score during rest at 2 h postoperatively.



The cumulative Z curve (blue) does not cross the monitoring boundary curve (red) and does not reach the required information size, indicating that firm evidence was not reached.

Fig. 5 Funnel plot of the primary outcome (pain score during rest at 2 h postoperatively).



SE (MD), standard error of the mean difference.

Table 2 **Secondary pain-related outcomes**

Outcome	Number of trials	References	Total number of patients		Mean difference (95% CI) or relative risk (95% CI)	I^2 (%)	*P* value for overall effect
			TAP block	Wound infiltration			
Pain score during rest at 12 h	6	Alemnew and Lemma[23]; Aydogmus *et al.* [24]; Das *et al.*[25]; Görkem *et al.*[26]; Tawfik *et al.* [27]; Telnes *et al.*[28]	205	210	−1.2 (−2.6 to 0.1)	96	0.08
Pain score during rest at 24 h	5	Alemnew and Lemma[23]; Aydogmus *et al.*[24]; Das *et al.*[25] ; Tawfik *et al.* [27]; Telnes *et al.*[28]	163	164	−1.3 (−2 to −0.6)	89	<0.001
Pain score during movement at 2 h	1	Tawfik *et al.*[27]	39	39	2 (0.8 to 3.2)	N/A	<0.001
Pain score during movement at 12 h	3	Aydogmus *et al.*[24]; Tawfik *et al.* [27]; Telnes *et al.*[28]	102	103	0.5 (−0.5 to 1.4)	71	0.34
Pain score during movement at 24 h	3	Das *et al.*[25]; Tawfik *et al.* [27]; Telnes *et al.*[28]	97	98	0.3 (−0.4 to 1)	39	0.45
Cumulative i.v. morphine[a] consumption at 2 h (mg)	1	Tawfik *et al.*[27]	39	39	0 (−0.2 to 0.2)	N/A	1
Cumulative i.v. morphine[a] consumption at 12 h (mg)	2	Tawfik *et al.* [27]; Telnes *et al.*[28]	67	68	0.2 (−2.7 to 3)	0	0.91
Cumulative i.v. morphine[a] consumption at 24 h (mg)	4	Alemnew and Lemma[23]; Görkem *et al.* [26] ; Tawfik *et al.* [27]; Telnes *et al.*[28]	140	145	−1.9 (−3.3 to −0.5)	25	0.007

All pain scores using 1 to 10 analogue scale. CI, confidence interval; N/A, not applicable. [a]Intravenous morphine-equivalent; see text for details.

the authors, we advocate the injection of bupivacaine 0.25% or ropivacaine 0.5% 40 ml for the TAP block, and 30 to 40 ml for wound infiltration.

Several weaknesses should be acknowledged in this report. In particular, we recognise there is unexplained heterogeneity in the data. Our hypotheses and subgroup analyses did not explain the elevated coefficient of heterogeneity within the primary outcome. We were unable to draw any conclusions regarding some of the predefined outcomes, such as postoperative infection, visceral injury, local anaesthetic systemic toxicity or hospital stay.

Indeed, these outcomes were not reported by any of the trials. In addition, three trials suffer from a high risk of selection, reporting and selecting biases. More research with well performed randomised controlled trials is needed to further investigate the complications of the local anaesthetic injection for each intervention, among others, and properly define the risk–benefit balance of each intervention. Finally, as none of the trials injected a long-acting opioid intrathecally, additional studies investigating the analgesic benefit of TAP block and wound infiltration in the setting of intrathecal morphine would be valuable.

Conclusion

There is moderate-level evidence that TAP block and wound infiltration provide similar postoperative analgesia after caesarean section. The choice of the analgesic option should be tailored to the individual patient, the procedure and the institutional setting.

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