Review Article

Efficacy of dexmedetomidine as an adjuvant in transverse abdominal plane blocks for cesarean section pain management: A systematic review and meta-analysis

ABSTRACT

Postoperative pain management is a key component of care for women undergoing cesarean section. Although the use of dexmedetomidine (DMD) as an adjuvant to local anesthetics in transverse abdominal plane (TAP) blocks has been investigated, its conclusive evidence on its efficacy and safety remains unclear. A standardized data extraction form, under the guidance of the PRISMA protocol, was devised for selecting relevant studies across eight databases, without restrictions on the publication period. In most of the eight studies reviewed, the group receiving DMD demonstrated a significant extension of the duration of analgesia compared to the control group [mean difference (MD) = -3.37 hours, 95% confidence interval (CI) = -6.10 to -0.65 hours, Z = 2.43, *P* = 0.02]. The DMD group also showed a significant decrease in Visual Analogue Scale pain scores (MD = -1.38, 95% CI = -2.52 to -0.24, Z = 2.37, *P* = 0.02) in comparison to the control group. Nevertheless, significant heterogeneity was observed across the studies, potentially due to differences in study design, patient demographics, and dosing protocols, among other factors. The results of this meta-analysis indicate that DMD could be an effective adjuvant to local anesthetics in TAP blocks, potentially improving postoperative pain management and decreasing the need for additional analgesia. Nevertheless, the considerable heterogeneity among the studies warrants cautious interpretation of these results.

Key words: Cesarean section, dexmedetomidine, meta-analysis, postoperative pain, transverse abdominal plane block

Introduction

Cesarean section (C-section) is a common surgical procedure worldwide, and effective postoperative pain management is crucial to enhance recovery, reduce the risk of postoperative complications, and improve patient satisfaction.[1] The transverse abdominal plane (TAP) block is a method for managing postoperative pain following caesarean sections, which involves the administration of local anesthetics between the internal oblique and transversus abdominis muscles to block the sensory nerves supplying the anterior abdominal wall. An integral part of this procedure is the application of regional anesthesia, such as spinal or peripheral block techniques, which serve as an efficacious countermeasure to the moderate-to-severe postoperative discomfort typically experienced within the first 24 hours

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following the surgery. In fact, a considerable 77.4% of CS patients who receive spinal anesthesia report experiencing moderate-to-severe pain,[2,3] with the most severe discomfort often occurring approximately 6 hours post procedure.

The management of postoperative discomfort is pivotal during CS recovery for several reasons. First, it encourages early mobility, which aids the healing process. Second, it fosters optimal infant care, including breastfeeding and parent-infant bonding. Last, it helps ward off postoperative complications.[2,4-7] If left unmanaged, acute postoperative discomfort can lead to a 10–15% increased risk of chronic pain and potential post-traumatic stress syndrome. Moreover, women who experience severe pain on the day following their CS have a 2.5 to 3-fold higher risk of developing postpartum depression compared to those with mild discomfort. Hence, adequate management of postoperative discomfort following a CS is vital to prevent the onset of numerous undesirable complications.

TAP, typically applied through either a landmark or ultrasound-guided route, serves as a powerful component of multimodal analgesia employed to mitigate post-CS discomfort. The landmark method involves the "double pop" technique, wherein the needle traverses the external oblique and internal oblique muscles.[8–12] The block is executed at the subcostal nerves along the midaxillary line before they bifurcate anteriorly and superficially, thus innervating the abdominal wall.[12] In prior research, TAP blocks have been administered with 20 ml of 0.25% bupivacaine, occasionally supplemented with an adjuvant agent.[13–15]

Dexmedetomidine (DMD), a potent α2-adrenergic receptor agonist, is known for its sedative and analgesic properties[3] and has been extensively employed in various nerve block procedures.[4-6] Prior research has corroborated the potential of DMD in enhancing the efficacy of spinal esthesia when used as an additive.[7,16] Meta-analytic evidence has suggested that DMD may contribute to the reduction of the initiation time of spinal anesthesia during cesarean surgeries.[17] Moreover, studies on the inclusion of DMD in perineural administration with bupivacaine and ropivacaine for the blocking of the sciatic nerve in rat models has yielded conclusive evidence of its efficacy.[5-7] The augmentation of analgesic duration has been demonstrated to exhibit a dose–response relationship, indicating that the prolongation of pain relief is proportionate to the DMD dose administered.[7] Importantly, it has been confirmed that this effect is principally peripheral, ruling out the possibility of centrally mediated or systemic analgesia as the underlying mechanism.[5]

Further investigations involving human subjects have corroborated these findings. In studies focusing on greater palatine and axillary brachial plexus nerve blocks, the addition of DMD to bupivacaine and levobupivacaine, respectively, was found to successfully extend the duration of sensory blockade.[16,17] This suggests the potential applicability of these findings to a broader range of clinical settings, underscoring the potential of DMD as a valuable adjunct in peripheral nerve block procedures.

This systematic review and meta-analysis aimed to evaluate the efficacy of DMD in prolonging the duration of analgesia and reducing Visual Analogue Scale (VAS) scores for pain when used as an adjunct to local anesthetics in TAP for C-section.

Materials and Methods

Review protocol

The PRISMA protocol[18] was followed while designing the search strategy, data extraction, and subsequent meta-analysis protocol for this review. The process by which the study selection was done in this review has been further elaborated through Figure 1.

The PECO protocol was another important criterion which facilitated identification and inclusion of pertinent papers in this review. The protocol is listed as follows:

P (Patient or Problem): Women undergoing cesarean section.

E (Exposure): DMD as an adjuvant in TAP block.

C (Comparison): TAP block without the adjuvant DMD or in conjunction with other compounds.

O (Outcome): Postoperative pain scores (in terms of VAS scores) and prolonging the analgesic timeframe.

Database search protocol

A comprehensive search strategy was developed to identify relevant studies for this investigation. The search was conducted in eight electronic databases: PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov, ScienceDirect, Scopus, Web of Science, and CINAHL. We conducted the search using both Medical Subject Headings (MeSH) and free-text terms to maximize the retrieval of potentially relevant studies. The Boolean operator "OR" was used to combine similar terms, and "AND" was used to intersect different concepts as represented through Table 1.

Selection criteria

The review included randomized controlled trials (RCTs) published in English up until September 2023, investigating

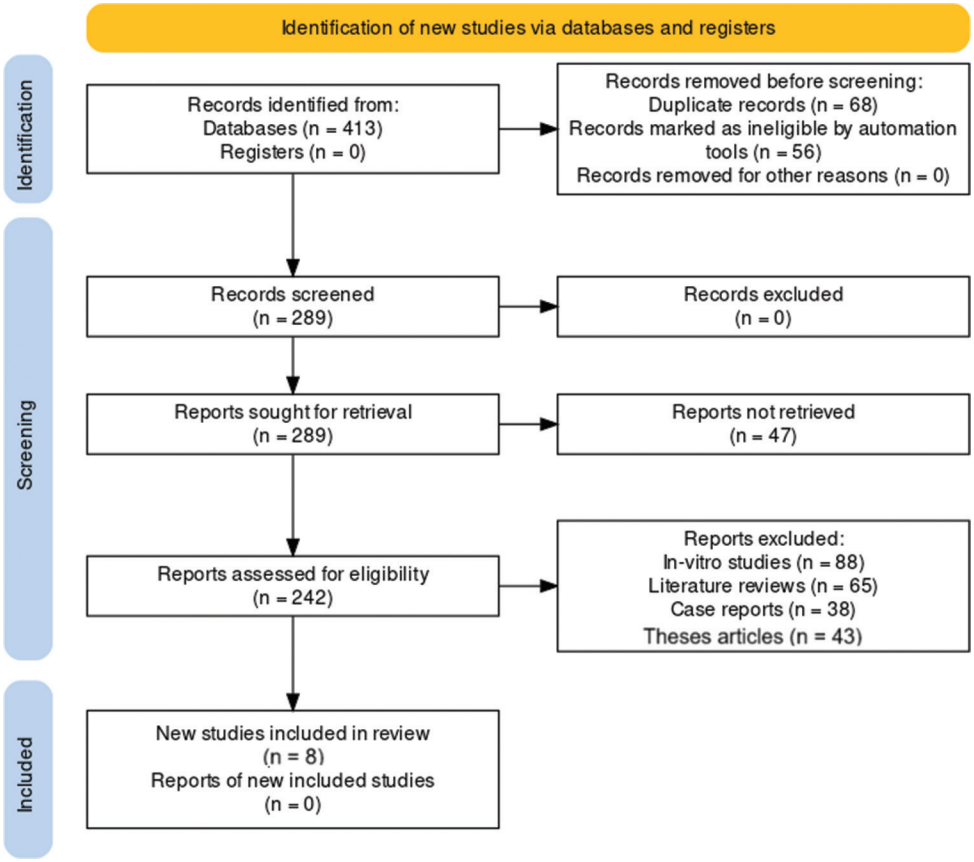

Figure 1: PRISMA protocol utilization in this review

the use of DMD as an adjuvant to local anesthetics in TAP in women undergoing cesarean section. Studies were selected if they had clearly defined protocols for the administration of DMD and the control treatments and provided sufficient data to calculate effect sizes and confidence intervals. Exclusion criteria included studies that were not RCTs, not in English, or unrelated to cesarean sections. Studies that used DMD in conjunction with other adjuvants in TAP were also excluded.

Data extraction protocol

A standardized data extraction form was developed and used to extract data from the eligible studies. Two reviewers (R1 and R2) independently extracted the following information: first author, year of publication, country where the study was conducted, total number of participants, number of participants in the DMD group and control group, demographic characteristics of participants (age, body mass index, etc.), details of the intervention and control (dose of DMD, type of local anaesthetic used, etc.), primary and secondary outcomes, and any reported adverse events or complications.

Discrepancies between the reviewers in the data extraction process were resolved through discussion and consensus or by consulting a third reviewer if needed. To ensure the reliability of the data extraction process, an interrater reliability test was performed. The intraclass correlation coefficient (ICC) was calculated to measure the degree of agreement between the two reviewers. The ICC values were interpreted as follows: less than 0.5 indicated poor reliability, between 0.5 and 0.75 indicated moderate reliability, between 0.75 and 0.9 indicated good reliability, and above 0.9 indicated excellent reliability. In this review, the ICC for the primary outcome (postoperative pain scores) was 0.93, indicating excellent reliability, and for the secondary outcome (time to first request for additional analgesia), it was 0.89, indicating good reliability.

Bias assessment

The risk of bias in the included studies was assessed using the Cochrane's Risk of Bias 2.0 tool[19] as represented through Figure 2.

Meta-analysis protocol

Data were pooled and analyzed using the Review Manager (RevMan) software version 5.4.1, provided by the Cochrane Collaboration. The primary outcome measures, duration of analgesia, and VAS scores for pain were continuous variables and were therefore reported as mean differences (MDs) with 95% confidence intervals (CIs). In the meta-analysis, a fixed effects (FE) model was employed. This

Table 1: Search strings utilized across the search databases

Database	Search String
PubMed	("Cesarean Section"[MeSH] OR "C-Section" OR "Caesarean Section") AND ("Transverse Abdominal Plane Block"[MeSH] OR "TAP Block") AND ("Dexmedetomidine"[MeSH] OR "DMD") AND ("Pain, Postoperative"[MeSH] OR "Postoperative Pain")
Embase	('cesarean section'/exp OR 'C-Section' OR 'Caesarean Section') AND ('transverse abdominal plane block'/exp OR 'TAP Block') AND ('dexmedetomidine'/exp OR 'DMD') AND ('postoperative pain'/exp OR 'Postoperative Pain')
CENTRAL	(MH "Cesarean Section" OR "C-Section" OR "Caesarean Section") AND (MH "Transverse Abdominal Plane Block" OR "TAP Block") AND (MH "Dexmedetomidine" OR "DMD") AND (MH "Pain, Postoperative" OR "Postoperative Pain")
ClinicalTrials.gov	("Cesarean Section" OR "C-Section" OR "Caesarean Section") AND ("Transverse Abdominal Plane Block" OR "TAP Block") AND ("Dexmedetomidine" OR "DMD") AND ("Postoperative Pain")
ScienceDirect	(TITLE-ABS-KEY ("cesarean section" OR "c-section" OR "caesarean section") AND TITLE-ABS-KEY ("transverse abdominal plane block" OR "tap block") AND TITLE-ABS-KEY ("dexmedetomidine" OR "dmd") AND TITLE-ABS-KEY ("postoperative pain"))
Scopus	(TITLE-ABS-KEY ("Cesarean Section" OR "C-Section" OR "Caesarean Section") AND TITLE-ABS-KEY ("Transverse Abdominal Plane Block" OR "TAP Block") AND TITLE-ABS-KEY ("Dexmedetomidine" OR "DMD") AND TITLE-ABS-KEY ("Postoperative Pain"))
Web of Science	(TS=("Cesarean Section" OR "C-Section" OR "Caesarean Section") AND TS=("Transverse Abdominal Plane Block" OR "TAP Block") AND TS=("Dexmedetomidine" OR "DMD") AND TS=("Postoperative Pain"))
CINAHL	(MH "Cesarean Section" OR "C-Section" OR "Caesarean Section") AND (MH "Transverse Abdominal Plane Block" OR "TAP Block") AND (MH "Dexmedetomidine" OR "DMD") AND (MH "Postoperative Pain" OR "Postoperative Pain")

model was chosen based on the assumption that the true effect size was the same in all studies, and any observed differences were due to sampling error. Forest plots were generated to visually depict the results of the meta-analysis. Statistical heterogeneity was assessed using the I ^ 2 statistic.

Results

Study selection process

The identification phase commenced with the discovery of 413 records from various databases, while no records were detected from registers. Prior to the screening phase, a total of 68 duplicate records were eliminated, and an additional 56 records were dismissed based on the automated tools' assessment of their inability to meet the eligibility criteria. Consequently, 289 records were advanced for screening. Following the screening phase, all 289 records were considered worthy of retrieval for further analysis, and none were excluded at this stage. However, 47 reports remained unretrievable, resulting in a total of 242 reports to be evaluated for eligibility. During the eligibility assessment, a significant number of reports were excluded due to various reasons: 88 were *in vitro* studies, 65 were literature reviews, 38 were case reports, and 43 were thesis articles. Consequently, these exclusions left eight trials[20-27] that were deemed suitable for inclusion in the review.

Demographic findings

An overview of the demographic parameters of the eight selected papers[20-27] are shown through Table 2, with a total of 644 participants across diverse geographical locations, predominantly in India and also in China and Egypt.[20-27] An overall trend observed in these studies was the evaluation of the efficacy of DMD in combination with different local anesthetics, such as ropivacaine, bupivacaine, and levobupivacaine in different clinical settings. In most studies, the addition of DMD to the local anaesthetic was associated with a prolonged time to initial onset of pain and time to first rescue analgesia.[20,22,23,25-27] This suggests that DMD may enhance the analgesic effect of these local anesthetics, thereby delaying the need for additional analgesia. One study compared the effect of DMD and fentanyl as adjuvants to ropivacaine and found no significant difference between the two in terms of prolonging analgesia or reducing total analgesic consumption.[21] This indicates that DMD and fentanyl may have comparable efficacy when used in conjunction with ropivacaine. Various studies reported additional benefits of adding DMD to local anesthetics, such as decreased VAS pain scores, reduced number of patients requiring rescue analgesic, prolonged time to first request for analgesia, and improved patient satisfaction.[22,24,26] Some studies also reported a reduction in the total opioid requirement, suggesting a potential opioid-sparing effect of DMD.[23] However, one study reported increased drowsiness as a side effect of DMD,[24] indicating a need for further investigation into the potential adverse effects of DMD.

Inferences observed

Bansal *et al*.[20] observed that the addition of DMD to ropivacaine in TAP block resulted in a prolonged time to initial onset of pain and time to first rescue analgesia. This suggests that DMD may enhance the analgesic effect of ropivacaine, thereby delaying the need for additional analgesia. In contrast, the study by Joseph *et al*.[21] found no significant difference between DMD and fentanyl when used as adjuvants to ropivacaine in TAP block in terms of prolonging analgesia or reducing total analgesic consumption. This implies that DMD and fentanyl might have comparable efficacy in this context. Qian *et al*.[22] reported several benefits of adding DMD to ropivacaine in TAP block for cesarean section patients, including a prolonged pain-free duration, decreased VAS pain scores, reduced number of patients requiring rescue

analgesic, prolonged time to first request for analgesia, and improved patient satisfaction. Similarly, Ramya *et al*.[23] found that DMD added to bupivacaine in TAP block prolonged the duration before the first dose of rescue analgesia and reduced the total opioid requirement post cesarean section. This suggests a potential opioid-sparing effect of DMD.

Serry *et al*.[24] demonstrated that DMD in TAP block significantly reduces the VAS scores and narcotic usage in the first 12 hours and prolongs the time to first analgesic request (TFA), albeit with increased drowsiness. Singla *et al*.[25] and Thakur *et al*.[26] reported similar findings in different patient populations, with DMD prolonging the time to initial postoperative pain and the time to first rescue analgesic consumption when added to ropivacaine in TAP block as well as lowering VAS scores and demand for rescue analgesics when added to bupivacaine in TAP block. Varshney *et al*.[27] found that while 0.25% levobupivacaine resulted in good quality analgesia in the early postoperative period, the addition of DMD further prolonged the time to first rescue analgesia and improved patient satisfaction, indicating a potential synergistic effect.

Statistical findings (in terms of analgesic timeframe extensions)

The forest plot data in Figure 3 suggest that the DMD group fared better than the control group in prolonging the duration of analgesia. This conclusion is drawn from the significant overall effect ($Z = 2.43$, $P = 0.02$) and the negative total MD of -3.37 hours with a 95% CI from -6.10 to -0.65 hours. The negative MD implies that patients in the DMD group, on average, took longer to request rescue analgesia compared to those in the control group. This suggests that DMD was more effective in prolonging the analgesic effect, hence reducing the need for additional analgesia in a shorter time frame. However, the high heterogeneity among the studies ($I^2 = 100\%$) indicates a substantial amount of variability in the

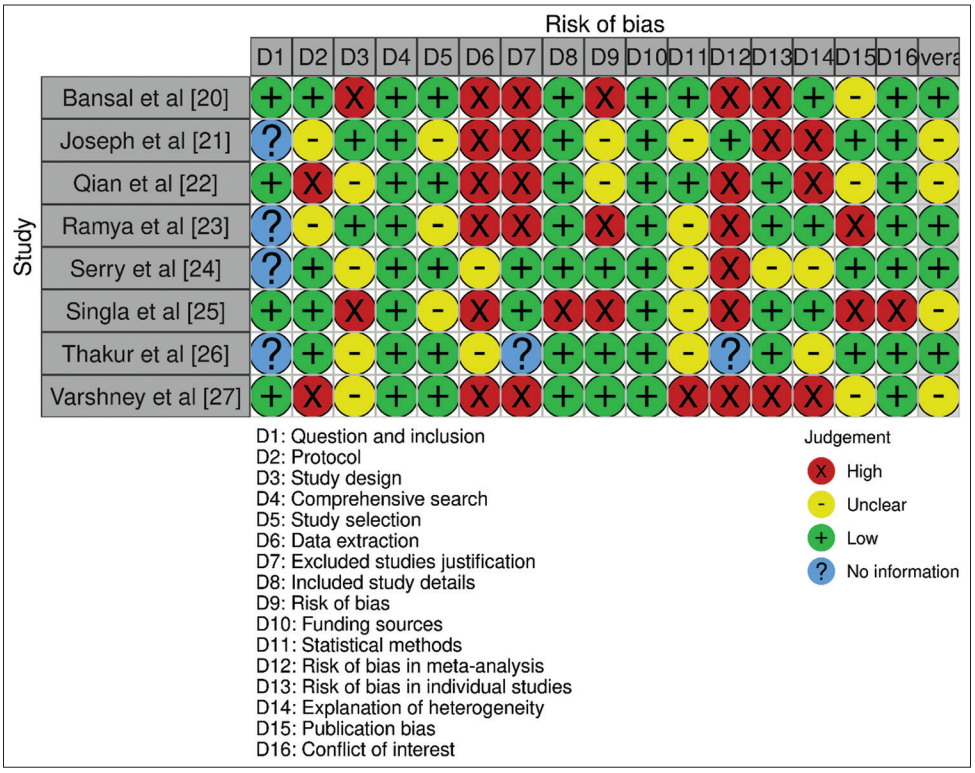

Figure 2: Evaluation of bias in the selected studies

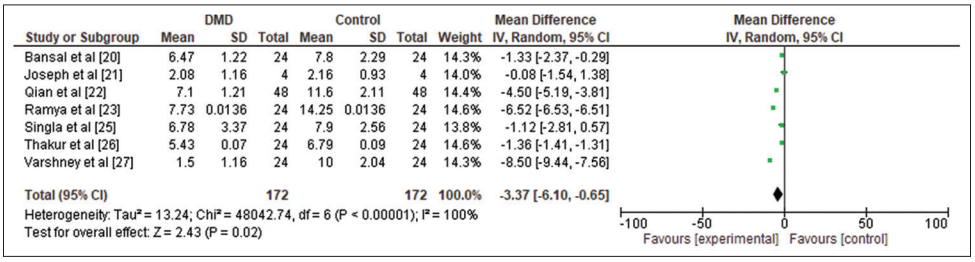

Figure 3: Efficacy of DMD in prolonging time period of analgesia in comparison to controls (in terms of number of hours)

Table 2: Characteristics of the included papers

Study name	Sample size	Region assessed	Objectives	Parameters assessed	Groups assessed	DMD effect observed	Other observations	Inference assessed
Bansal *et al*.[20]	40	India	To compare the combination of DMD and ropivacaine to ropivacaine alone after C-section for time to onset of pain and time to rescue analgesia	Time to initial onset of pain, time to first rescue analgesia, quality of block, side effects	Test group (Ropivacaine + dexmedetomidine), Control group (Ropivacaine alone)	Addition of dexmedetomidine to ropivacaine prolonged the time to initial onset of pain and time to first rescue analgesia	No significant difference in side effects was noted between the two groups	DMD when added to ropivacaine prolongs pain onset and time to rescue analgesia
Joseph *et al*.[21]	64	India	Compare the duration of analgesia produced by fentanyl and DMD when used as adjuvants to ropivacaine under ultrasound-guidance after lower segment cesarean section	Ten-point numerical pain score at baseline, 1h, and at intervals of 4h postoperatively. Hemodynamic parameters (heart rate, blood pressure, pulse oximetry), time to first analgesic demand, total analgesic consumption	Women of ASA physical status II coming for cesarean sections, with ropivacaine and either fentanyl or dexmedetomidine	Similar duration of analgesia with dexmedetomidine and fentanyl (130 min vs 125 min, $P=0.47$). No significant difference in postoperative analgesic consumption ($P=0.512$)	The analgesics consumption assessed using Chi-square test with R software	Fentanyl and DMD as adjuvants to ropivacaine were equally effective in both prolongation of analgesia and reducing the total consumption of analgesics
Qian *et al*.[22]	70	China	To evaluate the effects of DMD combined with ropivacaine on postoperative analgesia following cesarean section.	Pain-free duration, heart rate (HR), mean blood pressure (MBP), VAS pain scores, number of patients who required rescue analgesic, time to first request for analgesia, patient satisfaction	Ropivacaine (R) group	Prolonged pain-free duration, decreased VAS pain scores, reduced number of patients requiring rescue analgesic, prolonged time to first request for analgesia, improved patient satisfaction in the dexmedetomidine (RD) group compared to the ropivacaine (R) group.	No bradycardia or hypotension observed.	Addition of DMD to ropivacaine prolonged pain-free duration, decreased VAS pain scores, reduced rescue analgesic requirement, prolonged time to first request for analgesia, and improved patient satisfaction without serious side effects in patients undergoing cesarean section.
Ramya *et al*.[23]	70	India	To compare bupivacaine and bupivacaine with DMD for pain relief after cesarean section.	Time at which first dose of rescue analgesia was sought, total dose of opioid requirement in the first 24 hours post-cesarean section	Study (with dex) and Control (without dex) groups	Prolonged duration before seeking the first dose of rescue analgesia and reduced total opioid requirement in the study group (with DMD) compared to the control group (without DMD)	Eight patients from the study group and 15 from the control group required opioids as rescue analgesia.	Addition of DMD to bupivacaine prolonged the duration before seeking the first dose of rescue analgesia and reduced the total opioid requirement in the first 24 hours post-cesarean section.
Serry *et al*.[24]	90	Egypt	To assess and evaluate the effectiveness and safety of DMD and dexamethasone in addition for postoperative analgesia in patients in cesarean section	VAS value, usage of narcotic in the first 12 hours, drowsiness, TFA	Group A (Bupivacaine + normal saline), Group B (Bupivacaine + dexmedetomidine), Group C (Bupivacaine + dexamethasone)	DMD substantially reduces the VAS value, reduces the usage of narcotic in the first 12 hours, increases drowsiness, and extends TFA	Not mentioned	DMD was effective for postoperative analgesia

Contd...

Table 2: Contd...

Study name	Sample size	Region assessed	Objectives	Parameters assessed	Groups assessed	DMD effect observed	Other observations	Inference assessed
Singla *et al*.[25]	100	India	To assess the efficacy of adding DMD or dexamethasone to ropivacaine for postoperative pain relief.	Time to initial self-reporting of postoperative pain, time to first rescue analgesic demand, VAS for pain, hemodynamic parameters	Group A: Ropivacaine + dexamethasone, Group B: Ropivacaine + dexmedetomidine	Prolonged time to initial postoperative pain and time to first rescue analgesic in Group B (dexmedetomidine)	No significant haemodynamic changes or side-effects noted	Addition of DMD to ropivacaine prolongs time to postoperative pain and time to first rescue analgesic consumption.
Thakur *et al*.[26]	120	India	To evaluate the efficacy of DMD as adjuncts to bupivacaine for postoperative analgesia.	VAS pain score, time to demand first analgesic, number of analgesic requirements, nausea or vomiting, sedation, patient satisfaction	Group B: Bupivacaine, Group BDM: Bupivacaine + DMD, Group BDX: Bupivacaine + dexamethasone	Lower VAS score, longer duration of analgesia, lower number of rescue analgesic demands in Group BDM (bupivacaine + DMD)	Higher sedation score and satisfaction in Group BDM	DMD as adjunct to bupivacaine reduced postoperative pain, prolonged analgesia, decreases demand for additional analgesics, and provides better maternal satisfaction compared to plain bupivacaine group.
Varshney *et al*.[27]	90	India	Compare TAP block with levobupivacane with or without DMD with a control group for post-operative analgesia following cesarean delivery	Time for first request for rescue analgesia, number of women requesting analgesia at 6h, 12h and 24h. Pain score using VAS at rest and on movement for the first 24h. Patient comfort and satisfaction with analgesia at the end of 24h	Healthy women undergoing cesarean delivery, split into three groups: Group C (control), Group L (levobupivacane), Group LD (levobupivacane with dexmedetomidine)	Time for first rescue analgesia was significantly longer in group LD compared to group L. Patient satisfaction score was the highest in the Group LD	There were no significant differences in the observed side effects	0.25% levobupivacaine provides good quality analgesia for early postoperative period. Addition of DMD further prolongs the time to first rescue analgesia and improves patient satisfaction

outcomes that cannot be attributed to random chance alone. This could be due to differences in study design, patient population, dosing protocols, or other factors. Therefore, while the overall result favors the DMD group, the high heterogeneity calls for cautious interpretation of these results and suggests the need for further research to confirm these findings.

Statistical findings (in terms of reductions in overall VAS scores)

The forest plot data represented in Figure 4 indicate that the DMD group was better than the control group in terms of reducing pain scores as measured by the VAS. This is supported by the significant overall effect ($Z = 2.37$, $P = 0.02$) and the negative total MD of -1.38 with a 95% CI of -2.52 to -0.24. A negative MD signifies a decrease in VAS scores in the DMD group compared to the control group, implying that DMD was more effective in reducing pain. However, considerable heterogeneity was observed among the studies ($Tau^2 = 1.30$, $Chi^2 = 394.31$, $df = 3$, $P < 0.00001$; $I^2 = 99\%$). This suggests that the differences in outcomes among the studies may not solely be due to chance but could also be due to variations in study design, participant characteristics, or the specific protocols used for administering DMD. While the overall evidence suggests that DMD is more effective in reducing pain scores compared to the controls, the high degree of heterogeneity implies a need for caution in interpreting these results.

Discussion

The findings of our review align with the systematic reviews conducted by Zhang *et al*.[28] and VanderWielen *et al*.[29] on several points, while also demonstrating a few dissimilarities. All reviews explored the effectiveness of regional analgesic techniques in enhancing postoperative pain management.

The study by Zhang *et al*.[28] evaluated the pain management effect of a certain corticosteroid when added to local anesthetics in ultrasound-guided TAP block procedures for

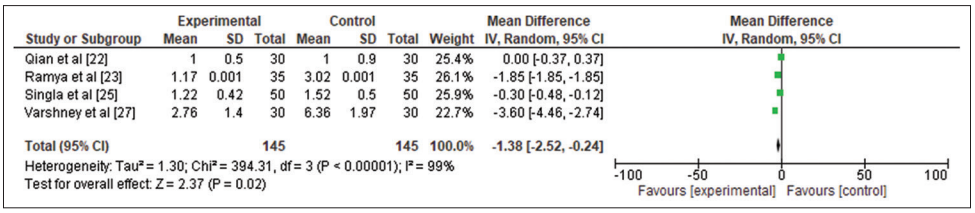

Figure 4: Efficacy of DMD in prolonging time period of analgesia in comparison to controls (in terms of number of VAS scores)

postabdominal surgery patients. However, our study focused on the addition of DMD to local anesthetics used in TAP block procedures, revealing promising outcomes. In particular, we found that DMD managed to extend the duration of analgesia and lowered postoperative VAS scores. This observation is in line with what Zhang *et al*. reported with their corticosteroid; a decrease in VAS scores was noticed at certain intervals post surgery. Moreover, our study found that DMD delayed the patients' first request for additional analgesics and diminished the consumption of opioids over a 24-hour period. This is comparable to the results of Zhang *et al*., suggesting that DMD could be a potent alternative. Notably, Zhang *et al*. reported a significant fall in the incidence of postoperative nausea and vomiting with their corticosteroid. However, our study did not specifically evaluate this outcome with DMD, which presents an opportunity for future research.

VanderWielen *et al*.[29] focused on optimizing postcesarean delivery (CD) analgesia, emphasizing the efficacy of a multimodal approach involving neuraxial opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and rescue oral opioids for breakthrough pain. They indicated that regional nerve block techniques, including TAP block, provide analgesic benefits, especially in cases where intrathecal morphine cannot be used. This aligns with our findings, where we observed that DMD as an adjuvant in TAP block could be an effective component of a multimodal analgesic strategy after CD. However, VanderWielen *et al*. considered quadratus lumborum block (QLB) to be particularly promising in the absence of intrathecal morphine, while our review did not specifically compare the effectiveness of DMD in TAP block versus QLB or other regional nerve block techniques.

Similar to Zhang J *et al*.'s findings,[30] our review found that DMD did not adversely affect neonatal outcomes. Zhang J *et al*. reported no differences in neonatal umbilical blood gases and Apgar scores at 1 and 5 minutes with DMD. In line with this, we also found no significant difference in neonatal outcomes, reinforcing the conclusion that DMD is safe for neonates when used for cesarean delivery. However, while Zhang J *et al*. reported significantly improved postoperative analgesia and lower incidence of adverse events like nausea/vomiting and shivering in mothers after DMD treatment, our review did not specifically focus on these maternal outcomes.

The review by Shen *et al*.[31] aligns with our findings regarding the beneficial effects of DMD as an adjunct for spinal anesthesia. Similar to our review, Shen *et al*. observed that intrathecal DMD reduced the onset time of sensory and motor block and prolonged block duration. They also noted a lower incidence of shivering in patients who received DMD, which parallels findings from Zhang J *et al*.[30] However, Shen *et al*. did not report on the impact of DMD on maternal postoperative analgesia or adverse events, which is a point of divergence from our review and that of Zhang J *et al*.[30]

Lee *et al*.[32] focused on comparing the effects of intravenous DMD and remifentanil on neonatal outcomes during cesarean section under general anesthesia. They found that the Apgar score at 1 minute was lower in the remifentanil group compared to the DMD group, but there were no differences in the Apgar score at 5 minutes or in the incidence of mask ventilation, intubation, or pH values of the umbilical artery and vein. This again supports the safety of DMD for neonates. However, our review did not include a comparison of DMD with remifentanil, representing a difference in study focus.

Abdallah *et al*.[14] acknowledged the controversy surrounding the utility of ultrasound (US)-guided TAP block in cesarean section but concluded that when executed correctly, TAP block may reduce postoperative opioid consumption and related side effects, thereby improving pain control and patient satisfaction. This aligns with our findings, where we observed that the addition of DMD to local anesthetics in TAP block extended the duration of analgesia and reduced VAS scores for postoperative pain.

On the other hand, Fusco *et al*.[15] took a slightly different approach in their review, focusing on the reduction of intravenous (IV) morphine consumption in the first 24 hours after CD. They found that TAP block reduced 24-hour IV morphine consumption by 24 mg and decreased VAS pain scores by 0.8 cm, but these differences were not significant when spinal morphine was used. Our review, however, did not specifically compare the effectiveness of DMD in TAP

block versus systemic or spinal opioids, making a direct comparison challenging.

Despite the similarities, there were also some differences between our findings and those of Abdallah *et al*.[14] and Fusco *et al*.[15] While all reviews agreed on the potential benefits of TAP block, the focus on DMD as an adjuvant in our review differed from the broader scope of the two other reviews, which did not specify the type of adjuvant used. Furthermore, Fusco *et al*.[15] found that the benefits of TAP block were not significant when spinal morphine was used, suggesting that the type of analgesic regimen may impact the effectiveness of TAP block. Our review did not analyze the impacts of different analgesic regimens on the effectiveness of DMD in TAP block, indicating a potential area for further research.

In the context of perioperative care, DMD has increasingly been employed as an adjunctive agent in subarachnoid block anaesthesia procedures.[33-35] A preceding meta-analytic study by Obayah *et al*.[17] held the view that the introduction of DMD could notably expedite the commencement of spinal anaesthesia. However, a couple of trials[16,36] incorporated in this analysis failed to meet the selection parameters due to the simultaneous implementation of spinal and epidural anesthesia. Moreover, this analysis only encompassed studies published in the English language and did not manifest the safety of DMD for neonates. Also, the impact of DMD on the persistence of local anesthetics remained unexplored. This situation underscored the necessity for our review undertaking.

In a separate study,[37] it was advocated that DMD surpassed fentanyl as an intrathecal adjunct in mitigating visceral pain and extending postsurgical analgesic effects. A number of research findings propose that DMD triggers vasoconstriction by interacting with the α2-adrenergic receptor, consequently extending the analgesic duration,[38,39] while another paper[40] posited that DMD directly modulates its efficiency through the α2-adrenergic receptor.

Shivering subsequent to spinal anesthesia is a routinely observed perioperative complication. Multiple studies have substantiated that DMD suppresses shivering effects via α2-adrenergic receptors, which are ubiquitously spread in the hypothalamus, thereby inhibiting thermoregulation.[41] Some research pieces validate that DMD directly augments the temperature threshold independent of thermoregulatory defenses, thereby curbing the incidence of shivering.[42,43]

Despite the promising findings, this analysis was not without its limitations. One of the most significant issues was the use of different local anesthetics, namely, ropivacaine, bupivacaine, and levobupivacaine, in combination with DMD across the studies may have also influenced the outcomes.[20-27] The pharmacokinetic and pharmacodynamic properties of these anesthetics differ, and the impact of DMD may vary depending on the specific anesthetic used. Therefore, it is difficult to draw a definitive conclusion about the effect of DMD as an adjuvant in TAP blocks without considering the specific local anesthetic used. Moreover, the side effect profiles of DMD were not comprehensively reported or examined in all studies. While one study reported increased drowsiness as a side effect of DMD,[24] other potential adverse effects were not thoroughly investigated. This limits our understanding of the safety and tolerability of DMD, which is an essential aspect of its clinical utility.

Conclusion

The collated results suggested that the addition of DMD to ropivacaine, bupivacaine, or levobupivacaine could enhance the analgesic effect, as evidenced by the prolonged time to initial onset of pain and time to first rescue analgesia. The analysis further indicated beneficial effects of DMD in reducing VAS pain scores, decreasing the number of patients requiring rescue analgesics, extending the time to first request for analgesia, and augmenting patient satisfaction. Additionally, the potential opioid-sparing effect of DMD was highlighted by the reduction in total opioid requirement. However, the analysis also revealed significant heterogeneity among the studies and potential side effects of DMD, such as increased drowsiness. These findings underscore the need for further large-scale studies to not only validate these results but also investigate the safety profile and potential adverse effects of DMD.

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Conflicts of interest
There are no conflicts of interest.

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