OPEN

Dexmedetomidine as an Adjuvant to Local Anesthetics in Transversus Abdominis Plane Block

A Systematic Review and Meta-analysis

Qianchuang Sun, MD, Shuyan Liu, MD,† Huiying Wu, PhD,‡ He Ma, MD,* Wei Liu, MD,* Meidan Fang, MD,* Kexiang Liu, PhD,§ and Zhenxiang Pan, MD**

Objectives: The objective of this meta-analysis was to evaluate the analgesic effects of dexmedetomidine (DEX) in transversus abdominis plane (TAP) blocks for abdominal surgery.

Methods: Electronic databases, including PubMed, EMBASE, Chinese National Knowledge Infrastructure (CNKI), Wan Fang, and the Cochrane Library, were conducted to collect the randomized controlled trials (RCTs) from inception to March 2018. RCTs investigating the impact of adding DEX to local anesthetics for TAP blocks were included in this analysis. Pain scores (at rest and movement), opioid consumption, the duration of the TAP block and the common adverse effects were analyzed.

Results: Twenty published trials including 1212 patients met the inclusion criteria. The addition of DEX significantly reduced pain scores 8 hours postoperatively at rest (WMD, −0.78; 95% CI, −1.27 to −0.30; $P = 0.001$), 4 hours postoperatively on movement (WMD, −1.13; 95% CI, −1.65 to −0.60; $P < 0.001$), and opioid consumption (WMD, −13.71; 95% CI, −17.83 to −9.60; $P < 0.001$) when compared with control group. Furthermore, perineural DEX significantly prolonged the duration of the TAP block (WMD, 3.33; 95% CI, 2.85 to 3.82; $P < 0.001$). It did not affect the incidence of postoperative nausea and vomiting, hypotension, bradycardia, somnolence, or pruritus.

Conclusions: DEX is a potential anesthetic adjuvant that can facilitate better postoperative analgesia, reduce postoperative analgesic requirements, and prolong the local anesthetic effect when administered in TAP blocks.

Key Words: transversus abdominis plane block, ropivacaine, bupivacaine, meta-analysis

(*Clin J Pain* 2019;35:375–384)

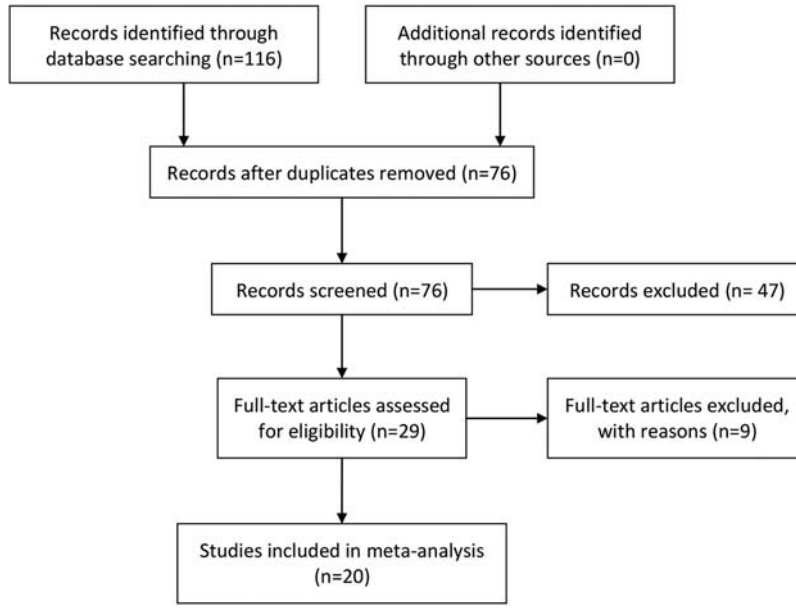

FIGURE 1. Flow chart of the review process.

Received for publication August 1, 2018; revised October 22, 2018; accepted November 11, 2018.
From the Department of *Anesthesiology; †Ophthalmology; ‡Ultrasonic Diagnosis; and §Cardiovascular Surgery, The Second Hospital of Jilin University, Changchun, China.
Supported by the grant from Jilin provincial finance department of China (201715603525).
The authors declare no conflict of interest.
Reprints: Kexiang Liu, PhD, Department of Cardiovascular Surgery and Zhenxiang Pan, MD, Department of Anesthesiology, The Second Hospital of Jilin University, Changchun 130041, China (e-mails: kexliu64@163.com; pzx6701@sohu.com).
Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website, www.clinicalpain.com.

DOI: 10.1097/AJP.0000000000000671

TABLE 1. Characteristics of the Included Studies

Reference	Country	Surgery	n	Anesthesia	Treatment (Unilateral Dosage)	Postoperative Analgesia	Main Outcomes
Nie et al[35]	China	Cesarean delivery	30 30 30	Spinal	1. DEX 1 μg/kg + 0.2% ropivacaine to 20 mL 2. 0.2% ropivacaine 20 mL 3. Saline 20 mL	Sufentanil PCA	VAS pain scores and sufentanil consumption at 6, 12, 24 & 48 h, PONV, pruritus
Hu & Xiao[17]	China	Hysterectomy	30 30	GA	1. DEX 0.5 μg/kg + 0.25% levobupivacaine to 20 mL 2. 0.25% levobupivacaine 20 mL	Sufentanil PCA	VAS pain scores at 1, 4, 8, 12, 24 h, 24 h sufentanil consumption, the duration of analgesia, PONV, hypotension, bradycardia
Zhai et al[25]	China	Kidney transplantation	20 20	GA	1. DEX 1 μg/kg + 0.375% ropivacaine to 20 mL 2. 0.375% ropivacaine 20 mL	Sufentanil and dezocine PCA	VAS pain scores (rest & movement) at 2, 4, 8, 24 & 48 h, time to first analgesia, the duration of sensory blockade, 24 h sufentanil and dezocine consumption, sedation
Li et al[18]	China	Inguinal hernia surgery	20 20	GA	1. DEX 0.5 μg/kg + 0.2% ropivacaine to 20 mL 2. 0.2% ropivacaine 20 mL	Tramadol	VAS pain scores (rest & movement) at 1, 3, 6, 12 & 18 h, tramadol consumption at 1, 3, 6, 12 h
Zhou et al[26]	China	Laparoscopic colon cancer surgery	20 20	GA	1. DEX 1 μg/kg + 0.25% ropivacaine to 20 mL 2. 0.25% ropivacaine 20 mL	Sufentanil PCA	VAS pain scores (rest & coughing) at 2, 6, 12, 24 & 48 h, time to first analgesia, the duration of sensory blockade, 24 h sufentanil consumption, sedation
Fang et al[27]	China	Hysterectomy	30 30	GA	1. DEX 1 μg/kg + 0.25% ropivacaine to 20 mL 2. 0.25% ropivacaine 20 mL	Sufentanil PCA	VAS pain scores (rest & coughing) at 2, 4, 8, 12, & 24 h, 24 h sufentanil consumption, sedation, PONV
Lan & Wang[28]	China	Hysterectomy	30 30	GA	1. DEX 1 μg/kg + 0.25% ropivacaine to 20 mL 2. 0.25% ropivacaine 20 mL	Fentanyl PCA	VAS pain scores (rest & movement) at 2, 6, 12, 24 & 48 h, 24 & 48 h sufentanil consumption, sedation, PONV
Ding et al[29]	China	Gastrectomy	30 30 31	GA	1. DEX 1 μg/kg + 0.33% ropivacaine to 15 mL 2. 0.33% ropivacaine 15 mL 3. Saline 15 mL	Tramadol	VAS pain scores (rest & movement) at 2, 4, 12 & 24 h, 36 h tramadol consumption, PONV
Luan et al[30]	China	Abdominal hysterectomy	25 25	GA	1. 2 mL DEX (0.5 μg/kg) + 0.3% ropivacaine 20 mL to 22 mL 2. 0.3% ropivacaine 20 mL + 2 mL saline to 22 mL	Sufentanil PCA	VAS pain scores at 2, 4, 6, 8, 12 & 24 h, 24 h sufentanil consumption, PONV
Xiao et al[19]	China	Abdominal hysterectomy	30 30	GA	1. DEX 0.5 μg/kg + 0.25% levobupivacaine to 20 mL 2. 0.25% levobupivacaine 20 mL	Sufentanil PCA	VAS pain scores at 1, 4, 8, 12 & 24 h, 24 h sufentanil consumption, the duration of analgesia, sedation
Aksu et al[31]	Turkey	Lower abdominal surgery	31 31 31	GA	1. 1 mL DEX (100 μg) + 0.5% bupivacaine 20 mL to 21 mL 2. 0.5% bupivacaine 15 mL + 1 mL saline to 21 mL 3. Saline 21 mL	Morphine PCA	VAS pain scores at 0, 2, 6, 8, 10, 12 & 18, morphine consumption at 2, 6, 12, 18 & 24 h, PONV
Ramya & Udayakumar[33]	India	Cesarean section	35 35	Spinal	1. DEX 0.5 μg/kg + 0.25% bupivacaine to 20 mL 2. 0.25% bupivacaine 20 mL	Paracetamol, Tramadol	VAS pain scores (rest & movement) at 1, 2, 4, 8, 12, 18 & 24, 24 tramadol consumption, time to first rescue analgesia, sedation, PONV
Almarakbi & Kaki[20]	Saudi Arabia	Abdominal hysterectomy	25 25	GA	1. 2 mL DEX (0.5 μg/kg) + 0.2% bupivacaine 20 mL to 22 mL 2. 0.2% bupivacaine 20 mL + 2 mL saline to 22 mL	Morphine PCA	VAS pain scores (rest & coughing) at 1, 4, 8, 12, 18 & 24 h, time to first analgesia, 24 h morphine consumption, PONV
Mishra et al[21]	Saudi Arabia	Abdominal hysterectomy	25 25	GA	1. 2 mL DEX (0.5 μg/kg) + 0.2% bupivacaine 20 mL to 22 mL 2. 0.2% bupivacaine 20 mL + 2 mL saline to 22 mL	Tramadol	VAS pain scores (rest & coughing) at 1, 3, 6, 12 & 18 h, PONV

(*Continued*)

TABLE 1. (*continued*)

Reference	Country	Surgery	n	Anesthesia	Treatment (Unilateral Dosage)	Postoperative Analgesia	Main Outcomes
Zhou et al[22]	China	Laparoscopic Radical Operation	30 30 30 30	GA	1. DEX 0.5 μg/kg + 0.25% ropivacaine to 15 mL 2. DEX 0.75 μg/kg + 0.25% ropivacaine to 15 mL 3. DEX 1 μg/kg + 0.25% ropivacaine to 15 mL 4. 0.25% ropivacaine 15 mL	Tramadol	VAS pain scores at 1, 6, 12, 24 & 48 h, Tramadol consumption, PONV
Wu et al[36]	China	Gynecological laparotomy	30 30 30	GA	1. DEX (0.75 μg/kg) + 0.4% ropivacaine to 15 mL 2. 0.4% ropivacaine 15 mL 3. Saline 15 mL	Dezocine and flurbiprofen PCA	VAS pain scores at 8, 12, 24 h, PONV
Zhang et al[34]	China	Laparoscopic hernia repair	30 30	GA	1. DEX (0.75 μg/kg) + 0.4% ropivacaine to 15 mL 2. 0.4% ropivacaine 15 mL	No	VAS pain scores (rest & coughing) at 0, 4, 6, 8, 12, 24 h, the duration of analgesia, PONV
Lang et al[32]	China	Gynecological surgery	30 30	GA	1. DEX (75 μg) + 0.375% ropivacaine to 10 mL 2. 0.375% ropivacaine 10 mL	No	VAS pain scores (rest & coughing) at 2, 4, 6, 12 & 24 h, the duration of analgesia, PONV
Chen et al[23]	China	Cesarean section	40 40 40	GA	1. DEX 0.5 μg/kg + 0.67% ropivacaine to 15 mL 2. DEX 1.0 μg/kg + 0.67% ropivacaine to 15 mL 3. 0.67% ropivacaine 15 mL	Tramadol	VAS pain scores at 1, 4, 8, 12, 24 h, additional analgesia, PONV
Sinha et al[24]	India	Endoscopic hernia repair	15 15	GA	1. DEX 0.5 μg/kg + 0.375% ropivacaine to 10 mL 2. 0.375% ropivacaine to 10 mL	Paracetamol, diclofenac, Tramazac hydrochloride	VAS pain scores at 1, 3, 6, 12, 24 h, PONV

DEX indicates dexmedetomidine; GA, general anesthesia; n, number of patients; PCA, patient-controlled analgesia; PONV, postoperative nausea and vomiting; VAS, visual analogue scale.

The transversus abdominis plane (TAP) block was first applied to abdominal surgery by Rafi[1] in 2001. The local anesthetic (LA) was injected between the internal oblique muscle and the transversus abdominis from the side of the abdomen to block the T7-L1 spinal nerve ventral branches, which improved postoperative analgesia after abdominal surgery.

Systemic dexmedetomidine (DEX) produces sedative, analgesic, sympatholytic, and anesthetic-sparing effects.[2] Recently, DEX as a local anesthetic adjuvant has been the subject of increasing interest as the potential to prolong blockade duration.[3–5] The combined use of a local anesthetic agent and DEX, applied in a TAP block, which targets peripheral nociceptive receptors may be an ideal protocol for pain control after abdominal surgery.

Some meta-analyses indicated that perineural DEX can prolong the durations of sensory block and motor block as well as analgesia when administered in brachial plexus block.[5–8] Unlike brachial plexus block, TAP block is a nondermatomal "field block," which requires a large volume of anesthetics to cover several spinal nerves.[9] To the authors' knowledge, there are no published meta-analyses investigating the effect of DEX as an adjuvant in TAP blocks on postoperative pain. This study was designed to determine the effect of DEX as a local anesthetic adjuvant in TAP blocks.

MATERIALS AND METHODS

Studies were performed in accordance with the PRISMA protocol[10] (Supplementary Table S1, Supplemental Digital Content 1, http://links.lww.com/CJP/A535).

Study Search Strategy

Two authors (QCS, SYL) independently searched the international databases (PubMed, EMBASE, and the Cochrane Library) and 2 Chinese databases (CNKI and Wan-Fang database) from inception to March 2018. Medical subject headings and text words of "dexmedetomidine" and "transversus abdominis plane block or TAP block" were used for databases searching. The details of the search strategies are summarized in Supplementary Table S2 (Supplemental Digital Content 2, http://links.lww.com/CJP/A536). No language restrictions were applied. In order to avoid omitting relevant clinical trials, we scanned conference summaries and reference lists of articles identified in the initial searches and contacted authors to obtain additional information for relevant trials.

Inclusion and Exclusion Criteria

Inclusion criteria were: (1) the study was a RCT; (2) adult patients undergoing abdominal surgery; (3) the test group was treated with TAP blocks using any LA agent combined with DEX, whereas the control group received LA agent alone; (4) outcomes: pain scores (at rest and movement), opioid consumption, the duration of analgesia, and incidence of postoperative nausea and vomiting (PONV), hypotension, bradycardia, somnolence, or pruritus.

Exclusion criteria were: (1) study designs other than a RCT; (2) reviews, letters, abstracts, editorials or studies that reported insufficient data; (3) DEX administered through nonperineural route. There were three disagreements about study selection were resolved by group discussion and consensus.

Data Extraction

Two reviewers independently extracted data from all included studies. The mean value and variance were for continuous variables, while proportions were for dichotomous outcomes. If data were presented as sample size, median, range or interquartile range, the author of the trial was contacted to inquire if they could provide raw data. Failing that, we used formulas to estimate the mean and standard deviation.[11,12] Extracted data included first author, publication year, country, sample size, type of anesthesia, postoperative analgesia, and outcome measures. Pain scores (at rest and movement) were defined as primary outcome measures. Pain scores presented as

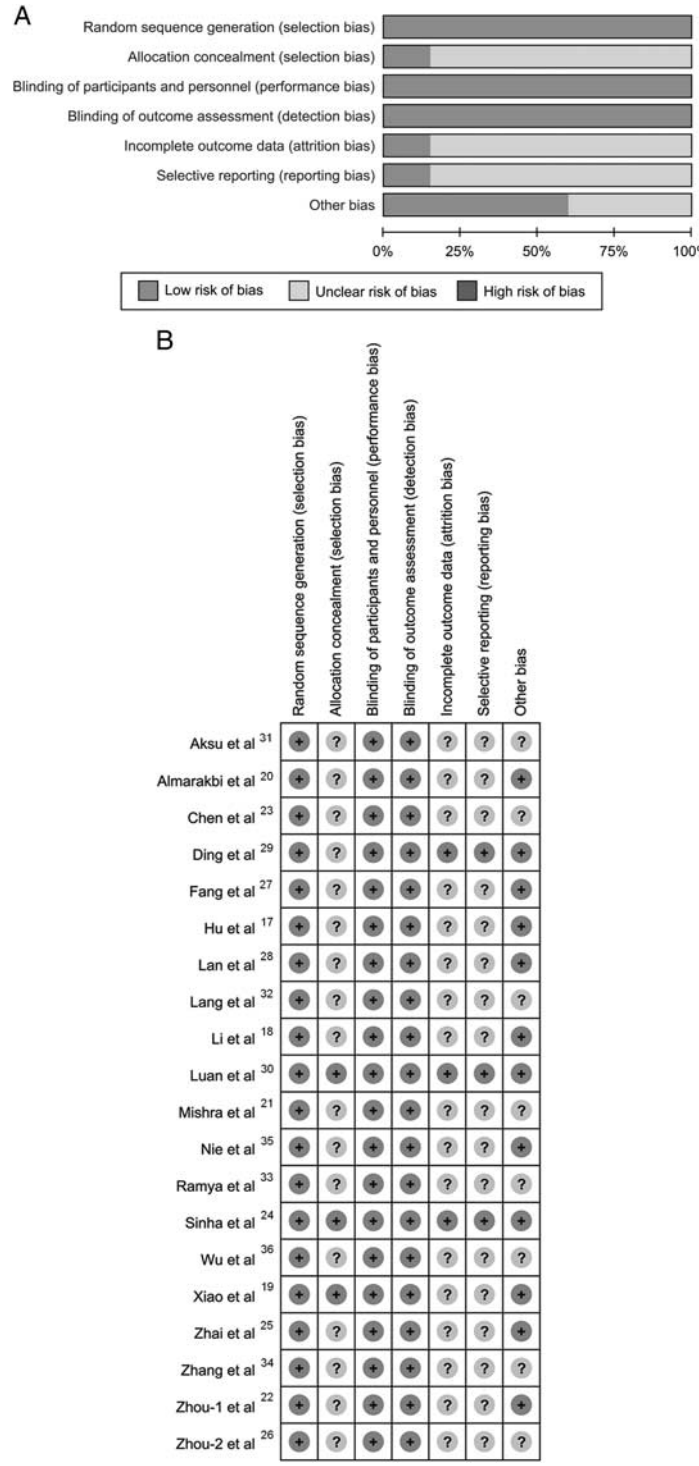

FIGURE 2. Risk of bias assessment. A, Risk of bias graph; B, Risk of bias summary.

TABLE 2. Pain Scores at Rest and on Movement at 7 Different Time Points for the Comparison of DEX Group and Control Group

Outcomes	Studies Included	DEX (n)	Control (n)	Estimated Benefit, WMD (95% CI)	*P*	I^2 test (%)
Pain at rest						
1 h postoperative	11-18,	315	215	−0.26 (−0.47, −0.057)	0.012	86.5
2 h postoperative	18-26	216	216	−0.33 (−0.83, 0.16)	0.19	92.5
4 h postoperative	11, 13-14, 17, 19, 21, 23, 24, 26-28	365	325	−0.53 (−1.24, 0.18)	0.15	99.0
6 h postoperative	12, 15, 16, 26, 28, 29	316	256	−0.65 (−0.94, −0.35)	< 0.001	84.3
8 h postoperative	11, 14, 17, 19, 21, 24, 25, 27, 28, 30	336	296	−0.78 (−1.27, −0.30)	0.001	97.8
12 h postoperative	11-13, 15, 16, 18, 20-28, 30	576	476	−0.58 (−0.80, −0.36)	< 0.001	90.2
24 h postoperative	11, 13, 16, 18-28, 30	611	511	−0.47 (−0.77, −0.16)	0.003	94.3
Pain on movement						
1 h postoperative	12, 14, 18	60	60	−0.008 (−0.11, 0.098)	0.88	0.0
2 h postoperative	19-26	130	130	−0.78 (−1.55, −0.015)	0.046	93.0
4 h postoperative	14, 19-23, 27	190	190	−1.13 (−1.65, −0.60)	< 0.001	90.2
6 h postoperative	12, 16, 18, 22	85	85	−0.94 (−1.87, −0.005)	0.049	89.7
8 h postoperative	14, 17, 19, 21	110	110	−0.73 (−1.50, 0.044)	0.065	96.3
12 h postoperative	12, 14, 17, 18, 20-23	205	205	−0.53 (−0.83, −0.23)	< 0.001	78.5
24 h postoperative	14, 17-23	205	205	−0.55 (−1.10, −0.007)	0.047	91.2

CI indicates confidence interval; DEX, dexmedetomidine; n, number of patients; RR, risk ratio; WMD, weighted mean difference.

a visual analog scale (VAS), where 0 = no pain and 10 = the most severe pain. Secondary outcomes were cumulative opioid consumption, the duration of analgesia and incidence of PONV, hypotension, bradycardia, somnolence, or pruritus. Using a published equivalence formula, cumulative opioid consumption, with opioid drugs other than morphine, was converted to morphine equivalent doses, where intravenous (i.v.) morphine 10 mg = i.v. sufentanil 10 μg = i.v. tramadol 100 mg = i.v. fentanyl 0.1 mg.[13,14] There were two disagreements were resolved by discussion.

Assessment of Quality and Bias

To determine the quality of the included studies, risk of assessment was performed, according to the Cochrane Collaboration's tool.[15] Seven evidence-based domains were evaluated: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; (7) other bias. Each of these domains was judged as low risk, high risk or unclear risk.

For the assessment of publication bias, both Begg's rank correlation and Egger's linear regression tests were performed.[10]

Statistical Analysis

All statistical analyses were performed in Stata 14.0 (Stata Corp, College Station, TX) and Review Manager 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2014). Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated for dichotomous data, and weighted mean differences (WMDs) with 95% CIs were calculated for continuous variables. Heterogeneity was measured by I^2, with $I^2 > 50\%$ indicating significant heterogeneity. If $I^2 < 50\%$, the fixed effects model was used; if $I^2 > 50\%$, a

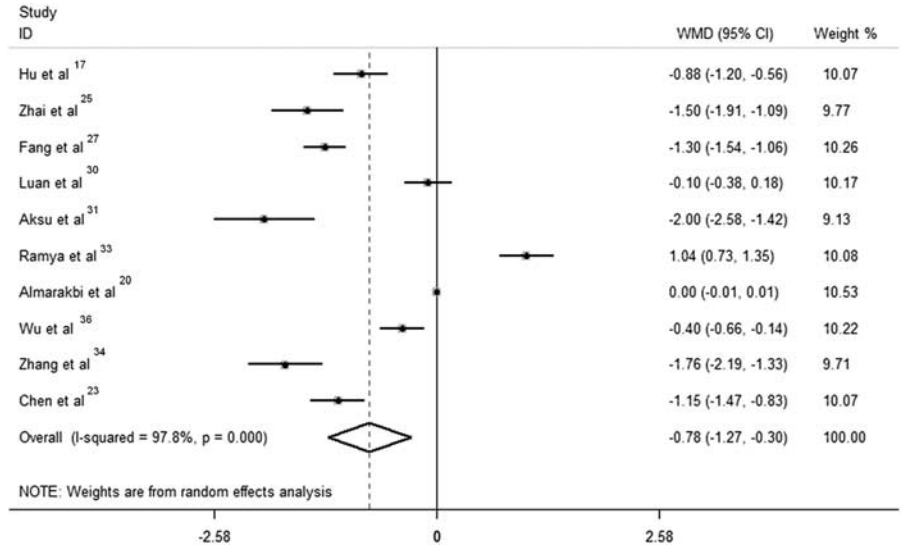

FIGURE 3. DEX versus control group: a forest plot of pain scores 8 hours postoperatively at rest. CI indicates confidence interval; DEX, dexmedetomidine; WMD, weighted mean difference.

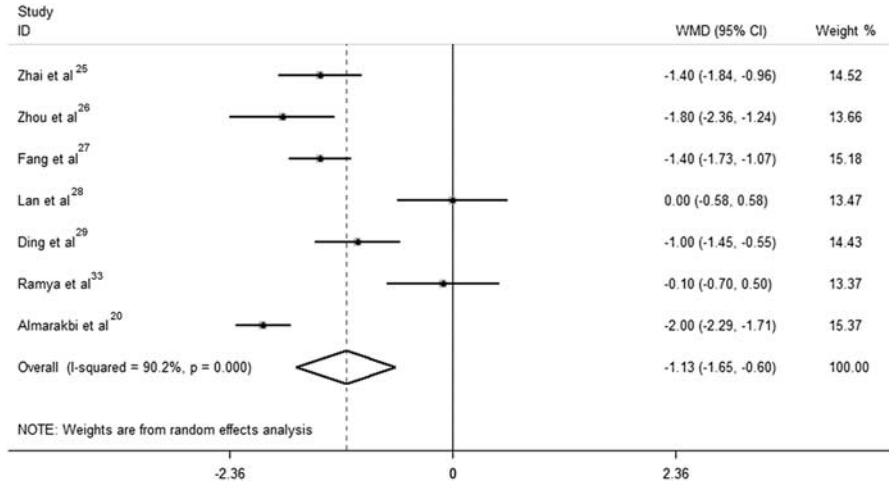

FIGURE 4. DEX versus control group: a forest plot of pain scores 4 hours postoperatively on movement. CI indicates confidence interval; DEX, dexmedetomidine; WMD, weighted mean difference.

random effects model was used, and the heterogeneity was assessed. Subgroup analyses were performed for the outcome measures, according to surgery types (open surgery or laparoscopic surgery) and anesthesia (general anesthesia or spinal). Furthermore, meta-regression was used to explore the origin of heterogeneity, such as postoperative patient-controlled analgesia (PCA, yes or no), LA types (ropivacaine, bupivacaine or levobupivacaine), surgery types, DEX doses (<1 μg/kg or ≥ 11 μg/kg) and anesthesia. Sensitivity analyses were performed by excluding one study each time to evaluate the influence of a single study on the overall estimate.[16]

RESULTS

In total, 116 articles were initially identified from the electronic search. Of these, 40 were excluded due to duplication; 47 were further excluded after screening the titles and abstracts. By reading the full text of the remaining 29 articles, 9 studies were excluded because they failed to meet the inclusion criteria. Ultimately, 20 eligible studies involving 1212 participants were included in this meta-analysis.[17–36] The search process is provided in Figure 1.

The characteristics of the included studies are shown in Table 1. Eighteen trials performed general anesthesia, while spinal anesthesia was used in 2 trials; 16 trials underwent open surgery, whereas 4 trials received laparoscopic surgery. Ropivacaine was used in 14 trials as the local anesthetic, while 4 trials used bupivacaine, and 2 others used levobupivacaine. The DEX dosage was various, with 1 μg/kg in 6 studies, 0.5 μg/kg in 8 studies, 0.75 μg/kg in 3 studies, 100 μg in 1 study, 2 doses in one study, and 3 doses in one study. Eleven studies received postoperative PCA (7 studies with PCA sufentanil, 2 studies with PCA morphine, 1 study with PCA fentanyl, and 1 study with PCA dezocine and flurbiprofen). Pain scores were reported in all included trials.

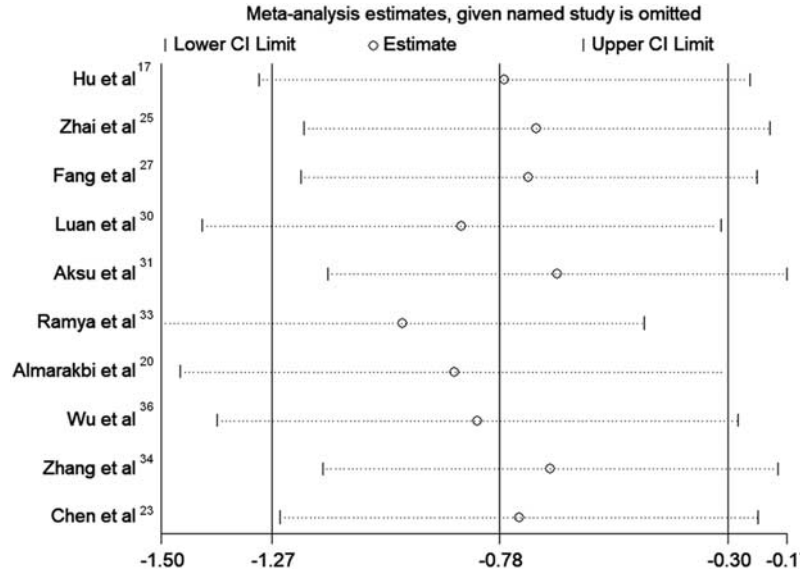

FIGURE 5. DEX versus control group: the sensitivity analysis of pain scores 8 hours postoperatively at rest. CI indicates confidence interval; DEX, dexmedetomidine.

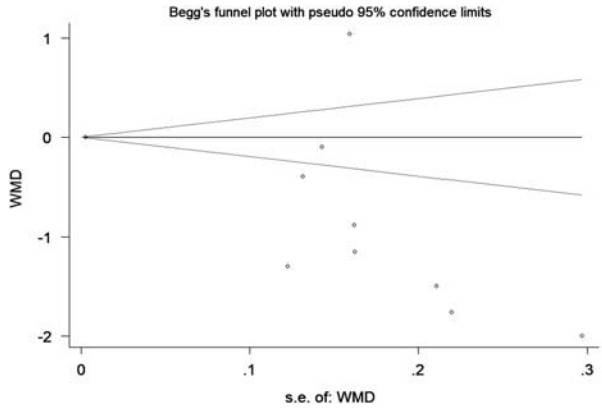

FIGURE 6. DEX versus control group: the Begg's funnel plot of pain scores 8 hours postoperatively at rest. DEX indicates dexmedetomidine; WMD, weighted mean difference.

Eleven studies reported pain scores at rest, whereas the other 9 reported pain scores at rest and on movement. The risk assessment of the included studies is presented in Figure 2.

The primary outcomes of pain scores at rest and on movement at 7 different time points are summarized in Table 2. Pooled analysis demonstrated significantly lower pain scores (WMD, −0.78; 95% CI, −1.27 to −0.30; $P=0.001$) 8 hours postoperatively at rest and 4 hours postoperatively on movement (WMD, −1.13; 95% CI, −1.65 to −0.60; $P<0.001$) in patients treated with combination of DEX and local anesthetic compared with local anesthetic alone (Figs. 3, 4). This statistically significant effect was also seen at 1, 6, 12, and 24 hours postoperatively at rest and at 2, 6, 12, and 24 hours postoperatively on movement. Meta-regression revealed that anesthesia ($P=0.027$) was associated with the significant heterogeneity 8 hours postoperatively at rest, while postoperative PCA ($P=0.29$), LA types ($P=0.45$), DEX doses ($P=0.077$) and surgery types ($P=0.393$) did not contribute to the heterogeneity. Sensitivity analysis was typically performed to check the robustness of these results, with pooled WMDs ranging from −0.50 (95% CI, −0.71 to −0.30) to −0.63 (95% CI, −0.85 to −0.40) (Fig. 5). Begg's funnel plot ($P = 0.152$, Fig. 6) showed no evidence of publication bias, however, Egger's test ($P=0.025$) indicated publication bias. The reasons of different statistical significance between these 2 test methods might derive from the small size of this study or the amount of included studies.

Twelve trials provided opioid consumption data at 24 hours. Pooled data found a statistically significant lower opioid consumption (WMD, −13.71; 95% CI, −17.83 to −9.60; $P<0.001$) in patients treated with combination of DEX and local anesthetic compared with local anesthetic alone (Fig. 7). Meta-regression showed that surgery types ($P<0.001$) were associated with the significant heterogeneity, whereas postoperative PCA ($P=0.27$), LA types ($P=0.51$), DEX doses ($P=0.60$) and anesthesia ($P=0.28$) did not contribute to the heterogeneity. Sensitivity analysis was typically performed to check the robustness of these results, with pooled WMDs ranging from −10.73 (95% CI, −14.90 to −71.68) to −15.14 (95% CI, −19.62 to −10.67). Begg's funnel plot ($P=0.41$) and Egger's test ($P=0.076$) showed no evidence of publication bias.

The duration of the TAP block was provided in 8 of the 20 included trials. Pooled results showed that DEX prolonged the block duration (WMD, 3.33; 95% CI, 2.85 to 3.82; $P<0.001$) (Fig. 8). Meta-regression showed that anesthesia ($P=0.013$) was associated with the significant heterogeneity, while surgery types ($P=0.68$), postoperative PCA ($P=0.34$), LA types ($P=0.25$) and DEX doses ($P=0.48$) did not contribute to the heterogeneity. Sensitivity analysis was typically performed to check the robustness of these results, with pooled WMDs ranging from 3.13 (95% CI, 2.74 to 3.53) to 3.49 (95% CI, 3.01 to 3.96). Begg's funnel plot ($P=0.9$) and Egger's test ($P=0.52$) showed no evidence of publication bias.

For adverse events, pooled analysis showed no difference in the incidence of PONV, hypotension, bradycardia, somnolence, hypotension, and pruritus between DEX and the control group (Table 3).

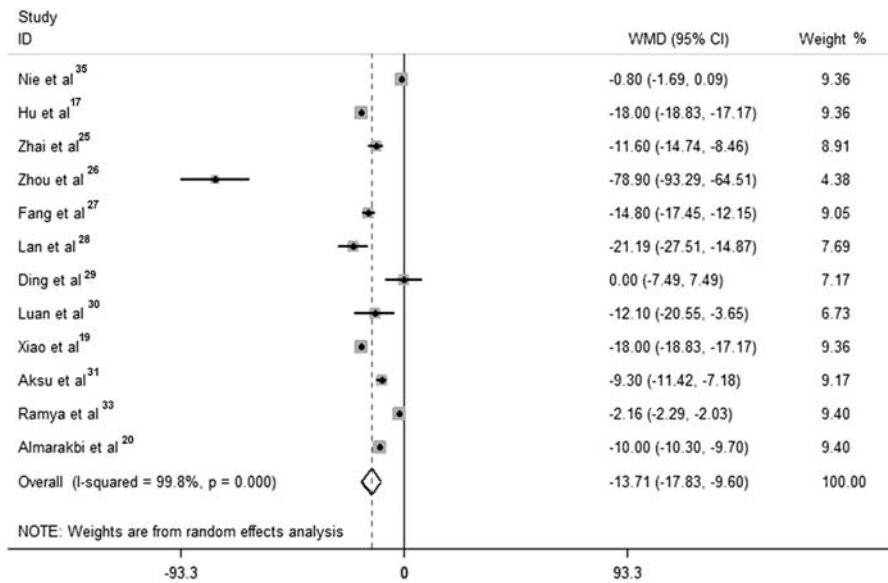

FIGURE 7. DEX versus control group: a forest plot of morphine equivalents 24 hours postoperatively. CI indicates confidence interval; DEX, dexmedetomidine; WMD, weighted mean difference.

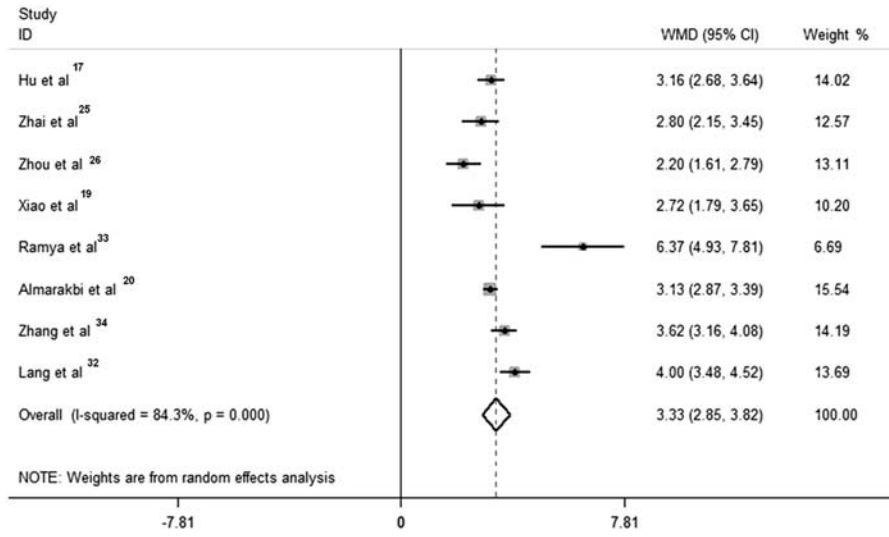

FIGURE 8. DEX versus control group: a forest plot of the duration of analgesia. CI indicates confidence interval; DEX, dexmedetomidine; WMD, weighted mean difference.

Subgroup analyses are shown in Table 4. Use of surgery and anesthesia types was performed to identify the origin of heterogeneity.

DISCUSSION

This meta-analysis demonstrated that DEX as a local anesthetic adjuvant on TAP block not only significantly reduced postoperative pain and opioid consumption but also prolonged the sensory block in patients undergoing abdominal surgery. There was no difference in the incidence of PONV, hypotension, bradycardia, somnolence, or pruritus between the DEX and control groups.

Postoperative pain remains a challenge worldwide. Inadequate treatment of pain can lead to patient anxiety, stress, extended hospital stays and dissatisfaction.[37–39] Much attention has been paid to management of acute postoperative pain in recent years. The TAP block is a regional anesthetic technique that provides postoperative analgesia for abdominal surgery.[40] The pooled results from our meta-analysis showed that DEX treatment reduced VAS pain scores by 0.78 points 8 hours postoperatively at rest and 1.13 points 4 hours postoperatively on movement. The lower pain scores can allow earlier ambulation after surgery and promote the satisfaction of analgesia of the patient. Meanwhile, opioid consumption was 13.71 mg lower in the DEX treatment group. Moreover, perineural DEX extended the duration of the TAP block by 3.33 hours compared with the control group.

Several recent studies demonstrated that DEX as potential LA adjuvant facilitates better and longer analgesia.[41–43] The spinal and peripheral analgesic mechanisms of DEX could be contributed to its highly selective affinity to alpha-2 adrenergic receptor (α2AR).[44] Similar to clonidine, DEX has an effect on presynaptic neuronal receptors and reduces norepinephrine release at peripheral afferent nociceptors.[45] Furthermore, some evidence indicated that DEX played an inhibitory role in delayed rectifier K+ current and Na+ current, which resulted in a reduction in neuronal activity.[46] Another study showed that adding DEX to ropivacaine increased the duration of analgesia by blocking the hyperpolarization-activated cation current.[4] Our results were consistent with some recent meta-analyses that DEX as an adjuvant could prolong the duration of brachial plexus block.[3–5] Currently, the safety of the perineural administration of DEX has received increased attention. In our study, DEX did not increase the incidence of hypotension or bradycardia. The low incidence of adverse events may be due to small dose of DEX administered.

Our study is the first to use meta-analysis to invest the effect of DEX as an adjuvant in TAP blocks on postoperative pain. However, there were several limitations of this meta-analysis. First, high heterogeneity was found in some outcome measures. Although subgroup and sensitivity analyses failed to change the heterogeneity, meta-regression indicated that anesthesia and surgery types were associated with the significant heterogeneity. Second, our study might be influenced by publication bias (Begg's funnel plot and Egger's test).

TABLE 3. The Incidences of Adverse Events

Adverse Events	No. Trial (Patients)	No. DEX Group/Total (%)	No. Control Group/Total (%)	RR (95% CI)	*P*	I^2 test (%)
PONV	11 (752)	42/381 (11.02)	58/341 (17.00)	0.70 (0.49-1.01)	0.053	7.5
Bradycardia	3 (240)	11/150 (0.073)	8/90 (0.089)	1.12 (0.24-5.79)	0.83	53.7
Somnolence	6 (480)	4/290 (0.014)	1/190 (0.0052)	1.87 (0.29-11.94)	0.51	0
Hypotension	2 (120)	7/60 (0.12)	8/60 (0.13)	0.86 (0.34-2.26)	0.78	0
Pruritus	4 (360)	3/230 (0.013)	1/130 (0.0076)	1.00 (0.11-9.26)	1.00	0

CI indicates confidence interval; DEX, dexmedetomidine; PONV, postoperative nausea and vomiting; RR, risk ratio.

TABLE 4. Subgroup Analyses

Subgroups	No. Studies	WMD (95% CI)	*P*	I^2 test (%)
Pain score 8 h postoperatively at rest				
Surgery types				
Open surgery	9	−0.68 (−1.16 to −0.20)	<0.001	97.6
Laparoscopic surgery	1	−1.76 (−2.19 to −1.33)	Not applicable	
Anesthesia				
GA	9	−0.99 (−1.50 to −0.48)	<0.001	97.8
Spinal	1	1.04 (−0.73 to −1.35)	Not applicable	
The duration of the TAP block				
Surgery types				
Open surgery	6	3.48 (2.91 to 4.05)	<0.001	83.3
Laparoscopic surgery	2	2.92 (1.53 to 4.31)	<0.001	92.8
Anesthesia				
GA	7	3.13 (2.74 to 3.53)	<0.001	76.9
Spinal	1	6.37 (4.93 to 7.81)	Not applicable	
Morphine equivalents 24 h postoperatively				
Surgery types				
Open surgery	11	−10.73 (14.90 to −6.56)	<0.001	99.8
Laparoscopic surgery	1	−78.90 (−93.29 to −64.51)	Not applicable	
Anesthesia				
GA	10	−15.95 (−19.71 to −12.19)	<0.001	88.7
Spinal	2	−1.55 (−2.88 to −0.23)	0.003	98.7

CI indicates confidence interval; GA, general anesthesia; TAP, transversus abdominis plane; WMD, weighted mean difference.

Since DEX is only approved intravenous administration by the US Food and Drug Administration and Health Canada, most of included studies were performed in developing countries.[47] Meanwhile, because of the language barrier, our search strategy is likely to include studies in English and Chinese database. Third, because of the limited number of included trials, a detailed meta-regression including all possible predictors could not be examined. Finally, the calculations of morphine equivalents may have introduced bias. These factors could affect our results. Therefore, the current results should be interpreted with caution.

In summary, this meta-analysis provided evidence that DEX is a favorable LA adjuvant with lower postoperative pain intensity and a significant reduction in opioid consumption as well as enhanced duration of the TAP block. More trials with strict design are required to confirm these findings.

REFERENCES

1. Rafi AN. Abdominal field block: a new approach via the lumbar triangle. *Anaesthesia*. 2001;56:1024–1026.
2. Gerlach AT, Murphy CV, Dasta JF. An updated focused review of dexmedetomidine in adults. *Ann Pharmacother*. 2009;43:2064–2074.
3. Marhofer D, Kettner SC, Marhofer P, et al. Dexmedetomidine as an adjuvant to ropivacaine prolongs peripheral nerve block: a volunteer study. *Br J Anaesth*. 2013;110:438–442.
4. Brummett CM, Hong EK, Janda AM, et al. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current. *Anesthesiology*. 2011;115:836–843.
5. El-Boghdadly K, Brull R, Sehmbi H, et al. Perineural dexmedetomidine is more effective than clonidine when added to local anesthetic for supraclavicular brachial plexus block: a systematic review and meta-analysis. *Anesth Analg*. 2017;124:2008–2020.
6. Hussain N, Grzywacz VP, Ferreri CA, et al. Investigating the efficacy of dexmedetomidine as an adjuvant to local anesthesia in brachial plexus block: a systematic review and meta-analysis of 18 randomized controlled trials. *Reg Anesth Pain Med*. 2017;42:184–196.
7. Ping Y, Ye Q, Wang W, et al. Dexmedetomidine as an adjuvant to local anesthetics in brachial plexus blocks: a meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2017;96:e5846.
8. Vorobeichik L, Brull R, Abdallah FW. Evidence basis for using perineural dexmedetomidine to enhance the quality of brachial plexus nerve blocks: a systematic review and meta-analysis of randomized controlled trials. *Br J Anaesth*. 2017;118:167–181.
9. Tsai HC, Yoshida T, Chuang TY, et al. Transversus abdominis plane block: an updated review of anatomy and techniques. *Biomed Res Int*. 2017;2017:8284363.
10. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ*. 2009;339:b2700.
11. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol*. 2005;5:13.
12. Wan X, Wang W, Liu J, et al. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14:135.
13. Pereira J, Lawlor P, Vigano A, et al. Equianalgesic dose ratios for opioids. A critical review and proposals for long-term dosing. *J Pain Symptom Manage*. 2001;22:672–687.
14. Knotkova H, Fine PG, Portenoy RK. Opioid rotation: the science and the limitations of the equianalgesic dose table. *J Pain Symptom Manage*. 2009;38:426–439.
15. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
16. Patsopoulos NA, Evangelou E, Ioannidis JP. Sensitivity of between-study heterogeneity in meta-analysis: proposed metrics and empirical evaluation. *Int J Epidemiol*. 2008;37:1148–1157.
17. Hu X, Xiao F. Effects of adding dexmedetomidine to levobupivacaine on transversus abdominis plane block. *Chin J New Drugs Clin Rem*. 2017;36:279–282.
18. Li L, Zheng T, Zheng X, et al. Ultrasound-guided transversus abdominis plane block with dexmedetomidine. *J Trauma Emerg*. 2017;5:68–71.
19. Xiao F, Liu L, Xu W, et al. Dexmedetomidine can extend the duration of analgesia of levobupivacaine in transversus abdominis plane block: a prospective randomized controlled trial. *Int J Clin Exp Med*. 2017;10:14954–14960.

20. Almarakbi WA, Kaki AM. Addition of dexmedetomidine to bupivacaine in transversus abdominis plane block potentiates post-operative pain relief among abdominal hysterectomy patients: a prospective randomized controlled trial. *Saudi J Anaesth*. 2014;8:161–166.
21. Mishra M, Mishra SP, Singh SP. Ultrasound-guided transversus abdominis plane block: what are the benefits of adding dexmedetomidine to ropivacaine. *Saudi J Anaesth*. 2017;11:58–61.
22. Zhou Q, Xu F, Li L, et al. Effects of different dosage of dexmedetomidine combined with ropivacaine for transversus abdominis plane block in Laparoscopic Radical Operation on patients with colon cancer. *J Pract Med*. 2016;32:4108–4110.
23. Chen M, Hou T, Chen P, et al. Observation on the time-effect of dexmedetomidine combined with ropivacaine for transversus abdominis plane block. *Chin J Mod Drug Appl*. 2017;11:87–89.
24. Sinha A, Jayaraman L, Punhani D, et al. Transversus abdominis plane block for pain relief in patients undergoing in endoscopic repair of abdominal wall hernia: a comparative, randomised double-blind prospective study. *J Minim Access Surg*. 2017;14:197–201.
25. Zhai M, Li J, Gu H, et al. Effect of ultrasound guided subcostal transverses abdominis plane block with dexmedetomidine mixed ropivacaine in related living kidney transplantation donor. *J Clin Anesthesiol*. 2016;32:441–444.
26. Zhou Y, Qian J, Xue L, et al. Effect of ultrasound-guided subcostal transverses abdominis plane block with dexmedetomidine after laparoscopic radical operation on colon. *Chin J Rehabil Theory Pract*. 2014;20:1171–1174.
27. Fang Z, Bao H, Si Y. Application of dexmedetomidine mixed with ropovacaine for transversus abdominis plane block in patients undergoing hysterectomy. *Jiangsu Med J*. 2016;42:2454–2457.
28. Lan F, Wang T. Evaluation on the postoperative analgesic effect of dexmedetomidine combined with ropivacaine for ultrasound. *Beijing Med J*. 2016;38:39–42.
29. Ding W, Li W, Zeng X, et al. Effect of adding dexmedetomidine to ropivacaine on ultrasound-guided dual transversus abdominis plane block after gastrectomy. *J Gastrointest Surg*. 2017;21:936–946.
30. Luan H, Zhang X, Feng J, et al. Effect of dexmedetomidine added to ropivacaine on ultrasound-guided transversus abdominis plane block for postoperative analgesia after abdominal hysterectomy surgery: a prospective randomized controlled trial. *Minerva Anestesiol*. 2016;82:981–988.
31. Aksu R, Patmano G, Biçer C, et al. Efficiency of bupivacaine and association with dexmedetomidine in transversus abdominis plane block ultrasound guided in postoperative pain of abdominal surgery. *Rev Bras Anestesiol*. 2018;68:49–56.
32. Lang S, Wu F, Liu X. Dexmedetomidine added to ropivacaine extends the duration of transversus abdominis plane blocks when compared with ropivacaine alone. *J Ningxia Univ*. 2017;39:1137–1139.
33. Ramya PA, Udayakumar P. Comparison of efficacy of bupivacaine with dexmedetomidine versus bupivacaine alone for transversus abdominis plane block for post-operative analgesia in patients undergoing elective caesarean section. *J Obstet Gynaecol India*. 2017;68:98–103.
34. Zhang L, Yuan J, Li J, et al. Postoperative analgesia of Ropivacaine combined Dexmedetomidine for transversus abdominis plane block in laparoscopic surgery. *China J Endosc*. 2017;23:16–20.
35. Nie L, Qiu Q, Zhang Q, et al. Effect of ropivacaine combined with dexmedetomidine fortransversus abdominis plane block after cesarean section. *Fujian Med J*. 2017;39:29–32.
36. Wu J, Peng J, He Q, et al. Application effects of ultrasound-guided transversus abdominis plane blocks with local anesthetics and Dexmedetomidine in patients with gynecological laparotomy. *Chin Med Herald*. 2017;14:62–65.
37. White PF, Kehlet H. Improving postoperative pain management: what are the unresolved issues. *Anesthesiology*. 2010;112:220–225.
38. Apfelbaum JL, Chen C, Mehta SS, et al. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. *Anesth Analg*. 2003;97:534–540.
39. White PF. Pain management after ambulatory surgery—where is the disconnect. *Can J Anaesth*. 2008;55:201–207.
40. Abdallah FW, Halpern SH, Margarido CB. Transversus abdominis plane block for postoperative analgesia after Caesarean delivery performed under spinal anaesthesia? A systematic review and meta-analysis. *Br J Anaesth*. 2012;109:679–687.
41. Wu HH, Wang HT, Jin JJ, et al. Does dexmedetomidine as a neuraxial adjuvant facilitate better anesthesia and analgesia? A systematic review and meta-analysis. *PLoS One*. 2014;9:e93114.
42. Abdallah FW, Brull R. Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: a systematic review and meta-analysis. *Br J Anaesth*. 2013;110:915–925.
43. Kirksey MA, Haskins SC, Cheng J, et al. Local anesthetic peripheral nerve block adjuvants for prolongation of analgesia: a systematic qualitative review. *PLoS One*. 2015;10:e0137312.
44. Bagatini A, Gomes CR, Masella MZ, et al. Dexmedetomidine: pharmacology and clinical application. *Rev Bras Anestesiol*. 2002;52:606–617.
45. Al-Metwalli RR, Mowafi HA, Ismail SA, et al. Effect of intra-articular dexmedetomidine on postoperative analgesia after arthroscopic knee surgery. *Br J Anaesth*. 2008;101:395–399.
46. Chen BS, Peng H, Wu SN. Dexmedetomidine, an alpha2-adrenergic agonist, inhibits neuronal delayed-rectifier potassium current and sodium current. *Br J Anaesth*. 2009;103:244–254.
47. Abdallah FW, Dwyer T, Chan VW, et al. IV and perineural dexmedetomidine similarly prolong the duration of analgesia after interscalene brachial plexus block: a randomized, three-arm, triple-masked, placebo-controlled trial. *Anesthesiology*. 2016;124:683–695.