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META-ANALYSIS

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Combining Spinal-Epidural Anesthesia *versus* Single-Shot Spinal Anesthesia for Cesarean Delivery: A Meta-Analysis of 5 Randomized Controlled Trials

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Background: This study compared combined spinal-epidural anesthesia (CSEA) and single-shot spinal anesthesia (SSSA) by performing a meta-analysis.

Material/Methods: An electronic search of relevant studies was done through 2017. Primary endpoints included duration of surgery, and time for (1) sensory recovery to thoracic vertebra (T10), (2) maximal sensory, (3) motor blockade, and (4) motor recovery. Secondary endpoints were the adverse effects. RevMan 5.3 analytical software was used with odds ratios (OR) and 95% confidence intervals (CIs) as the analytic parameters. Standard deviation and mean were used to evaluate data by weighted mean differences (WMDs) with 95% CI.

Results: A total of 370 patients were analyzed. A similar duration of surgery was observed with CSEA and SSSA (WMD: 0.24, 95%CI: −3.41–3.89; P=0.90). Time to maximal sensory blockade (WMD: 0.96, 95%CI: −2.91–4.83), time to maximal motor blockade (WMD: 0.25, 95%CI: −2.46–2.96), time for complete motor recovery (WMD: −6.28, 95%CI: −29.42–16.86), and time for sensory recovery to T10 vertebra (WMD: 0.42, 95%CI: −11.07–11.91) were not significantly different. Adverse effects such as hypotension (OR: 1.49, 95%CI: 0.27–8.31), pruritus (OR: 0.23, 95%CI: 0.03–2.18), nausea/vomiting (OR: 0.84, 95%CI: 0.12–5.99). and shivering (OR: 0.53, 95%CI: 0.11–2.56) were also similar with CSEA and SSSA.

Conclusions: CSEA was not associated with significantly different maximal duration of sensory/motor blockade, complete motor recovery, sensory regression to T10, or adverse drug events compared to SSSA. Hence, both should be considered effective in cesarean delivery.

MeSH Keywords: Anesthesia • Anesthesia, Spinal • Hypotension • Meta-Analysis

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Background

Even if the World Health Organization recommends cesarean delivery based only on medical needs [1,2], whereby a normal vaginal delivery could be harmful to the mother or the baby's life [3], for example as suggested by the Maternal Fetal Medicine Committee of the Society of Obstetricians and Gynecologists of Canada [4], many C-sections are nowadays performed upon request under local anesthesia, without any medical reason to do so [5].

Combined spinal-epidural anesthesia (CSEA) and epidural anesthesia (EA) during labor have previously been compared in systematic reviews [6]. Although CSEA was associated with a rapid onset rate, no difference was observed in terms of maternal satisfaction, ability to mobilize and maternal hypotension when compared to EA. Moreover, no meaningful conclusion could be drawn regarding rare complications which could be associated with these 2 different anesthetic techniques. Spinal anesthesia was also commonly preferred due to its rapid onset and reliable blockade [7]. However, due to a larger dose of bupivacaine used as a precaution to ensure adequate anesthetic effect, post-anesthesia complications were possible with spinal anesthesia [8]. Recently, a study [9] showed intrathecal block to be similar in duration and extent whether given as single-shot spinal anesthesia (SSSA), or used as a CSEA with or without epidural volume extension during elective cesarean delivery. A study by D'Ambrosio [10] that compared the effectiveness and anesthetic recovery times after isobaric levobupivacaine (L) 0.25% versus L 0.50% spinal anesthesia during elective cesarean deliveries found that L 0.25% may be used as a suitable alternative to L 0.50% for spinal anesthesia for cesarean deliveries.

Since CSEA and SSSA have seldom been compared through meta-analyses, the present compared CSEA with SSSA for cesarean delivery using a large number of patients obtained from previously published studies.

Material and Methods

Ethics approval

Neither ethics approval nor patient consents were required during this analysis.

Searched databases and strategies

Two authors independently searched 3 electronic databases (Cochrane Library of Randomized Controlled Trials, PubMed, and EMBASE) for English publications comparing CSEA with SSSA for cesarean delivery by entering the phrase 'combined spinal-epidural anesthesia versus single-shot spinal anesthesia for cesarean delivery' and by searching the words 'combined spinal-epidural anesthesia, single-shot spinal anesthesia and cesarean delivery' from database inception to the year 2017. To further enhance this search, abbreviations such as CSE anesthesia and SSS anesthesia were also used in the search process. References were also checked for relevant publications. Any inconsistencies were settled by group discussion.

Inclusion and exclusion criteria

Studies were included if:

a. They were considered as randomized trials or observational studies.
b. They compared CSEA with SSSA.
c. They involved patients undergoing cesarean delivery.
d. They reported duration of surgery, intraoperative adverse drug effects or sensory/motor blockage/regression time duration as their endpoints.

Studies were excluded if:

a. They were case studies/meta-analyses/letter to editors.
b. Comparison between CSEA and SSSA was not made.
c. Patients undergoing cesarean delivery were not included.
d. They did not report the above-mentioned endpoints.
e. They were duplicates.
f. Only their abstracts were made available.

Data extraction and review

Two authors assessed the titles, abstracts, and data of relevant studies. The authors' names, year of publication, and reported endpoints, as well as data concerning the total number of patients involved, the baseline features, and the number of events or time duration of anesthetic procedure durations were systematically extracted. If any of these 2 authors disagreed about including certain studies or data, disagreements were discussed and resolved by consensus.

Bias risk was briefly assessed by referring to the recommendations in the Cochrane Collaboration handbook [11]. A grade (A to C) was allocated depending upon the quality (low risk to high risk of bias) of the trials strictly in accordance to what the authors observed. Note that the authors tried to be fair during this quality assessment, but a slight upward or downward bias in grading was possible. This study adhered to the applicable Equator guidelines [12].

Statistical analysis

The Cochrane Q statistic test and the I^2 test were used to assess heterogeneity. A P value greater than 0.05 was considered insignificant whereas a P value less or equal to 0.05

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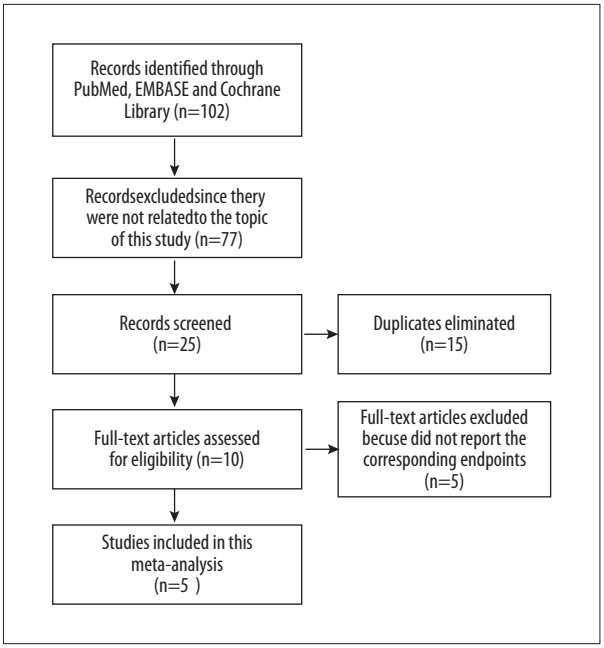

Figure 1. Flow diagram representing study selection.

was significant. For the I^2 value, a high percentage indicated a high heterogeneity whereas a low percentage showed a lower heterogeneity. In this analysis, a fixed-effects model (I^2<50%) or a random-effects model (I^2>50%) was used based on the value of I^2.

RevMan 5.30 software was used to calculate odds ratios (OR) with 95% confidence intervals (CIs) for discontinuous variables, whereas for continuous variables, standard deviation and mean were used to evaluate the data by weighted mean differences (WMDs) with 95% CI.

Since only 5 trials were included in this analysis, funnel plots were used to assess publication bias.

Results

Search result

The electronic literature search produced a total of 102 articles. Seventy-seven articles were eliminated based on intense assessment of the summarized version (abstract) of the articles. Fifteen articles which were duplicates were also eliminated. Finally, eligibility assessment was carried out for 10 full-text articles. Five full-text articles were further rejected since they did not report the required endpoints. Only 5 trials [9,13–16] were finalized for this analysis (Figure 1).

Main features of the studies

Table 1 summarizes the type of study reported and the total number of patients associated with each group. This analysis consisted of a total of 370 patients obtained from 5 randomized trials (206 patients associated with the CSEA group and 164 patients associated with the SSSA group).

Baseline features of the patients involved

The baseline features of the patients are summarized in Table 2. The mean ages ranged from 24.7 to 33.0 years and the average body weight was between 57.8 and 77.5 kg. Body mass index was above 24 kg/m^2. As shown in Table 2, no significant difference was observed in baseline features between the CSEA group and the SSSA group.

Endpoints assessed

The analyzed endpoints are listed in Table 3.

The primary endpoints included:
a. Duration of surgery
b. Time for sensory recovery to T10
c. Time to maximal motor blockade

Table 1. General features of the studies included.

Studies	Type of study	No. of patients who underwent CSEA (n)	No. of patients who underwent SSSA (n)	Quality assessment grade
Choi 2006 [13]	RCT	50	50	B
Girotra 2009 [9]	RCT	20	20	B
Ithnin 2006 [14]	RCT	15	15	B
Lew 2004 [15]	RCT	31	31	B
Salman 2013 [16]	RCT	90	48	B
Total no. of patients (n)		206	164	

RCT – randomized controlled trials; CSEA – combined spinal-epidural anesthesia; SSSA – single-shot spinal anesthesia.

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Table 2. Baseline features of the studies included.

Studies	Age (years)	Weight (kg)	Height (cm)	BMI (kg/m²)	Baseline SP (mmHg)	Duration of surgery (min)
	C/S	C/S	C/S	C/S	C/S	C/S
Choi2006 [13]	30.1/31.8	68.8/69.0	160.2/159.5	–	–	46.7/48.6
Girotra2009 [9]	26.0/24.7	60.0/57.8	153/153	25.6/24.4	127/120	51.5/50.3
Ithnin2006 [14]	31.0/33.0	73.0/69.0	156/153	30.0/29.0	127/134	42.0/47.0
Lew2004 [15]	32.0/33.0	69.0/69.0	158/157	27.6/28.0	–	42.0/38.0
Salman2013 [16]	29.6/31.0	76.7/77.5	163/163	28.8/29.0	–	–

C – combined spinal-epidural anesthesia; S – single-shot spinal anesthesia; BMI – body mass index; kg – kilograms; cm – centimeters; SP – systolic pressure.

Table 3. Endpoints reported in the studies analyzed.

Studies	Endpoints assessed
Choi 2006 [13]	Incidence of intraoperative side effects: hypotension, nausea and vomiting, shivering, pruritus, sensory recovery to T10, complete motor recovery, duration of surgery
Girotra 2009 [9]	Duration of surgery, time to maximum motor blockade, time to complete regression of motor blockade, time to maximum sensory block, time for sensory block to regress to T10, adverse effects: hypotension, nausea and vomiting, shivering, pruritus
Ithnin 2006 [14]	Duration of surgery, time to maximal sensory block, time for block to recede to T10, time to maximal motor block, hypotension, nausea, vomiting, shivering
Lew 2004 [15]	Duration of surgery, time for sensory regression to T10, hypotension
Salman 2013 [16]	Time to onset of sensory block, time to maximum sensory block, time for sensory block to regress to T10, time to maximum motor block, time to recovery for motor block

Table 4. Results of this analysis.

Endpoints analyzed	OR or WMD with 95% CI		P value	I² (%)
Duration of surgery	0.24	[–3.41–3.89]	0.90	0
Time for sensory recovery to T10	0.42	[–11.07–11.91]	0.94	83
Time to maximal motor blockade	0.25	[–2.46–2.96]	0.86	94
Time for complete motor recovery	–6.28	[–29.42–16.86]	0.59	91
Time to maximum sensory blockade	0.96	[–2.91–4.83]	0.63	93
Hypotension	1.49	[0.27–8.31]	0.65	79
Pruritus	0.23	[0.03–2.18]	0.20	–
Nausea and vomiting	0.84	[0.12–5.99]	0.86	80
Shivering	0.53	[0.11–2.56]	0.43	52

OR – odds ratios; CI – confidence intervals; WMD – weight mean difference.

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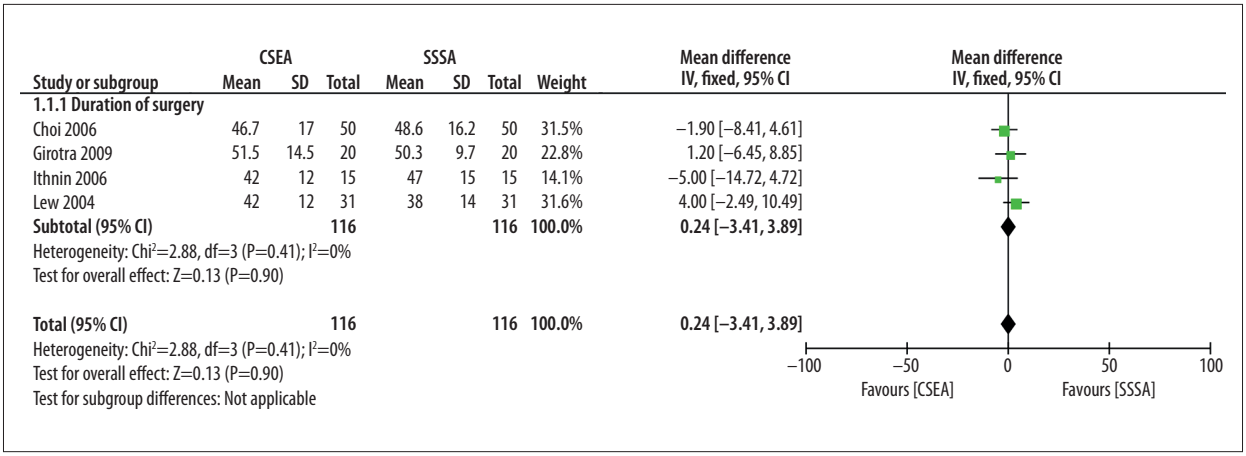

Figure 2. Forest plot showing the duration of surgery between CSEA and SSSA groups.

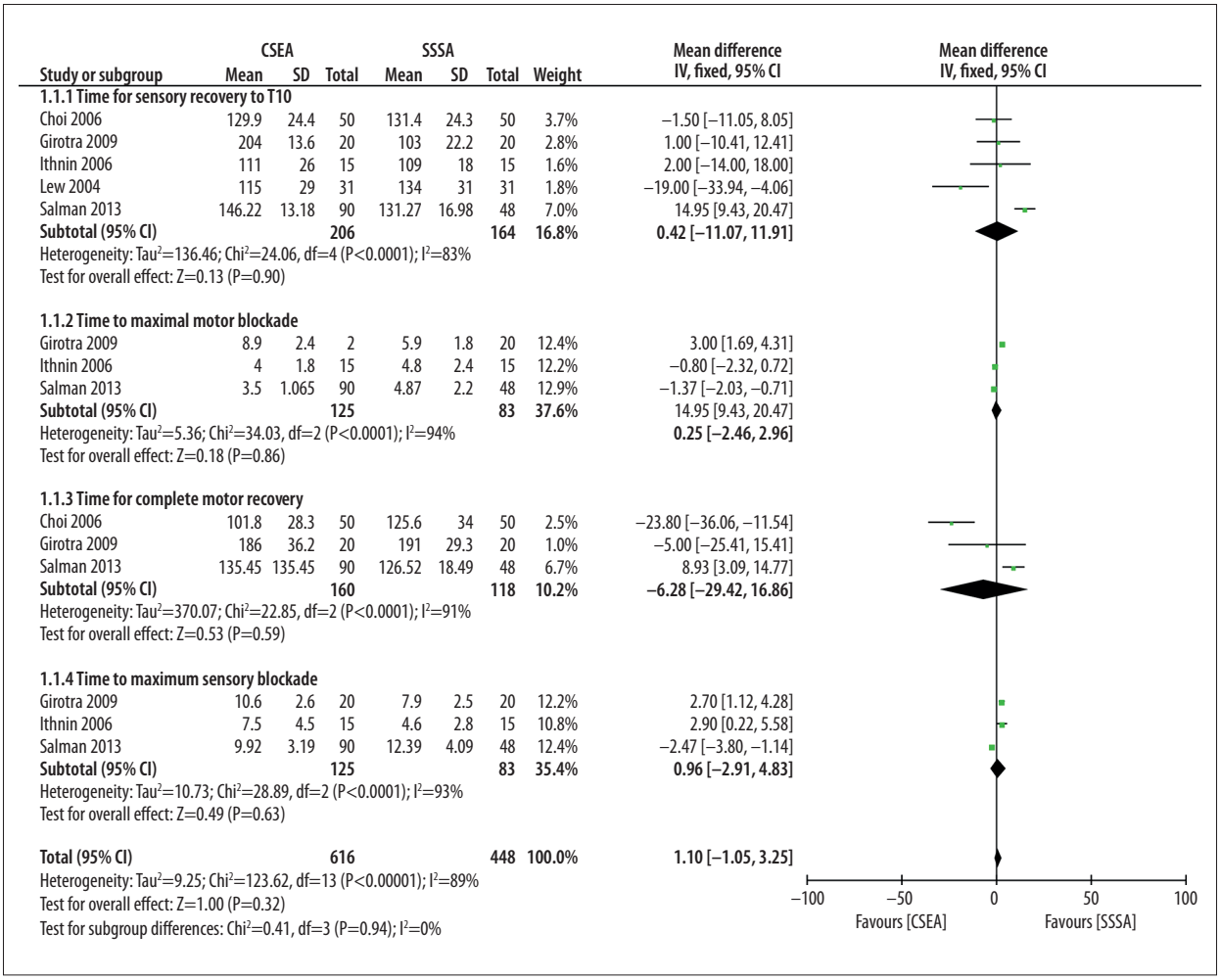

Figure 3. Forest plot comparing the primary endpoints between CSEA and SSSA groups.

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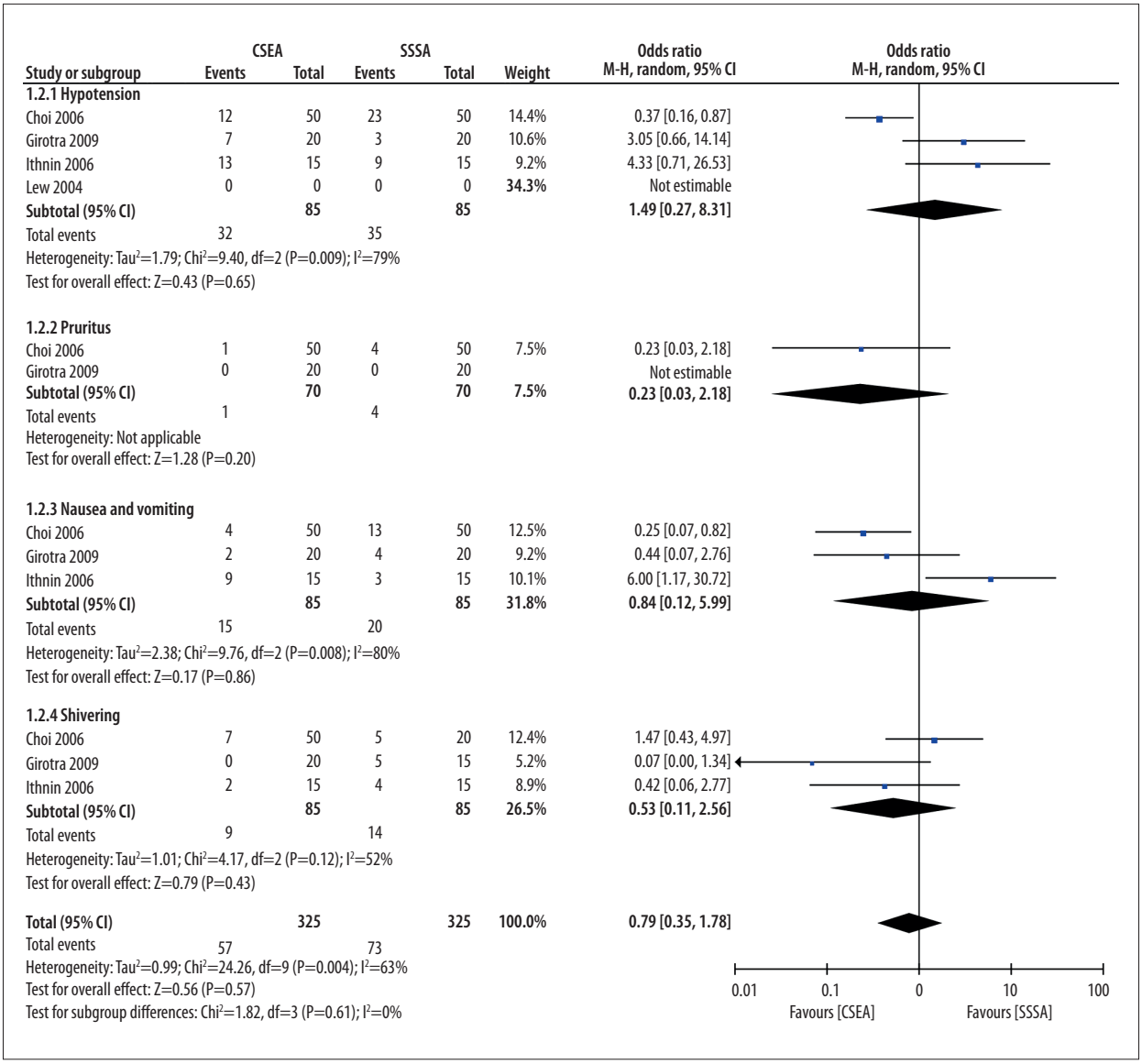

Figure 4. Forest plot comparing the adverse drug effects (secondary outcomes) between CSEA and SSSA groups.

d. Time for complete motor recovery
e. Time to maximum sensory blockade

The secondary endpoints which consisted of adverse drug effects:
a. Hypotension
b. Pruritus
c. Nausea and vomiting
d. Shivering

According to Table 3, there were 4 studies that reported duration of surgery, time for sensory regression to T10, and hypotension, and only 3 studies reported time to maximal sensory and motor blockade, time for complete motor recovery, nausea/vomiting, and shivering. Pruritus was reported in only 2 studies.

Analysis of CSEA versus SSSA

Table 4 summarizes the results of this meta-analysis.

This analysis, which included data only from randomized trials, showed that a similar duration of surgery was associated with CSEA and SSSA, (WMD: 0.24, 95% CI: –3.41–3.89; P=0.90) (Figure 2).

No significant difference has been observed when CSEA and SSSA were compared in terms of time to maximal sensory blockade, time to maximal motor blockade, time for complete motor recovery, and time for sensory recovery to T10 vertebra (WMD: 0.96, 95% CI: –2.91–4.83; P=0.63), (WMD: 0.25, 95% CI: –2.46–2.96; P=0.86), (WMD: –6.28, 95% CI: –29.42–16.86;

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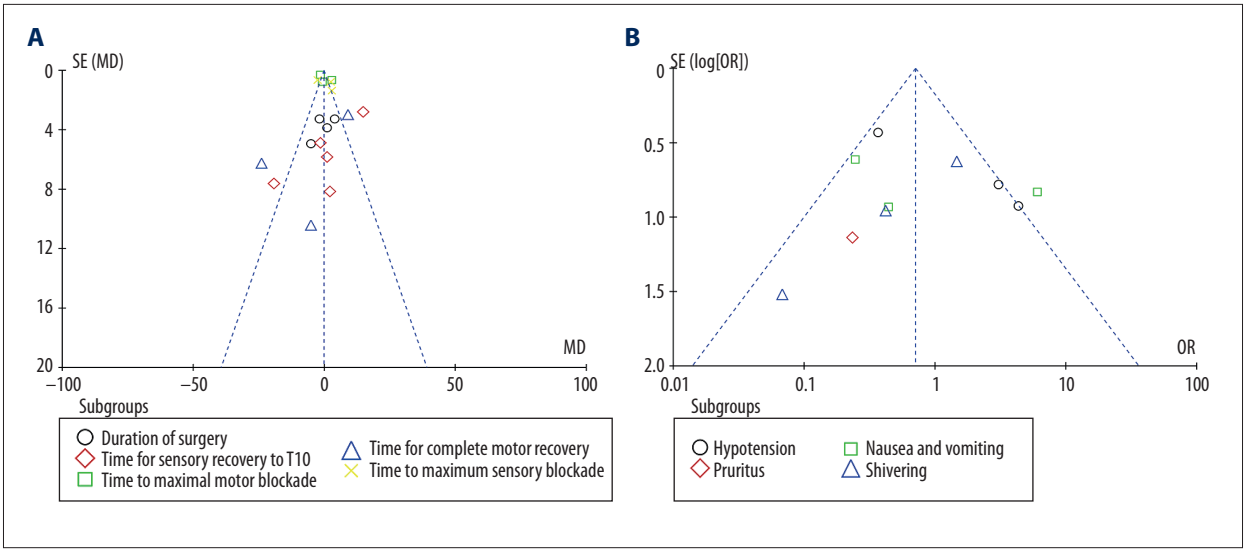

Figures 5. Funnel plots representing publication bias.

P=0.59) and (WMD: 0.42, 95% CI: −11.07–11.91; P=0.94), respectively (Figure 3).

In addition, even when the adverse drug effects were analyzed (secondary endpoints), no significant differences were observed between CSEA and SSSA (OR: 1.49, 95% CI: 0.27–8.31; P=0.65), (OR: 0.23, 95% CI: 0.03–2.18; P=0.20), (OR: 0.84, 95% CI: 0.12–5.99; P=0.86) and (OR: 0.53, 95% CI: 0.11–2.56; P=0.43) for hypotension, pruritus, nausea/vomiting and shivering, respectively (Figure 4).

Publication bias

The funnel plots showing visually estimated publication bias are shown in Figure 5.

Discussion

Our aim was to compare CSEA with SSSA. We found no significant difference in terms of duration of surgery, time to maximal sensory and motor blockade, time for complete motor recovery, or time for sensory regression to T10. Moreover, hypotension, pruritus, nausea/vomiting, and shivering were also not significantly different between the CSEA and SSSA groups.

In agreement with the results of the present analysis, Horstman et al. also demonstrated a similar blockade associated with CSEA and SSSA among 30 parturients (18–45 years old) who underwent elective cesarean delivery [17], and they also showed no significant differences in median pinprick sensory block height (T4 [T4-2] and T3 [T4-1]) or cerebrospinal fluid pressures. In addition, Macfarlane et al. showed CSEA placement was not associated with hemodynamic advantages when compared to SSSA, even when the same dose of local anesthetic agent was administered [18]. In their study, hyperbaric bupivacaine (12.5 mg) and diamorphine (0.3 mg) were administered intrathecally via CSEA or SSSA in 70 women who underwent cesarean delivery. However, the authors further stated that no block was higher than T4 in their study, which could have been responsible for such a result [19].

Another study, involving 44 obese patients, also showed no significant difference when CSEA and SSSA were compared [20]. However, its main focus was on the technique of anesthesia, which was not the case in the present analysis. Moreover, a recently published study by Singh et al. also showed no significant difference associated with CSEA and non-CSEA for cesarean delivery [21], but their study mainly focused on the duration of labor, rate of instrumental vaginal delivery, and neonatal outcomes, whereby emergency lower-segment cesarean section including fetal distress was higher with CSEA (14.5%) compared to non-CSEA (10.9%), which were not assessed in the present analysis.

In contrast to the result of our analysis, a study by Choi et al. showed SSSA to be associated with a denser motor block, whereas motor recovery was faster with CSEA [13]. In addition, even sensory blockade was more prominent with SSSA for the first 5 min, whereas no significant difference was observed afterwards. The authors also observed SSSA to be associated with a higher maternal hypotension, whereas the other adverse drug effects were similar between these 2 groups, demonstrating several benefits observed with CSEA when compared to SSSA, among the 102 women (52 allocated to receive CSEA and 50 allocated to SSSA) undergoing cesarean delivery at term.

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Our study has several new features. First, CSEA and SSSA for cesarean delivery have not been previously compared through meta-analyses. Being the first analysis comparing CSEA with SSSA could be a new feature of this study. Secondly, this analysis included a more randomized patient population compared to previously published studies. This could add to the novelty of our study. Moreover, because it is clinically important, anesthesiologists might further decide about the correct technique of anesthesia to be considered appropriate in patients undergoing cesarean delivery, which is gradually increasing, depending on the women's preference or clinical conditions [22–24].

Nevertheless, even if other anesthetic agents might be used in combination with bupivacaine, for spinal route, with reduced adverse drug events [25–29], the results of the present analysis are fully supported by several randomized trials. Unfortunately, due to the very limited number of patients analyzed, and the high level of heterogeneity among almost all the subgroups analyzed (possibly due to the different dosages of drugs used in different studies, selection and language bias, contributing to the main limitations of this study), further research is warranted in this field, which could be beneficial to future deliveries.

Conclusions

This analysis showed that CSEA was not associated with significantly different maximal duration of sensory or motor blockade, maximal duration of complete motor recovery, or time duration for sensory regression to T10 compared to SSSA for cesarean delivery. In addition, no significant differences in adverse drug effects were observed between these 2 techniques of anesthesia. Hence, both can be considered effective in cesarean delivery.

Conflict of interest

None.

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