Meta-Analysis

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Intravenous dexmedetomidine during spinal anaesthesia for caesarean section: A meta-analysis of randomized trials

Zeqing Bao[1,*], Chengmao Zhou[1,*], Xianxue Wang[2,*] and Yu Zhu[1]

Abstract

Objective: To evaluate the efficacy and safety of spinal anaesthesia using dexmedetomidine for caesarean section.

Methods: PubMed, The Cochrane Library, and CNKI were searched for relevant literature.

Results: The incidence of nausea and vomiting in the dexmedetomidine group was significantly lower than that in the control group (OR = 0.21, 95% CI: 0.12–0.35, $P < 0.00001$). No difference was found in the incidence of pruritus between the two groups (OR = 1.21, 95% CI: 0.36–4.09, $P = 0.76$).The dexmedetomidine group had a higher incidence of bradycardia than did the control group (OR = 2.20, 95% CI: 1.02–4.77, $P = 0.05$). The incidence of shivering in the dexmedetomidine group was significantly lower than that in the control group (OR = 0.20, 95% CI: 0.13–0.32, $P < 0.00001$). The incidence of hypotension was not different between the two groups (OR = 0.88, 95% CI: 0.49–1.56, $P = 0.65$).

Conclusion: Dexmedetomidine can decrease the incidence of nausea, vomiting, bradycardia, and shivering with spinal anaesthesia during caesarean section.

Keywords

Dexmedetomidine, caesarean section, spinal anaesthesia, meta-analysis

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Spinal anaesthesia is widely used in caesarean section because of its simple operation and minimal effects on physiological function in humans.[1] To improve sedative and postoperative analgesic effects, opioids and

[1]Zhaoqing Medical College, Zhaoqing, China
[2]Department of Anesthesiology, The First People's Hospital of Changde, Changde, China

*These authors contributed equally to this work.

Corresponding author:
Chengmao Zhou, Zhaoqing Medical College, No. 5 Xijiangnan Road, Zhaqing, Guangdong, China.
Email: 564099474@qq.com

other drugs often need to be administrated through the spinal canal during anaesthesia. However, opioids have many adverse reactions, including pruritus. The incidence of nausea and vomiting caused by caesarean section is as high as 60%, causing discomfort to patients. For full-stomach patients, reflux and aspiration may occur during caesarean section.[2] Additionally, shivering, a common complication of patients who undergo caesarean section, can increase patients' oxygen consumption, produce large amounts of CO_2, and increase the metabolic rate by 400%.[3] If heart and lung diseases are discovered in patients, serious complications may occur. Prevention of intraoperative and postoperative shivering caused by caesarean section is an effective measure to prevent obstetric complications.[4] Moreover, the majority of puerperas may suffer from hypotension when self-regulation of blood flow is inhibited and support of abdominal muscles for the uterus disappear when the subarachnoid space is blocked.[5] Dexmedetomidine, which is a selective α2-receptor agonist, is used for sedation, analgesia, and inhibition of shivering during the extubation phase of general anaesthesia. This study aimed to investigate the effects of dexmedetomidine on adverse reactions caused by spinal anaesthesia during caesarean section.

Materials and methods

Inclusion criteria

With regard to the type of study, we included randomized, controlled trials (RCTs), which adopted a blinding method. Criteria for inclusion of studies were as follows: (1) original and independent studies; (2) RCTs; (3) the groups were comparable and balanced; and (4) spinal anaesthesia was used. For interventions, the experimental group was administered dexmedetomidine, while a control group received placebo or saline. Evaluation indicators of adverse reactions included the following: (1) shivering; (2) nausea and vomiting; (3) hypotension; (4) bradycardia; and (5) pruritus.

Exclusion criteria

Any studies with one of the following conditions were excluded: (1) non-RCTs; (2) retrospective studies; (3) descriptive literature reviews or systematic reviews; and (4) no data provided for calculating adverse reactions.

Search strategy

We searched PubMed, the Cochrane Library, CNKI, and other Chinese and foreign databases. We conducted comparative studies on specific clinical trials (from 1989 to 2016) of dexmedetomidine during spinal anaesthesia for caesarean section. We also manually searched the full texts of all studies to obtain the primary data. The English search terms included "dexmedetomidine", "cesarean section", and "spinal anesthesia." The retrievals ranged from January 1989 to August 2016.

Criteria for assessing the quality of literature

All RCTs that met the inclusion criteria were evaluated according to the Jadad scale. Two reviewers separately assessed the quality, and consulted a third party or negotiated with each other when there was a disagreement. The evaluated items included the following: (1) whether randomization was performed and whether the method was correct; (2) whether allocation concealment was used and whether the method was correct; (3) whether blinding was performed and in whom the method was used; and (4) whether there were withdrawals or dropouts.

Data extraction

All of the data were independently extracted using standard data tables by two investigators. They consulted a third party when there was a disagreement. The following contents were extracted from each article: the first author, the published year, the number of cases, grouping, and indicators of adverse reactions.

Statistical analysis

We performed a meta-analysis using Review Manager 5.2 and examined heterogeneity by conducting the chi-square test. In this study, the criteria and analytical method for determining heterogeneity were as follows. (1) If I^2 was $<50\%$, there was homogeneity, and the fixed-effects model was used to conduct the meta-analysis. (2) If I^2 was $\geq 50\%$ and heterogeneity between the groups needed to be combined, the random-effects model was selected for performing the meta-analysis. Subgroup analyses or sensitivity analyses were performed on factors that may contribute to heterogeneity. The data were analysed by means of the weighted mean difference if the continuous data were achieved by using measurement tools or by means of the standardized mean difference if the continuous data were obtained by using different measurement tools. For categorical data, the odds risks (ORs) were calculated. All data were calculated with 95% confidence intervals (CIs). The funnel plot was used to analyse publication bias.

Results

Literature screening

In accordance with the search strategy, 401 articles were included in the initial search. A total of 94 articles were selected after excluding non-relevant literature and non-original studies by reading titles and abstracts. Finally, only 12 articles[6–17] were included after further reading the full text (Figure 1).

Data extraction and evaluation of quality

The basic information of the included RCTs is shown in Table 1. Two researchers independently evaluated the quality using the Jadad scale. The quality of the original literature is shown in Table 1. We also

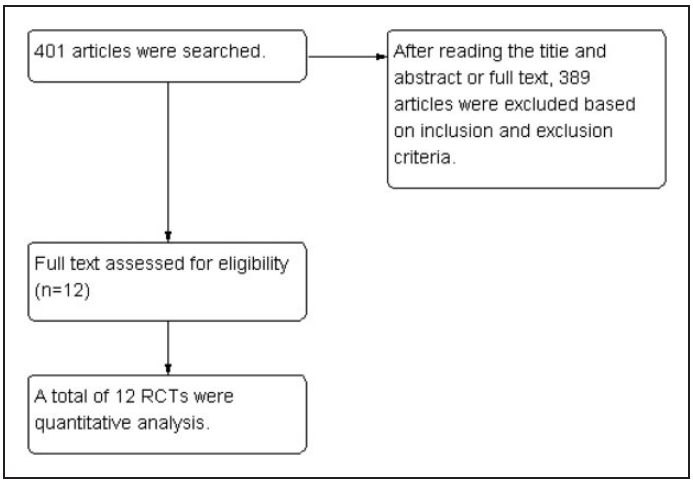

Figure 1. Flow diagram of the study.

Table 1. Characteristics and Jadad scores of the included studies in the meta-analysis.

Authors	Country	Number of patients	Groups	Target	Jadad score	Blinding	Concealment allocation	Randomised	Follow-up
Bai, 2015	China	50	Dexmedetomidine Saline	1	4	1	1	1	1
Chen, 2014	China	40	Dexmedetomidine Saline	1	4	1	1	1	1
Deng, 2011	China	90	Dexmedetomidine Saline Tramadol	1, 2	4	1	1	1	1
Ge, 2012	China	60	Dexmedetomidine Saline	1, 2, 3, 4	4	1	1	1	1
Hanoura, 2013	Egypt	50	Dexmedetomidine Saline	1, 2, 3, 4, 5	6	2	1	2	1
Li, 2013	China	120	Dexmedetomidine Saline	1, 2	4	1	1	1	1
Li, 2015	China	90	Dexmedetomidine Fentanyl Fentanyl plus clonidine Saline	2, 3, 4, 5	6	2	1	2	1
Liu, 2015	China	120	Dexmedetomidine Saline	2, 3	6	2	1	2	1
Lu, 2015	China	60	Dexmedetomidine Saline	1, 2	4	1	1	1	1
Sun, 2015	China	90	Dexmedetomidine Saline Fentanyl	1, 2, 3, 4, 5	6	2	1	2	1
Yousef, 2015	Egypt	80	Dexmedetomidine Saline	2, 3, 4, 5	5	2	1	1	1
Zhang, 2014	China	136	Dexmedetomidine Saline	1, 3, 4	4	1	1	1	1

1: shivering, 2: nausea and vomiting, 3: hypotension, 4: bradycardia, 5: pruritus.

used the Jadad score for randomization, allocation concealment, blinding, and withdrawals or dropouts of all enrolled studies.

Meta-analysis results

2.3.1 Effect of dexmedetomidine on nausea and vomiting: Nine studies were included. We compared the incidence of nausea and vomiting, which was introduced by spinal anaesthesia during caesarean section, between the dexmedetomidine and control groups. The heterogeneity test showed that $I^2 = 45\%$, and thus the fixed-effects model was used for the meta-analysis. We found that the dexmedetomidine group had a significantly lower incidence of nausea and vomiting than did the control group (OR = 0.21, 95% CI: 0.12–0.35, $P < 0.00001$) (Figure 2).

2.3.2 Effect of dexmedetomidine on pruritus: Four studies were included. We compared the incidence of pruritus, which was caused by spinal anaesthesia during caesarean section, between the dexmedetomidine and control groups. The heterogeneity test showed that $I^2 = 0\%$, and thus the fixed-effects model was used to conduct the meta-analysis. We found that the incidence of pruritus was not significantly different between the dexmedetomidine group and the control group (OR = 1.21, 95% CI: 0.36–4.09, $P = 0.76$) (Figure 3).

2.3.3 Effect of dexmedetomidine on bradycardia: Six studies were included. We compared the incidence of bradycardia, which was induced by spinal anaesthesia during caesarean section, between the dexmedetomidine and control groups. The heterogeneity test showed that $I^2 = 0\%$, and thus the fixed-effects model was used to perform the meta-analysis. We found that the incidence of bradycardia in the dexmedetomidine group was significantly higher than that in the control group (OR = 2.20, 95% CI: 1.02–4.77, $P = 0.05$) (Figure 4).

2.3.4 Effect of dexmedetomidine on shivering: Nine studies were included. We compared the incidence of shivering, which was caused by spinal anaesthesia during caesarean section, between the dexmedetomidine and control groups. The heterogeneity test showed that $I^2 = 32\%$, and thus the fixed-effects model was used to conduct the meta-analysis. We found that the incidence of shivering in the dexmedetomidine group was significantly lower than that in the control group (OR = 0.20, 95% CI: 0.13–0.32, $P < 0.00001$) (Figure 5).

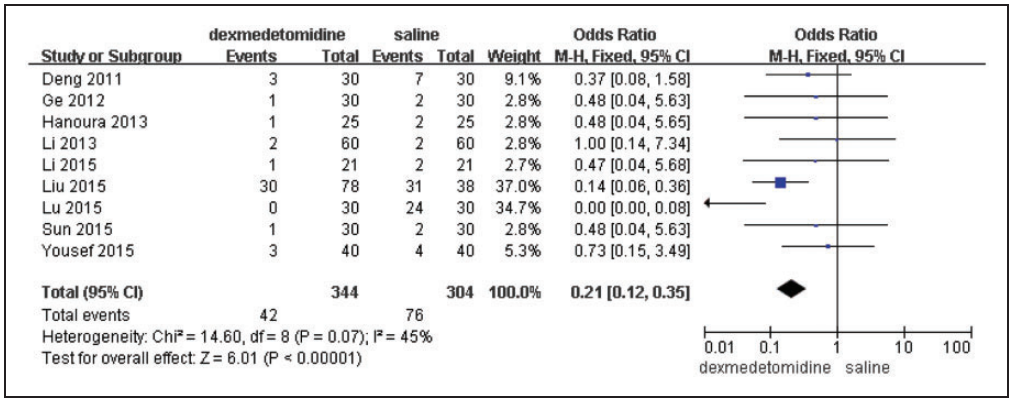

Figure 2. Effect of dexmedetomidine on nausea and vomiting.

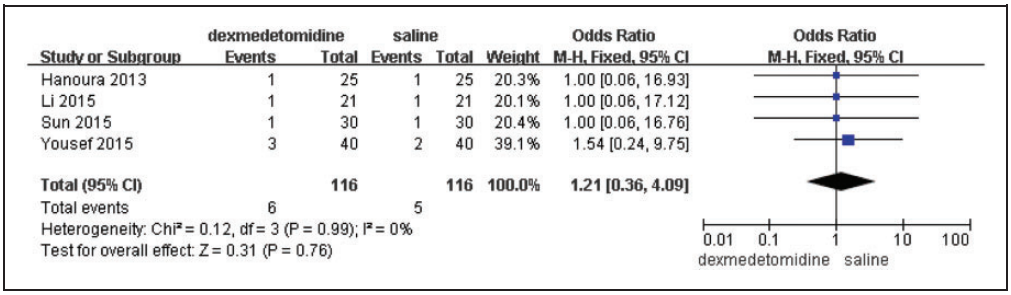

Figure 3. Effect of dexmedetomidine on pruritus.

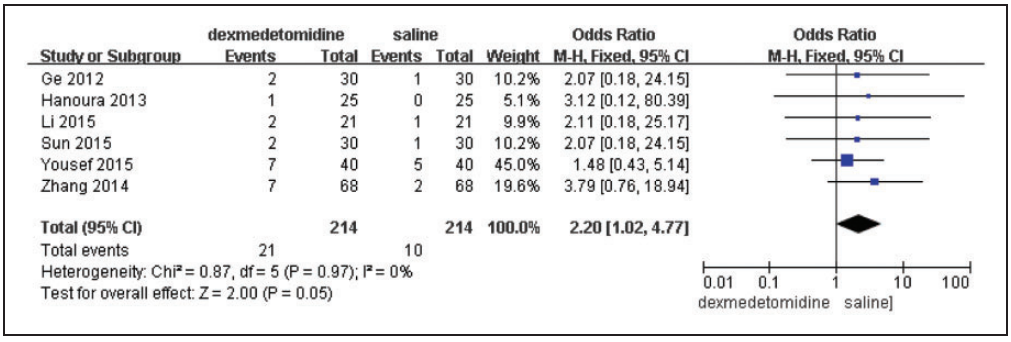

Figure 4. Effect of dexmedetomidine on bradycardia.

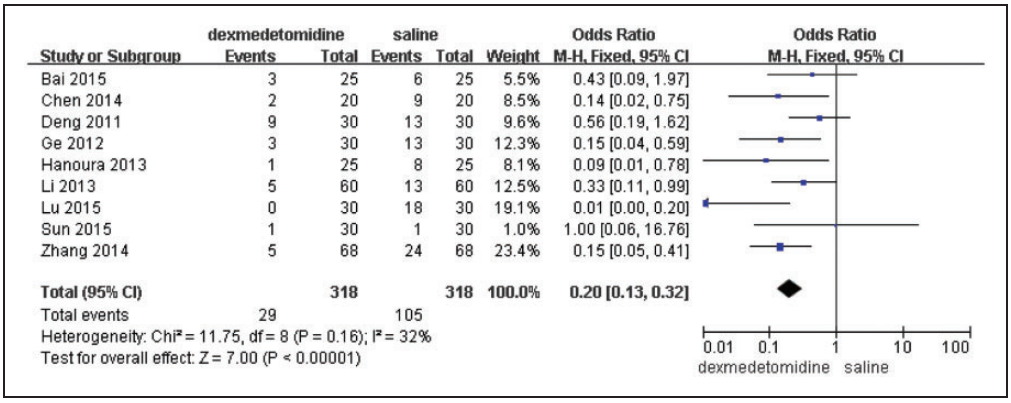

Figure 5. Effect of dexmedetomidine on shivering.

2.3.5 Effect dexmedetomidine on hypotension: Seven studies were included. We compared the incidence of hypotension, which resulted from spinal anaesthesia during caesarean section, between the dexmedetomidine and control groups. The heterogeneity test showed that $I^2 = 13\%$, and thus the fixed-effects model was used to

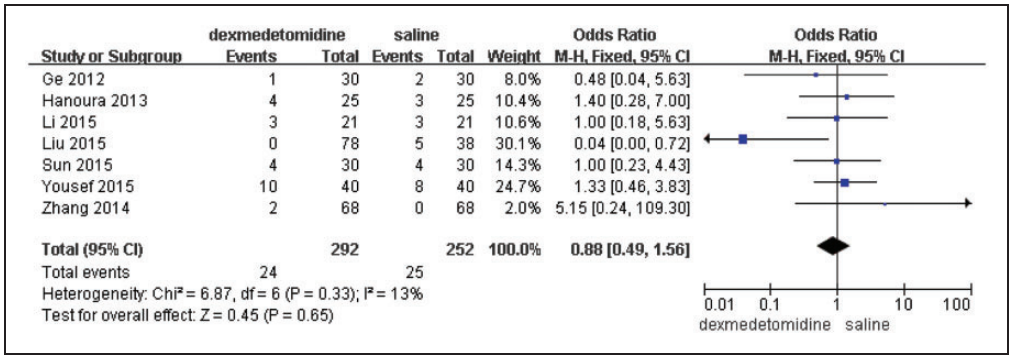

Figure 6. Effect of dexmedetomidine on hypotension.

perform the meta-analysis. We found that there was no significant difference in the incidence of shivering between the dexmedetomidine and control groups (OR = 0.88, 95% CI: 0.49–1.56, $P = 0.65$) (Figure 6).

Discussion

An increasing amount of studies[18–20] have shown that the anaesthetic efficacy of α2-receptor agonists, such as clonidine and dexmedetomidine, is satisfactory. Dexmedetomidine is a highly selective α2-adrenergic receptor agonist. Dexmedetomidine inhibits the release of norepinephrine through stimulating the α2-adrenergic receptor in the presynaptic membrane, thus terminating the delivery of pain signals. Dexmedetomidine also reduces the activity of sympathetic nerves via the α2-adrenergic receptor in the postsynaptic membrane, reduces blood pressure and heart rate, and produces the effects of sedation and relieving anxiety. Additionally, dexmedetomidine in combination with the α2-adrenergic receptor in the spinal cord is an effective analgesia.[19]

Shivering is a common complication of caesarean section. The incidence of shivering ranges from 5% to 65% in caesarean section. The main reasons for shivering include partial inhibition of the spinal reflex, decreased sympathetic activity, suppressed adrenal function, and surgical stimulation and pain. For puerperas, severe shivering can lead to increased consumption of oxygen, a rise in production of CO_2 and blood sugar, acceleration of heart rate, and in severe cases, severe hypoxaemia and acidosis. Dexmedetomidine is a highly selective and a novel α2-adrenergic receptor agonist. Dexmedetomidine acts on the α2-adrenergic receptor in the brain and spinal cord, inhibiting the discharge of nerve cells to hypnotize, sedate, resist anxiety, and mitigate the patient's poor mood.[21] Phan et al.[22] reported that dexmedetomidine curbs the thermoregulatory centre in the brain by suppressing delivery of information via body temperature at the spinal cord level, thus inhibiting shivering.

Nausea and vomiting during perioperation are adverse events for patients, obstetricians, and anaesthesiologists. Uncontrolled abdominal movement during surgery can increase the risk of visceral injury. The exact aetiology of perioperative nausea and vomiting remains unclear. A variety of factors are likely to cause nausea and vomiting.[23] Cerebral ischaemia tends to trigger vomiting during combined spinal and epidural anaesthesia for caesarean section. Blocking of sympathetic nerves and hypotension secondary to spinal anaesthesia, visceral pain, and vagal stimulation are the most important factors in caesarean

section. Hypotension may be the most important cause of nausea and vomiting. Studies have demonstrated that dexmedetomidine has effects of analgesia and sedation during spinal anaesthesia. Intravenously injected dexmedetomidine leads to hyperpolarization of nerve tissue to produce an analgesic effect and enhance regional anaesthesia by changing the transmembrane and ionic conductivity of blue-spot in the brainstem. The stable haemodynamic effects of dexmedetomidine are mainly related to the enhanced stability of the sympathetic adrenergic system. Steady haemodynamics may reduce the incidence of nausea and vomiting.

Dexmedetomidine has little effect on hypotension and pruritus during caesarean section. Moreover, dexmedetomidine reduces the activity of sympathetic nerves via the α2-adrenergic receptor in the postsynaptic membrane and reduces heart rate, and thus increases the incidence of bradycardia.

Several limitations of this meta-analysis should be taken into account. First, the quality of the included studies was uneven. Additionally, the number of included RCTs was too small. Moreover, the methodological quality used in evaluating the 13 RCTs was not high. Because we only included published literature, the search strategy and publication bias also could have affected the results of this study.

In summary, dexmedetomidine can reduce the incidence of nausea, vomiting, and shivering in spinal anaesthesia for caesarean section, but it does not reduce the incidence of pruritus and hypotension. Dexmedetomidine can raise the incidence of bradycardia.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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