

# Effects of colloid preload on the incidence of hypotension in spinal anesthesia for cesarean section: a systematic review and meta-analysis

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## Abstract

**Background:** Hypotension is a common complication caused by spinal anesthesia (SA), which may have adverse impacts on the condition of the parturient and fetus. Liquid infusion was found to be relatively effective for reducing the incidence of hypotension. However, the question of whether colloid preload can optimize hemodynamic variables in the cesarean section remains controversial. This study aims to determine the effects of colloid preload on the incidence of hypotension induced by SA in elective cesarean section.

**Methods:** Related keywords were searched on PubMed, EMBASE, and Cochrane Library from inception dates to May 2020. Studies included were evaluated for eligibility and quality. The primary outcome was the intra-operative incidence of hypotension and severe hypotension. The secondary outcomes included the lowest intra-operative systolic blood pressure, the maximal intra-operative heart rate, the intra-operative needs of ephedrine and phenylephrine, the incidence of maternal nausea and/or vomiting, and neonatal outcomes (umbilical artery pH and Apgar scores). Apart from the above, RevMan 5.3 was used for the data analysis.

**Results:** Altogether nine randomized controlled trials were included in the meta-analysis. There were no significant differences in the incidence of intra-operative hypotension, severe hypotension, or neonatal outcomes between the colloid preload group and control group, except for the umbilical artery pH.

**Conclusion:** This meta-analysis suggests that colloid preload does not significantly reduce the incidence of hypotension associated with SA in elective cesarean section.

**Keywords:** Colloid; Preload; Spinal anesthesia; Cesarean section

## Introduction

Cesarean section is one of the most commonly undertaken surgical procedures. Rates of cesarean section continue to rise worldwide: 24.5% in Western Europe, 32% in North America, and 41% in South America in 2016.<sup>[1]</sup> In China, the overall annual rate of cesarean sections rose from 2008 to 2014 by 34.9%.<sup>[2]</sup> The anesthetic management of patients who receive cesarean section becomes a challenging problem.

About 80% to 90% of the cesarean sections are performed under spinal anesthesia (SA).<sup>[3,4]</sup> Although SA may have significant benefits compared to general anesthesia, it frequently leads to hypotension, with an incidence up to 60% to 70% due to sympathetic nervous system blockade.<sup>[5-7]</sup> In addition, during late pregnancy, supine

positioning causes the gravid uterus to compress the inferior vena cava, resulting in drastic hemodynamic changes. A reduction of blood-flow through the inferior vena cava occurs during the supine position, which subsequently reduces cardiac output and blood pressure.<sup>[8]</sup> Prolonged hypotension leads to organ ischemia and cardiovascular collapse in parturients.<sup>[9]</sup> Furthermore, the decrease of the blood-flows to the uterine vascular bed leads to hypoxia, acidosis, fetal distress, reduced Apgar scores, and risk for the baby's health.<sup>[10]</sup> Since intra-operative hypotension has been associated with the increase of patient mortality and morbidity,<sup>[5]</sup> maintaining of blood pressure is very important during cesarean section, especially for the perinatal period before fetus delivery.

Multiple studies have assessed fluid infusion, vasopressor administration, and maternal positioning, which can

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10.1097/CM9.0000000000001477

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Chinese Medical Journal 2021;134(9)

Received: 26-01-2021 Edited by: Peng Lyu

attenuate the hypotension during cesarean section. Still, the methods to prevent and treat hypotension vary from one anesthesia practice to another.<sup>[11]</sup> Anesthetists can choose from different fluids loading regimens. There are two types of fluids (colloid or crystalloid), and both can be administered either before SA (preload) or with SA (coload),<sup>[12]</sup> while the better way to administer fluids is still subject to controversy. Colloid has been widely used in surgeries since it can provide swifter volume expansion in the intravascular space,<sup>[13]</sup> but the appropriate infusion time of colloid is unclear. Therefore, the aim of our research is to determine whether colloid preload can prevent hypotension during elective cesarean section under SA.

## Methods

### Study design

This review was presented according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines.<sup>[14]</sup> Our study was registered on PROSPERO, with a registration number of CRD42020191758. The selection of literature was based on the following inclusion criteria:

**Participants:** Healthy women with normal term pregnancy receiving elective cesarean section under SA.

**Intervention:** Colloid preload given to the parturients receiving elective cesarean section under SA.

**Comparator:** Instead of colloid preload, the parturients will get fluid coload when receiving elective cesarean section under SA.

**Outcomes:** The primary outcome was the incidence of hypotension and severe hypotension. Hypotension was defined as a decrease of more than 20% from the baseline in systolic blood pressure (SBP) <90 mmHg. Severe hypotension was defined as a decrease of more than 30% from the baseline in SBP, or SBP <80 mmHg. The secondary outcomes included the lowest SBP, the maximal heart rate (HR), the intra-operative needs of ephedrine and phenylephrine, the incidence of nausea and/or vomiting, umbilical arterial pH, and Apgar scores at 1 min and 5 min after birth.

**Type of studies:** Published randomized controlled trials (RCTs).

**Exclusion criteria:** The intervention group or control group was set to apply vasoactive drugs or other treatments from the beginning of anesthesia to the end of the operation continuously; studies showed no relevant outcomes mentioned above; study published in a non-English language.

### Data sources and search strategies

The literature search was based on the following electronic databases from their inception dates to May 2020: PubMed, EMBASE, and Cochrane Library. The following are the keywords searched: colloid, preload, spinal anesthesia, and cesarean section. Synonyms, including succinylated gelatin,

hydroxyethyl starch, HES, 2-hydroxyethyl starches, hydroxyethyl starch 130-0.4, hydrocolloids, preloading, cesarean delivery, abdominal delivery, C-section, and post-cesarean section, were also searched.

### Selection of articles and extraction of data

Two independent investigators reviewed each title and abstract to eliminate all irrelevant clinical trials and identify the potentially relevant publications. The latter in turn were thoroughly analyzed to select those which can meet the inclusion criteria mentioned above. All discrepancies were analyzed and verified again by a third investigator. After that, studies were evaluated for eligibility and quality. Data analysis was double-checked to avoid any possible transcription errors. The following data were extracted: author, publication year, country, sample size, study design (randomization, blind, allocation concealment, and follow-up), anesthetic method, interventions, and outcome measures of interest, etc. Additional elements of information were requested from authors via email if the required data were not available from the articles.

### Assessment of the risk of bias in individual studies

The Cochrane Collaboration tool was used independently by two researchers to assess randomization bias, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. Studies were classified as “low,” “unclear,” or “high risk” of bias according to each of these six criteria, and consensus was reached through discussions among the three reviewers, and when consensus could not be reached, “unclear risk of bias” was the label given. Detailed criteria for making judgments about the risk of bias from each of the items in the tool are available in the Cochrane Handbook.

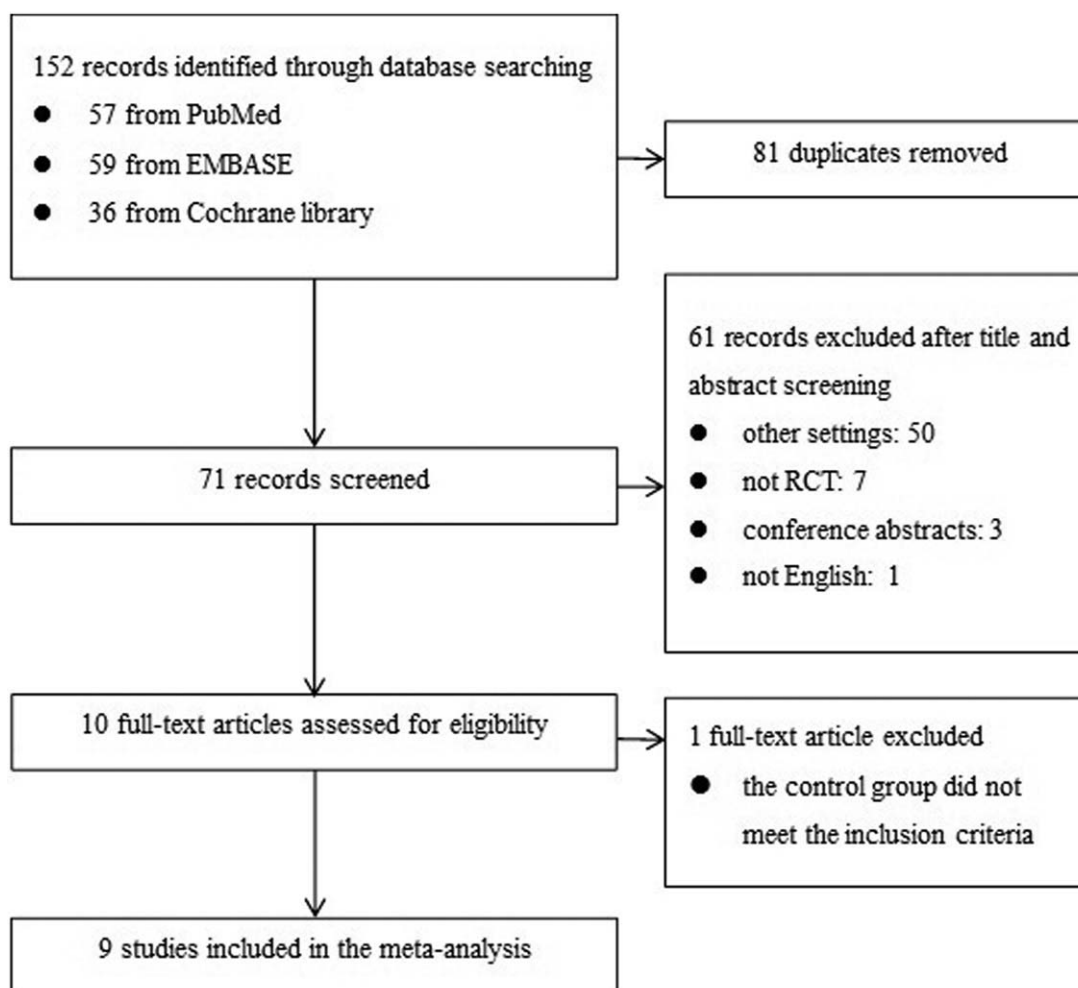
### Statistical analysis

Review Manager 5.3 (RevMan 5.3) was used for the statistical analysis. For continuous data, mean difference (MD) with 95% confidence intervals (CIs) was used; for dichotomous outcomes, odds ratio (OR) with 95% CIs was used. A random-effects model was used in this meta-analysis. We evaluated the statistical heterogeneity of the results with the Chi-squared test and the  $I^2$  statistic.  $I^2$  values which were <25%, 25% to 50%, or >75% were defined as indicating low, moderate, and high heterogeneity respectively. A  $P$  value of <0.05 was considered to be statistically significant. If data were reported as a median or range, we used formulas to calculate the mean and standard deviation (SD).<sup>[15,16]</sup>

## Results

### Study selection and characteristics

The search strategy identified 152 articles, after which 71 were selected by title and abstract screen after duplicates were removed. Following an initial evaluation, 61 articles were excluded: 50 articles were other settings



**Figure 1:** The PRISMA flow diagram of the study selection. PRISMA: Preferred reporting items for systematic reviews and meta-analysis; RCT: Randomized controlled trial.

(the authors discussed other topics), seven were not RCTs, three were conference abstracts, and one was not in English. Ten articles were selected for full-text review, after which nine articles were finally selected.<sup>[17-25]</sup> The flow diagram is shown in Figure 1.

Nine trials with 871 patients were eligible for this study. These articles were published from 2001 to 2019 with sample sizes ranging from 36 to 205. All trials enrolled healthy parturients who were scheduled for elective surgery and applied SA for elective cesarean section: two trials<sup>[22,24]</sup> from India, two<sup>[23,25]</sup> from Egypt, one<sup>[17]</sup> from China, one<sup>[18]</sup> from Japan, one<sup>[19]</sup> from America, one<sup>[20]</sup> from Singapore, and one<sup>[21]</sup> from Lebanon.

In three trials,<sup>[17,18,20]</sup> the infusion volume of intervention groups was set as 15 mL/kg colloid preload, two<sup>[22,24]</sup> as 10 mL/kg, and the other four as<sup>[19,21,23,25]</sup> 500 mL. As for the control groups, the infusion methods were set as 15 mL/kg colloid coload in two trials,<sup>[18,20]</sup> 10 mL/kg colloid coload in two trials,<sup>[22,24]</sup> 500 mL colloid coload in two trials,<sup>[19,21]</sup> and 1000 mL crystalloid coload in two trials.<sup>[23,25]</sup> Another trial did not specify the amount of crystalloid coload in the control group.<sup>[17]</sup>

Eight trials<sup>[17-19,21-25]</sup> recorded the number of patients with hypotension throughout the surgery, among which three trials<sup>[21,23,25]</sup> were recorded as severe hypotension. As for the other hemodynamic variables, five trials<sup>[18-22]</sup> recorded the lowest intra-operative SBPs, and two<sup>[21,22]</sup> recorded the maximal intra-operative HRs. With regard to intra-operative needs of vasoactive agents, four trials<sup>[18,21,24,25]</sup> reported the needs for ephedrine, and three<sup>[20-22]</sup> reported the needs for phenylephrine. In addition, six trials<sup>[17,19-21,23,25]</sup> showed the incidence of nausea and/or vomiting during surgery. For neonatal outcomes, umbilical arterial pH was analyzed in seven trials,<sup>[17-23]</sup> and Apgar scores were analyzed in four trials.<sup>[19,21,23,25]</sup> The characteristics of the RCTs included in the meta-analysis are summarized in Table 1.

### Risk of bias in studies

The risk of bias assessment is presented in Figure 2A, and the risk of bias summary is shown in Figure 2B. Overall, most studies had a low or unclear risk of bias, and all studies were RCTs. Two studies,<sup>[17,19]</sup> however, had high risks of bias due to blinding of participants and personnel.

**Table 1: Characteristics of included studies.**

Study (year)	Country	Number of patients	Interventions		Outcomes data available for meta-analysis								
			Type of colloid	Volume of colloid	Hypotension	Severe hypotension	Lowest SBPs	Maximal HRs	Needs of ephedrine	Needs of phenylephrine	Nausea and/or vomiting	Umbilical artery pH	Apgar scores
Ngan Kee <i>et al</i> <sup>[17]</sup> (2001)	China	68	Succinylated gelatin	15 mL/kg	✓						✓	✓	
Nishikawa <i>et al</i> <sup>[18]</sup> (2007)	Japan	36	HES	15 mL/kg	✓		✓			✓			✓
Carvalho <i>et al</i> <sup>[19]</sup> (2009)	America	46	HES	500 mL	✓		✓				✓	✓	✓
Siddik-Sayyid SM <i>et al</i> <sup>[21]</sup> (2009)	Lebanon	178	HES	500 mL	✓	✓	✓	✓	✓	✓	✓	✓	✓
Teoh <i>et al</i> <sup>[20]</sup> (2009)	Singapore	40	HES	15 mL/kg			✓			✓	✓	✓	
Varshney and Jain <sup>[22]</sup> (2013)	India	40	HES	10 mL/kg	✓		✓	✓		✓		✓	
Tawfik <i>et al</i> <sup>[23]</sup> (2014)	Egypt	205	HES	500 mL	✓	✓					✓	✓	✓
Arora <i>et al</i> <sup>[24]</sup> (2015)	India	60	HES	10 mL/kg	✓				✓				
Tawfik <i>et al</i> <sup>[25]</sup> (2019)	Egypt	198	HES	500 mL	✓	✓			✓		✓		✓

HR: Heart rate; HES: Hydroxyethyl starch; SBP: Systolic blood pressure.

**Incidence of hypotension**

As shown in Figure 3A, the incidence of hypotension was analyzed in eight studies,<sup>[17-19,21-25]</sup> including a total of 831 patients. The results indicated that there were no differences between the colloid preload group and control group (OR 0.83, 95% CI 0.53 to 1.28,  $P = 0.39$ ). Furthermore, three studies<sup>[21,23,25]</sup> showed that colloid preload might not affect the incidence of severe hypotension (OR 0.88, 95% CI 0.51 to 1.53,  $P = 0.66$ ) [Figure 3B].

Colloid preload was not given to the parturients in the control group. Six selected studies<sup>[18-22,24]</sup> used colloid coload in the control groups, among which five<sup>[18,19,21,22,24]</sup> reported the incidence of hypotension. The results showed that there were no differences between colloid preload and coload regimens (OR 0.81, 95% CI 0.51 to 1.30,  $P = 0.39$ ).

In addition, we analyzed the effects of different colloid volume preload on the incidence of hypotension. The subgroup results showed that there were no differences between the colloid preload group and control group whether the infusion volume was set as 500 mL<sup>[19,21,23,25]</sup> (OR 1.07, 95% CI 0.69 to 1.65,  $P = 0.76$ ) or 10 mL/kg<sup>[22,24]</sup> (OR 0.68, 95% CI 0.28 to 1.67,  $P = 0.40$ ). However, two studies<sup>[17,18]</sup> demonstrated that 15 mL/kg colloid preload can significantly reduce the occurrence of hypotension (OR 0.32, 95% CI 0.13 to 0.77,  $P = 0.01$ ) [Figure 3C].

**Hemodynamic variables**

The lowest intra-operative SBPs are shown in Figure 4A. Five studies<sup>[18-22]</sup> of 340 patients found no significant differences between two groups (MD = 1.95 mmHg, 95% CI -0.65 to 4.55,  $P = 0.14$ ).

The maximal intra-operative HRs are shown in Figure 4B. Two studies<sup>[21,22]</sup> of 218 patients found no significant differences between two groups (MD = -3.10 beats/min, 95% CI -7.41 to 1.21,  $P = 0.16$ ).

**Intra-operative needs of vasoactive agents**

Four studies<sup>[18,21,24,25]</sup> compared the intra-operative needs of ephedrine between the colloid preload and control groups. The results showed that there were no significant decreases in the needs of ephedrine in patients receiving colloid preload (MD = 0.08 mg, 95% CI -0.50 to 0.66,  $P = 0.79$ ) [Figure 5A].

Three studies<sup>[20-22]</sup> recorded the intra-operative needs of phenylephrine for the colloid preload and control groups. The results showed that there were no differences between the two groups. (MD = 15.04 µg, 95% CI -65.82 to 95.90,  $P = 0.72$ ) [Figure 5B].

**Incidence of nausea and/or vomiting**

Figure 6 shows the results about the incidence of nausea and/or vomiting for the two groups. Six of the included studies<sup>[17,19-21,23,25]</sup> reported this endpoint. No differences were found between the two groups (OR 0.84, 95% CI 0.50 to 1.40,  $P = 0.50$ ).

**Neonatal outcomes**

**Umbilical artery pH**

Data from seven studies<sup>[17-23]</sup> showed that the umbilical arterial pH was significantly lower in the colloid preload group (MD = -0.01, 95% CI -0.02 to -0.00,  $P = 0.04$ ) [Figure 7].

**Apgar scores**

Apgar scores were analyzed in four studies<sup>[19,21,23,25]</sup>, and formulas<sup>[15,16]</sup> were used to calculate the mean and SD through the values for median and range reported in the articles. Apgar scores at 1 min (MD = 0.01, 95% CI -0.09 to 0.12,  $P = 0.83$ ) [Figure 8A] and 5 min (MD = 0.00, 95% CI -0.04 to 0.04,  $P = 1.00$ ) [Figure 8B] after birth were not influenced by colloid preload.



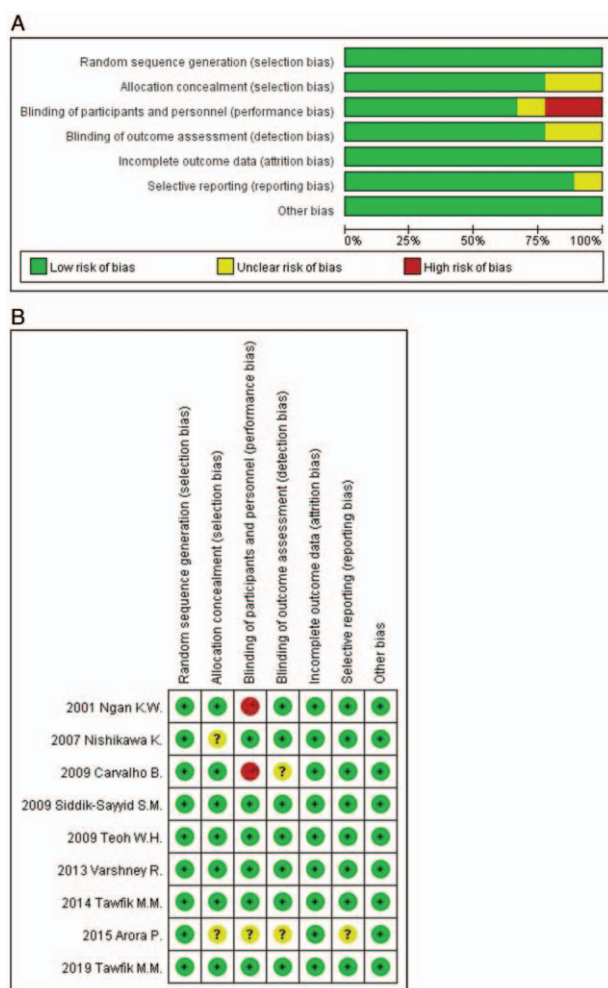


Figure 2: The risk of bias in studies. (A) Assessment and (B) summary.

**Discussion**

This study intended to study the effects of colloid preload on the incidence of hypotension caused by SA during cesarean section. The findings of this systematic review and meta-analysis suggest that currently published evidences do not favor the colloid preload in elective cesarean section, in terms of preventing hypotension, or improving other hemodynamic variables and perinatal outcomes.

Hypotension is mainly caused by SA and supine hypotension syndrome. In included studies, all the participants laid supine with a slight left lateral tilt to prevent supine hypotension syndrome. The supine position prevents the well blood-returning to the heart of the mother. Even if the blood volume increases, it will cover up the effects of reducing the incidence of hypotension. A research suggests that more studies are needed on the prevention of hypotension, and focusing only on the type and effects of preloading liquid cannot effectively remove or prevent the hypotension following SA.<sup>[26]</sup>

Colloid preload was given to patients in all intervention groups in all nine studies. There were two types of colloid

used in the studies, succinylated gelatin was employed in one study,<sup>[17]</sup> and hydroxyethyl starch (HES) in eight.<sup>[18-25]</sup> The volume of colloid preload was not the same in each study; therefore, subgroup analyses were conducted to ascertain if it has an impact on the results. In three studies,<sup>[17,18,20]</sup> the infusion volume was set as 15 mL/kg, two<sup>[22,24]</sup> as 10 mL/kg, and the other four as<sup>[19,21,23,25]</sup> 500 mL. The three subgroup analyses showed that 15 mL/kg colloid preload can reduce the incidence of hypotension, while 500 mL or 10 mL/kg cannot. The average weight of pregnant women is about 70 kg in the included studies, and the blood volume accounts for 7% to 8% of the body weight, which is equivalent to 4.9 to 5.6 L. If the preload volume is 500 mL or 10 mL/kg, it accounts for about 10% to 15% of the blood volume, and thus the volume of preloaded colloid was not enough to compensate for the decrease in the amount of venous return and cardiac output. Further, the results are in line with Davies' study, which proved that 10 mL/kg of colloid solution was significantly more effective than 5 mL/kg in preventing the development of hypotension following SA,<sup>[27]</sup> meaning that a larger volume of liquid is more conducive to improving hemodynamic variables. Moreover, it should be noted that 15 mL/kg colloid infused 15 to 20 min before the anesthesia is at the upper end of the range of volumes investigated previously.<sup>[17]</sup> It may cause heart failure if the preload volume exceeds this range in clinical practice. So, such a large-volume infusion is not recommended in cesarean sections by this research, and whether this infusion strategy is appropriate for parturients remains still to be studied. We moderately recommend that the volume of colloid preload which is based on the patient's physical condition and weight, combined with crystalloid and/or prophylactic vasopressors, is the most appropriate fluid regimen.

In addition, we compared the time of colloid infusion of two groups. In six included studies,<sup>[18,19,21,23-25]</sup> where colloid coload was used in the control groups, it was found that colloid preload was similarly effective in reducing hypotension when compared with colloid coload in the cesarean section. It means that if the amount of fluid infusions is the same in two groups throughout the operation, only changing the time of colloid infusion (before or after anesthesia) cannot effectively avoid the occurrence of hypotension.

As for the secondary outcomes, there were no statistically significant differences between the colloid preload and control groups with respect to the lowest SBPs or the maximal HRs, as well as the intra-operative dose of ephedrine and phenylephrine. In all the included studies, ephedrine or phenylephrine was administered if hypotension occurred. So, the needs for vasoactive agents in the two groups were directly related to the occurrence of hypotension.

Furthermore, outcomes such as nausea and/or vomiting in the patients of both groups were also evaluated, indicating that there were no statistically significant differences between the colloid preload and control groups. Hypotension that occurs during SA is one of the most important etiological factors for intra-operative nausea and/or vomiting, because hypotension leads to gut ischemia and release of emetogenic substances such as serotonin from

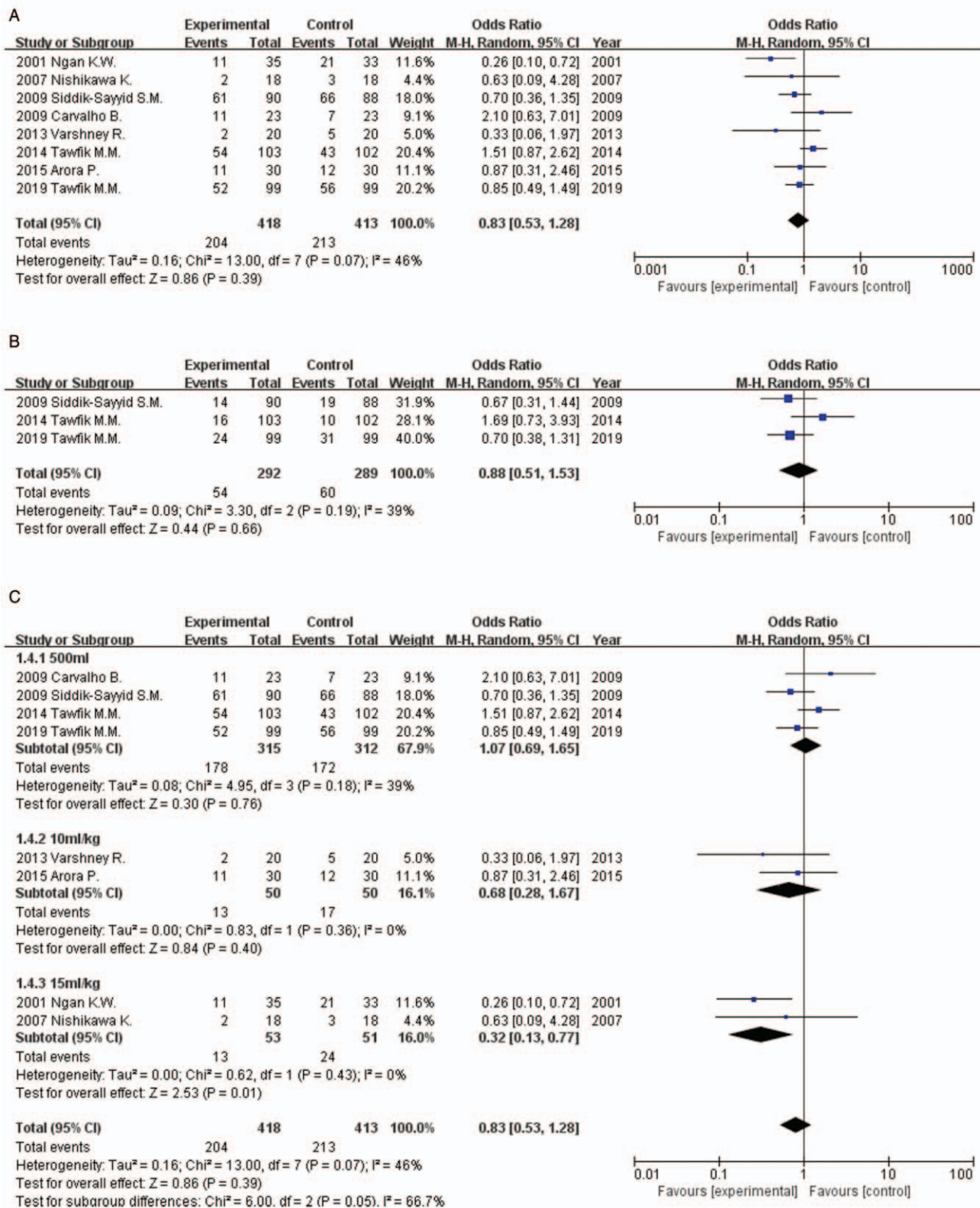


Figure 3: Forest plot for intra-operative hypotension. (A) Hypotension, (B) severe hypotension; and (C) hypotension in subgroup analyses. CI: Confidence interval.



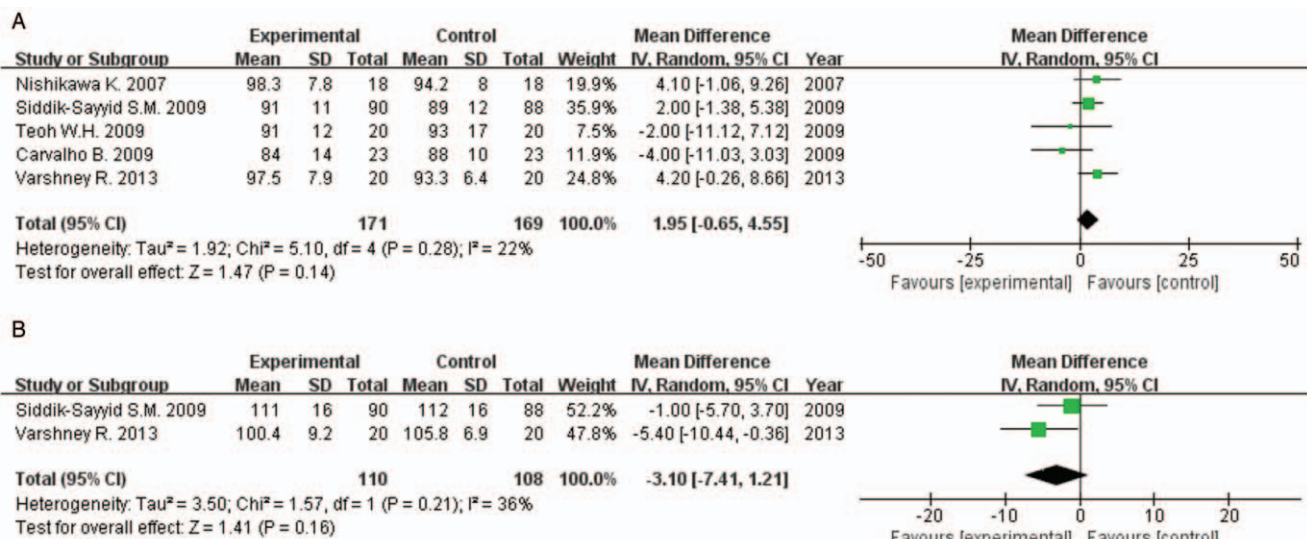


Figure 4: Forest plot for the hemodynamic variables. (A) Lowest intra-operative SBPs and (B) maximal intra-operative HRs. CI: Confidence interval; SD: Standard deviation.

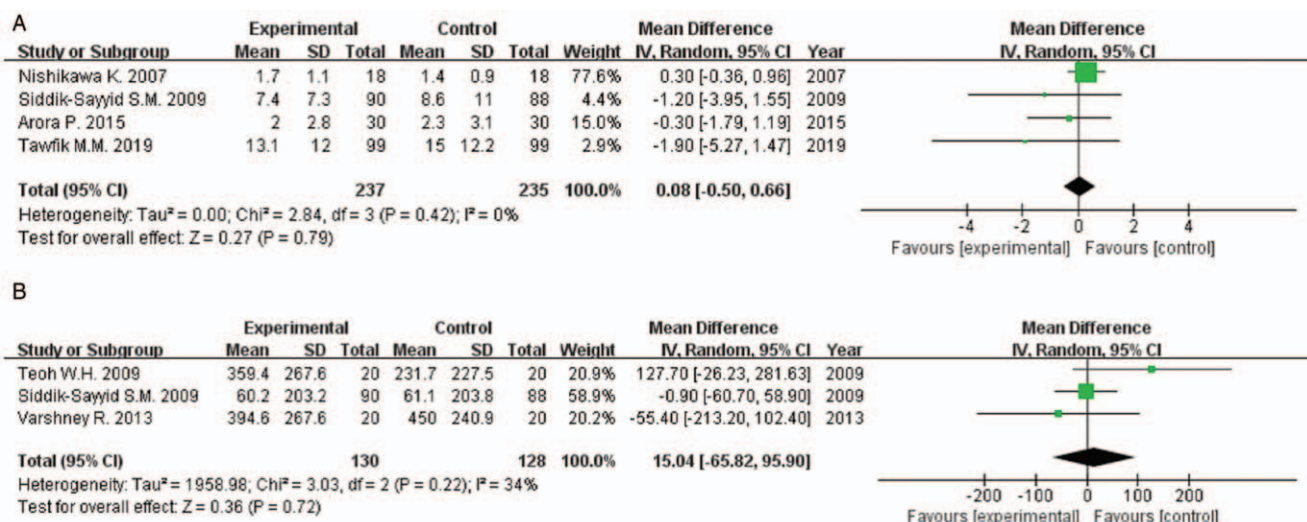


Figure 5: Forest plot for needs of vasoactive agents. (A) Ephedrine and (B) phenylephrine. CI: Confidence interval; SD: Standard deviation.

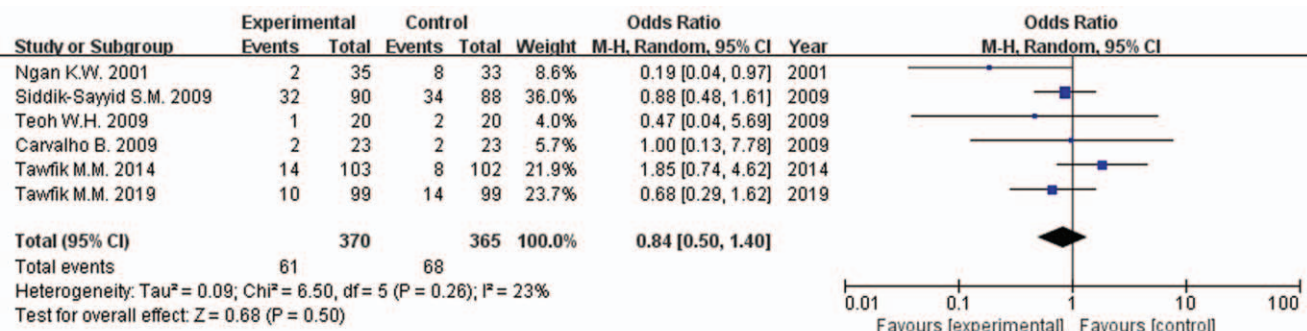


Figure 6: Forest plot for the incidence of nausea and/or vomiting. CI: Confidence interval.

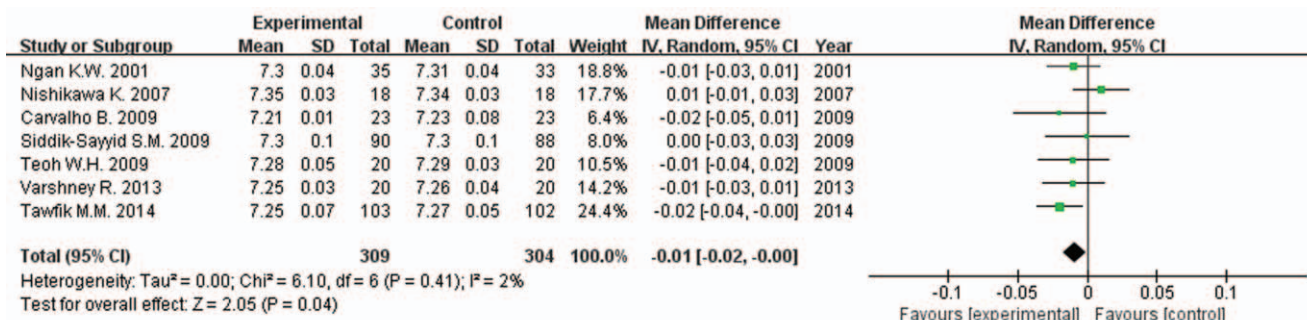


Figure 7: Forest plot for umbilical artery pH. CI: Confidence interval; SD: Standard deviation.

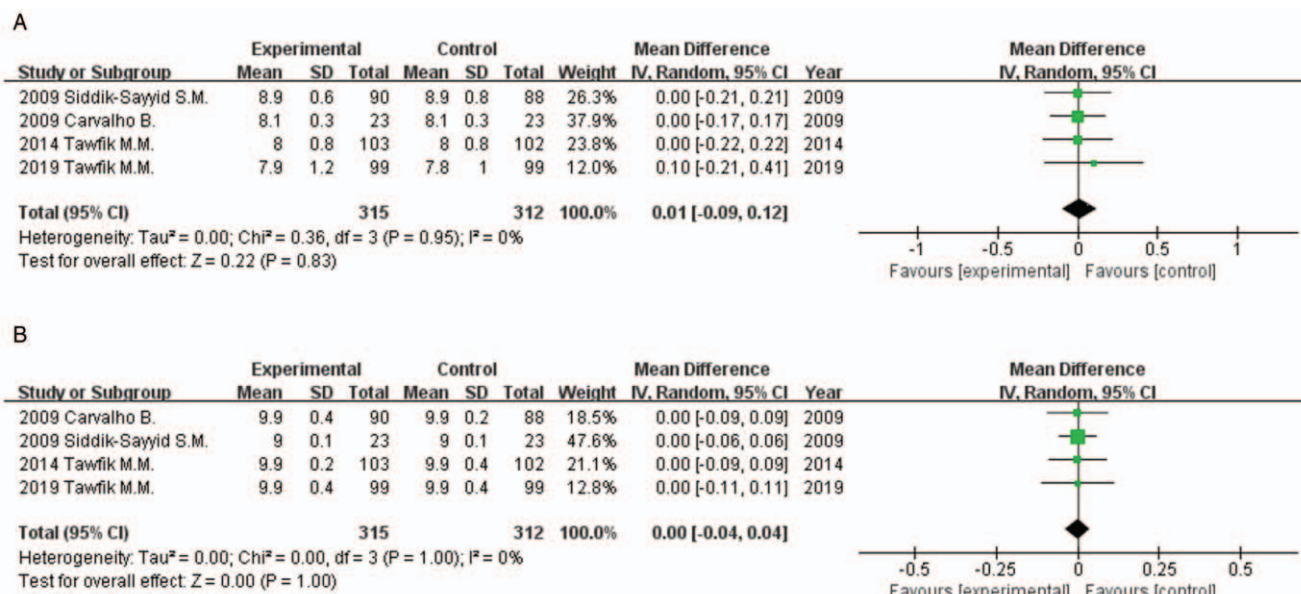


Figure 8: Forest plot for Apgar scores (A) 1 min and (B) 5 min. CI: Confidence interval; SD: Standard deviation.

the intestine.<sup>[28]</sup> Since there were no significant differences in the incidence of hypotension between the two groups, the results in the occurrence of nausea and/or vomiting are understandable. In this regard, the findings in our study were consistent with the studies conducted by Banerjee *et al*,<sup>[29]</sup> since there were no differences in nausea and/or vomiting between preload and coload regimens.

As for the neonatal outcomes, the results of Apgar scores showed no significant differences between the two groups in our study. However, the umbilical arterial pH was lower in the colloid preload group. Umbilical arterial pH is sensitive in detecting fetal hypoxia.<sup>[6]</sup> Umbilical arterial pH < 7.1 will be considered an abnormal outcome, which happened neither in the colloid preload groups nor the control groups. The umbilical arterial pH-values in the two groups are both at normal levels (pH > 7.1). The slight difference, although statistically significant, has little clinical significance for infants.

### Limitations

There were several limitations in this meta-analysis. First, participants or personnel were not blinded in the two studies, which may cause selection bias. Second, the differences in the amount and speed of fluids infusion among studies may have an impact on the final results. Finally, this study does not observe any beneficial effects of colloid preload regimens on long-term outcomes after cesarean delivery. Therefore, further studies with larger sample size, investigating the short-term as well as long-term outcomes in this population, are needed.

### Conclusions

In summary, colloid preload does not reduce the incidence of hypotension in women undergoing elective cesarean section. Only if the colloid preload volume attains 15 mL/kg, will the occurrence of hypotension be decreased. However, the safety of such a large-volume infusion needs



to be further studied. Since the above conclusions are limited by the number and quality of included studies, they necessitate verification through more high-quality studies.

### Funding

This work was supported by the Scientific Research Fund of China-Japan Friendship Hospital (No. 2017-RC-3).

### Conflicts of interest

None.

### References

- Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: systematic review and meta-analysis. *PLoS Med* 2018;15:e1002494. doi: 10.1371/journal.pmed.1002494.
- Gu C, Wang X, Zhang Z, Schwank S, Zhu C, Zhang Z, *et al.* Pregnant women's clinical characteristics, intrapartum interventions, and duration of labour in urban China: a multi-center cross-sectional study. *BMC Pregnancy Childbirth* 2020;20:386. doi: 10.1186/s12884-020-03072-x.
- Jaafarpour M, Taghizadeh Z, Shafiei E, Vasigh A, Sayehmiri K. The effect of intrathecal meperidine on maternal and newborn outcomes after cesarean section: a systematic review and meta-analysis study. *Anesth Pain Med* 2020;10:e100375. doi: 10.5812/aapm.100375.
- McDonnell NJ, Paech MJ, Muchatuta NA, Hillyard S, Nathan EA. A randomised double-blind trial of phenylephrine and metaraminol infusions for prevention of hypotension during spinal and combined spinal-epidural anaesthesia for elective caesarean section. *Anaesthesia* 2017;72:609–617. doi: 10.1111/anae.13836.
- Ferre F, Martin C, Bosch L, Kurrek M, Lairez O, Minville V. Control of spinal anesthesia-induced hypotension in adults. *Local Reg Anesth* 2020;13:39–46. doi: 10.2147/LRA.S240753.
- Ni HF, Liu HY, Zhang J, Peng K, Ji FH. Crystalloid coload reduced the incidence of hypotension in spinal anesthesia for cesarean delivery, when compared to crystalloid preload: a meta-analysis. *Biomed Res Int* 2017;2017:3462529. doi: 10.1155/2017/3462529.
- Khosravi F, Alishahi M, Khanchemehr Y, Jarineshin H. A comparison between the effects of preloading with ringer's solution and voluven on hemodynamic changes in patients undergoing elective cesarean section under spinal anesthesia. *Med Arch* 2019;73:44–48. doi: 10.5455/medarch.2019.73.44-48.
- Humphries A, Mirjalili SA, Tarr GP, Thompson JMD, Stone P. Hemodynamic changes in women with symptoms of supine hypotensive syndrome. *Acta Obstet Gynecol Scand* 2020;99:631–636. doi: 10.1111/aogs.13789.
- Macarthur A, Riley ET. Obstetric anesthesia controversies: vasopressor choice for postspinal hypotension during cesarean delivery. *Int Anesthesiol Clin* 2007;45:115–132. doi: 10.1097/AIA.0b013e31802b8d53.
- Alimian M, Mohseni M, Safaiean R, Faiz SH, Majedi MA. Comparison of hydroxyethyl starch 6% and crystalloids for preloading in elective caesarean section under spinal anesthesia. *Med Arch* 2014;68:279–281. doi: 10.5455/medarch.2014.68.279-281.
- Pellegrini JE. Treatment and prevention of spinal-induced hypotension in the cesarean section patient: what does the evidence say? *Annu Rev Nurs Res* 2017;35:159–178. doi: 10.1891/0739-6686.35.159.
- Ripolles MJ, Espinosa A, Hurtado EM, Francés RC, Pérez RN, Gurumeta AA, *et al.* Colloids versus crystalloids in the prevention of hypotension induced by spinal anesthesia in elective cesarean section. A systematic review and meta-analysis. *Minerva Anesthesiol* 2015;81:1019–1030.
- Lewis SR, Pritchard MW, Evans DJ, Butler AR, Alderson P, Smith AF, *et al.* Colloids versus crystalloids for fluid resuscitation in critically ill people. *Cochrane Database Syst Rev* 2018;8:CD000567. doi: 10.1002/14651858.CD000567.pub7.
- Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1. doi: 10.1186/2046-4053-4-1.
- Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res* 2018;27:1785–1805. doi: 10.1177/0962280216669183.
- Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol* 2014;14:135. doi: 10.1186/1471-2288-14-135.
- Ngan Kee WD, Khaw KS, Lee BB, Ng FF, Wong MM. Randomized controlled study of colloid preload before spinal anaesthesia for caesarean section. *Br J Anaesth* 2001;87:772–774. doi: 10.1093/bja/87.5.772.
- Nishikawa K, Yokoyama N, Saito S, Goto F. Comparison of effects of rapid colloid loading before and after spinal anesthesia on maternal hemodynamics and neonatal outcomes in cesarean section. *J Clin Monit Comput* 2007;21:125–129. doi: 10.1007/s10877-006-9066-4.
- Carvalho B, Mercier FJ, Riley ET, Brummel C, Cohen SE. Hetastarch co-loading is as effective as pre-loading for the prevention of hypotension following spinal anesthesia for cesarean delivery. *Int J Obstet Anesth* 2009;18:150–155. doi: 10.1016/j.ijoa.2008.12.006.
- Teoh WHL, Sia ATH. Colloid preload versus coload for spinal anesthesia for cesarean delivery: the effects on maternal cardiac output. *Anesth Analg* 2009;108:1592–1598. doi: 10.1213/ane.0b013e31819e016d.
- Siddik-Sayyid SM, Nasr VG, Taha SK, Zbeide RA, Shehade JM, Al AAA, *et al.* A randomized trial comparing colloid preload to coload during spinal anesthesia for elective cesarean delivery. *Anesth Analg* 2009;109:1219–1224. doi: 10.1213/ane.0b013e3181b2bd6b.
- Varshney R, Jain G. Comparison of colloid preload versus coload under low dose spinal anesthesia for cesarean delivery. *Anesth Essays Res* 2013;7:376–380. doi: 10.4103/0259-1162.123248.
- Tawfik MM, Hayes SM, Jacoub FY, Badran BA, Gohar FM, Shabana AM, *et al.* Comparison between colloid preload and crystalloid coload in cesarean section under spinal anesthesia: a randomized controlled trial. *Int J Obstet Anesth* 2014;23:317–323. doi: 10.1016/j.ijoa.2014.06.006.
- Arora P, Singh RM, Kundra S, Gautam PL. Fluid administration before caesarean delivery: does type and timing matter? *J Clin Diagn Res* 2015;9:UC01–UC04. doi: 10.7860/JCDR/2015/12083.6008.
- Tawfik MM, Tarbay AI, Elaidy AM, Awad KA, Ezz HM, Tolba MA. Combined colloid preload and crystalloid coload versus crystalloid coload during spinal anesthesia for cesarean delivery: a randomized controlled trial. *Anesth Analg* 2019;128:304–312. doi: 10.1213/ANE.0000000000003306.
- Saghafinia M, Jalali A, Eskandari M, Eskandari N, Lak M. The effects of hydroxyethyl starch 6% and crystalloid on volume preloading changes following spinal anesthesia. *Adv Biomed Res* 2017;6:115. doi: 10.4103/abr.abr\_151\_16.
- Davies P, French GW. A randomised trial comparing 5 mL/kg and 10 mL/kg of pentastarch as a volume preload before spinal anaesthesia for elective caesarean section. *Int J Obstet Anesth* 2006;15:279–283. doi: 10.1016/j.ijoa.2006.03.009.
- Balki M, Carvalho JCA. Intraoperative nausea and vomiting during cesarean section under regional anesthesia. *Int J Obstet Anesth* 2005;14:230–241. doi: 10.1016/j.ijoa.2004.12.004.
- Banerjee A, Stocche RM, Angle P, Halpern SH. Preload or coload for spinal anesthesia for elective cesarean delivery: a meta-analysis. *Can J Anaesth* 2010;57:24–31. doi: 10.1007/s12630-009-9206-7.

**How to cite this article:** Gong RS, Liu XW, Li WX, Zhao J. Effects of colloid preload on the incidence of hypotension in spinal anesthesia for cesarean section: a systematic review and meta-analysis. *Chin Med J* 2021;134:1043–1051. doi: 10.1097/CM9.0000000000001477