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Research article

Left-lateral position versus phenylephrine prophylactic treatment for hypotension following combined spinal epidural anesthesia during elective cesarean section

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ABSTRACT

Background: Hypotension is one of the most common and dangerous complications following combined spinal epidural anesthesia during elective cesarean delivery. Many methods are used to prevent or treat the hypotension with pharmacological or non-pharmacological measures. Our aim was to assess left-lateral position and phenylephrine prophylactic treatment for the prevention or treatment of maternal hypotension.

Methods: A total of 127 pregnant women were enrolled to be analyzed. The primary outcome measure was the incidence of maternal hypotension and secondary outcome measures included maternal demographic characteristics, anesthesia-to-incision time interval, birthweight and Apgar scores.

Results: The incidence of hypotension was 65.4 % in sequential reactive treatment and only 11.3 % achieved complete anesis after left-lateral position, significantly higher than 17.4 % in left-lateral position combined phenylephrine prophylactic treatment ($P < 0.001$). The increasing in gestational age may decrease the hypotension risk ($P < 0.001$). There were no significantly differences with maternal age, gravidity, parity, BMI before pregnancy, BMI before cesarean section, anesthesia-to-incision time interval, birthweight and Apgar scores ($P > 0.05$). The univariate logistic regression analysis revealed a significant association between treatment and hypotension (OR 0.11, 95 % CI 0.05–0.27). After adjusting for confounding variables, the risk of hypotension was decreased in subjects with treatment (OR 0.1, 95 % CI 0.04–0.25; OR 0.15, 95 % CI 0.05–0.43; OR 0.16, 95 % CI 0.05–0.46). The results of stratified and interaction analyses of the association between treatment between treatment revealed no interactive role from maternal age, gravidity and BMI before cesarean section ($P > 0.05$).

Conclusions: Single use of left-lateral position had limited effective and left-lateral position combined prophylactic phenylephrine used may be much better to prevent or treat hypetension, but larger studies with more robust data are needed to confirm these findings.

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1. Introduction

Though combined spinal epidural anesthesia is often selected as a more acceptable and less risky method during elective cesarean delivery, hypotension is still one of the most common and dangerous complications which frequently followed combined spinal epidural anesthesia during cesarean section and causes both maternal and fetal/neonatal adverse effects [1,2]. The incidence of hypotension can be as high as 70–80 % when pharmacological prophylaxis was not used and 14.8 % experienced sustained spinal hypotension, even if prophylactic pharmacological or non-pharmacological measures were used before the appearance of hypotension, the incidence was also up to 34%–56 % [3–5].

Many methods are used to prevent or treat the maternal hypotension such as pharmacological treatment, non-pharmacological measures and fluid administration. Vasopressors were the most commonly used to prevent or treat the maternal hypotension [6–8]. But maternal positions and crystalloid pre-hydration were also used though there were limited evidences to support or clearly disprove [9–11].

Therefore, we performed this retrospective study to compare the totally different procedures used to prevent the maternal hypotension in two hospitals. One procedure was sequential reactive treatment performed in a particular sequence (when onset of hypotension, first, table tilted left laterally to 15°, continued hypotension, and then phenylephrine administered); Another procedure was maternal left-lateral position combined with phenylephrine prophylactic treatment (table tilted left laterally to 15° combined initial solution of norepinephrine administered, when onset of hypotension, solution of norepinephrine added). Our aim was to assess the two different procedures in their effectiveness for the prevention or treatment of maternal hypotension following combined spinal epidural anesthesia at elective cesarean section and evaluate the effect on maternal and fetal outcomes.

2. Methods

2.1. Study population

A retrospective study was performed between 1 January 2019 and April 30, 2021 at Shandong Province Maternal and Child Health Care Hospital and Qingdao Central Hospital. The common inclusion criteria were singleton pregnancy, gestational age >37 weeks, elective cesarean section, using combined spinal epidural anesthesia. Exclusion criteria were multiple pregnancy, urgent cesarean section, elevated blood pressure no matter the cause. An absolute blood pressure was got by measuring in the arm in a variety of body positions and hypotension was diagnosed by either '< 80 % baseline', or '< 100 mmHg OR < 80 % baseline'.

The characteristics of combined spinal epidural anesthesia were as follows: after the L3-4 vertebral interspace puncture was perfectly performed in the right-side position using a 25-G spinal needle, 2 ml of 7.5 mg/ml ropivacaine or 1.8 ml of 0.5 % bupivacaine was administered. And then, catheterization of epidural catheter was perfectly performed.

2.2. Procedures of preventing or treating maternal hypotension

Sequential reactive treatment used at Shandong Province Maternal and Child Health Care Hospital (Treatment 1).

The procedures of this treatment were performed by one anesthetist at Shandong Province Maternal and Child Health Care Hospital. After perfect combined spinal epidural anesthesia, blood pressure, heart rate and oxyhemoglobin saturation of the pregnancy women at a supine position were measured every 3 min. Hypotensive episode was defined as the period from onset of hypotension and then the table was tilted left laterally to 15°. If there were continued hypotension for 15–20 s after the table tilted, a dose of 80 μg

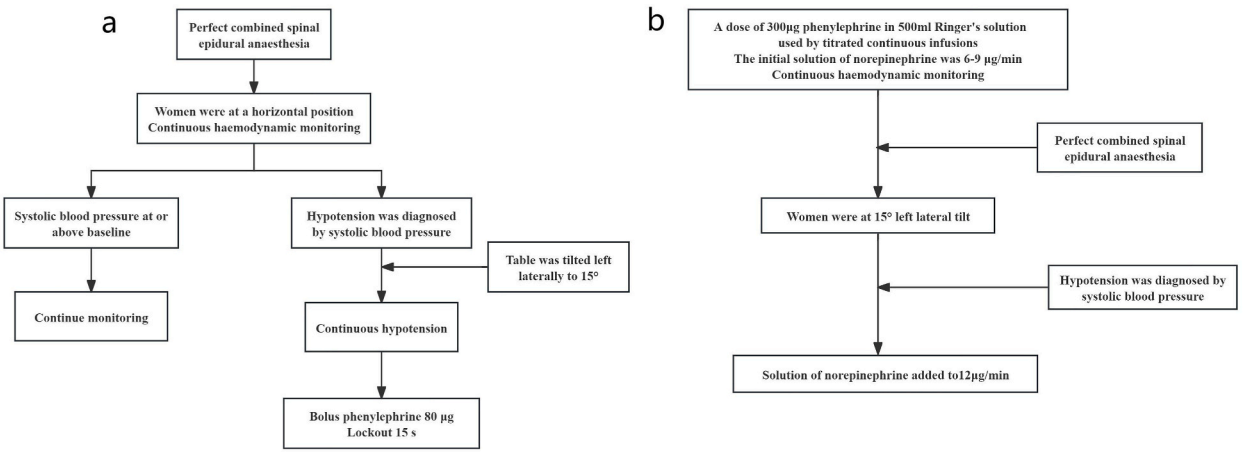

Fig. 1. a Schematic diagram of sequential reactive treatment used in the Department of Anesthesiology at Shandong Province Maternal and Child Health Care Hospital. b Schematic diagram of maternal left-lateral position combined phenylephrine prophylactic treatment used in the Department of Anesthesiology at Qingdao Central Hospital.

phenylephrine was administered (Fig. 1a).

Maternal left-lateral position combined phenylephrine prophylactic treatment used at Qingdao Central Hospital (Treatment 2).

The procedures were performed by one anesthetist at Qingdao Central Hospital. A dose of 300 μg phenylephrine in 500 ml Ringer's solution was used by titrated continuous infusions at the beginning of epidural puncture. The initial solution of norepinephrine was 6–9 μg/min as prophylactic measures and added to 12 μg/min lasting until delivery from the onset of hypotension as treatment. After perfect combined spinal epidural anesthesia, blood pressure, heart rate and oxyhemoglobin saturation of the pregnant women were measured every 3 min and the women were always at left-lateral position tilting to 15°until delivery (Fig. 1b).

2.3. Outcomes

The primary outcomes were the incidence of maternal hypotension after administration and the procedure of preventing or treating the maternal hypotension. The secondary outcome measures included age, gestational age, gravidity, parity, body mass index (BMI) before pregnancy and cesarean section, anesthesia-to-incision time interval, birthweight and Apgar scores.

2.4. Statistical analyses

All the analyses were performed with the statistical software packages R (http://www.R-project.org, The R Foundation) and Free Statistics software versions 1.3. Data are presented as mean ± standard deviation (SD) or median (interquartile range) for continuous variables, and as frequency or percentage for categorical variables. For baseline characteristics analysis, the statistical differences among groups were tested with *t*-test or one-way ANOVA for continuous variables and chi-square or fisher test for categorical variables. A two-tailed test was performed and $P < 0.05$ was considered statistically significant.

3. Results

One hundred and seventy-six women were assessed and 49 women were excluded because of multiple pregnancy, gestational age <37 weeks, epidural anesthesia and general anesthesia. A total of 127 women were enrolled to be analyzed (Fig. 2). Additional explanations for sequential reactive treatment was that only 6 of 53 (11.3 %) women with hypotension achieved complete anesis after left-lateral position.

3.1. Baseline characteristics between two groups

Characteristics of the patients at baseline were shown in Table 1. The incidence of hypotension was 65.4 % in sequential reactive treatment, and significantly higher than 17.4 % in left-lateral position combined phenylephrine prophylactic treatment ($P < 0.001$). The increasing in gestational age may decrease the hypotension risk ($P < 0.001$). There were no significantly differences with maternal age, gravidity, parity, BMI before pregnancy, BMI before cesarean section, anesthesia-to-incision time interval, birthweight and Apgar

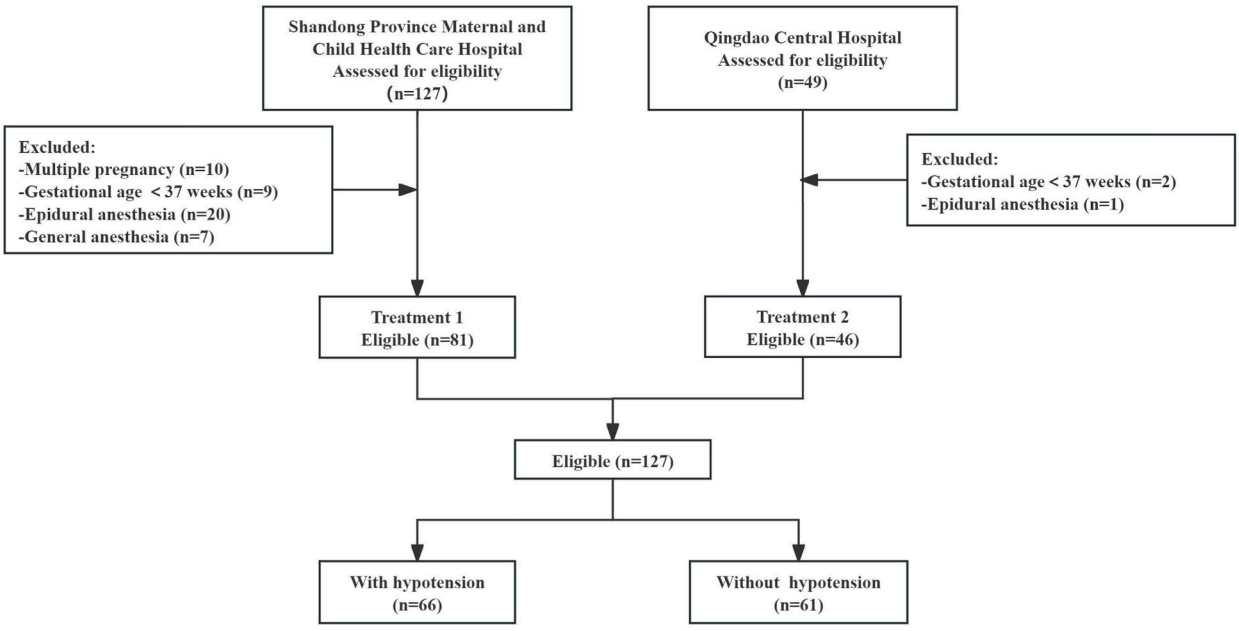

Fig. 2. Flow diagram of study.

Table 1
Characteristics of the patients at baseline.

Variables	With hypotension (n = 61)	Without hypotension (n = 66)	t/F/χ^2	P value
Age (years)	31.2 ± 4.0	32.0 ± 4.1	1.457	0.23
Gestational age (weeks)	38.7 ± 0.8	39.4 ± 1.1	13.631	<0.001
Gravidity (n)	2.0 (1.0, 3.0)	1.0 (1.0, 2.0)	3.594	0.058
Parity (n)	1.0 (0.0, 1.0)	0.0 (0.0, 1.0)	0.119	0.73
BMI before Caesarean section	29.9 ± 4.4	28.8 ± 3.3	2.201	0.14
BMI before pregnancy	24.0 ± 4.1	23.1 ± 3.5	1.902	0.17
anesthesia-to-incision time interval (min)	14.6 ± 4.1	15.9 ± 6.1	2.095	0.15
Treatment (n, %)			25.236	<0.001
1	53 (65.4)	28 (34.6)		
2	8 (17.4)	38 (82.6)		
Birthweight (g)	3450.2 ± 399.1	3553.3 ± 465.0	1.783	0.184
Apgar scores (n,%)				0.48[a]
9	1 (1.6)	0 (0)		
10	60 (98.4)	66 (100)		

[a] Fisher-test.

scores ($P > 0.05$).

3.2. Relationship between treatments and hypotension

The relationship between treatments and hypotension was presented in Table 2. The univariate logistic regression analysis revealed a significant association between treatment and hypotension (OR 0.11, 95 % CI 0.05–0.27). After adjusting for confounding variables, the risk of hypotension was decreased in subjects with treatment (OR 0.1, 95 % CI 0.04–0.25; OR 0.15, 95 % CI 0.05–0.43; OR 0.16, 95 % CI 0.05–0.46). Excellent robustnesses were revealed in logistic regression analyses evaluating the effects of treatment.

3.3. Stratified and interaction analyses of association between treatment and hypotension

The association between treatment and hypotension in stratified analysis was consistent with that in the multivariable logistic regression analysis. The stratified analysis demonstrated no statistically significant association between treatments in age ($P = 0.85$), gravidity ($P = 0.095$) and BMI before cesarean section ($P = 0.524$). The interaction analysis revealed no interactive role in the association between treatment and these variables (Fig. 3).

4. Discussion

During combined spinal epidural anesthesia, hypotension was caused by reduced venous return because of an increasing venous capacitance due to sympathetic block and aortocaval compression in the supine position. In this study, the procedure of combined spinal epidural including the use of drug and dose was one of the most commonly used methods. Vasopressors were usually given to healthy women to prevent hypotension during cesarean section with spinal anesthesia, but other added measures like left lateral tilt position were still in use [12,13]. The using methods, doses and timing of application of vasopressors and the using modes and timing of maternal position were variously [14].

In our study, we found that both treatments were safe and effective because there were no maternal and fetal/neonatal adverse effects in all women, but more women (65.4 %) experienced hypotension in sequential reactive treatment. These results suggested that prophylactic phenylephrine used by infusion decreased the incidence of hypotension. Though phenylephrine used by intermittent boluses or by infusion was both effective to prevent and treat spinal hypotension [13,15,16]. We also used multivariable logistic regression models to evaluate the two treatments and found that left-lateral position combined phenylephrine prophylactic treatment was much better than sequential reactive treatment.

Maternal positions, mainly refer to left lateral tilted position were also widely used though there were limited evidences to support or clearly disprove [9,10]. In our study, we also found that only 11.3 % of women experiencing hypotension achieved complete anesis

Table 2
Multivariable logistic regression models evaluating the association between treatment and hypotension.

Variable	crude.OR_95CI	crude.P_value	adj.OR_95CI	adj.P_value
Treatment 1	1(Ref)		1(Ref)	
Model1[a]	0.11 (0.05–0.27)	<0.001	0.1 (0.04–0.25)	<0.001
Model2[b]			0.15 (0.05–0.43)	<0.001
Model3[c]			0.16 (0.05–0.46)	0.001

a: Adjusted for Age, BMI before Caesarean section, BMI before pregnancy. b: Adjusted for Age, BMI before Caesarean section, BMI before pregnancy, Gestational age, Gravidity, Parity, Anesthesia-to-incision time interval. c: Adjusted for Age, BMI before Caesarean section, BMI before pregnancy, Gestational age, Gravidity, Parity, Anesthesia-to-incision time interval, Birthweight and Apgar scores.

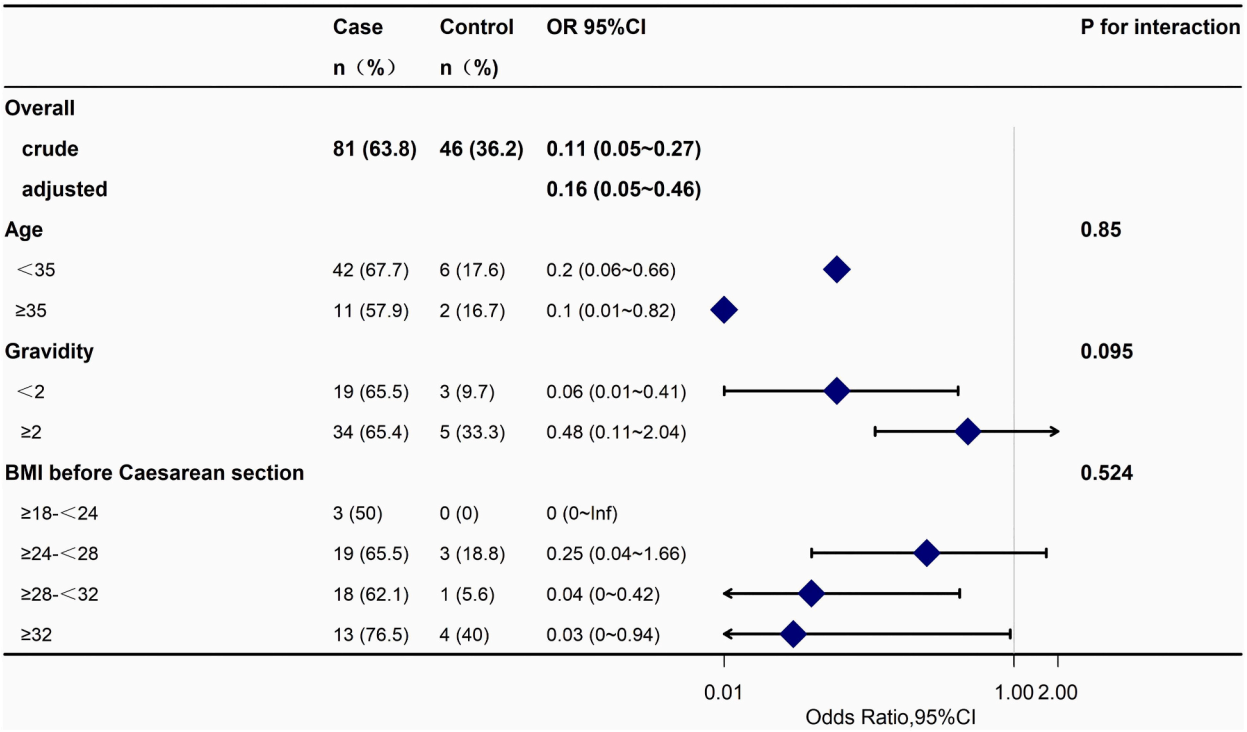

Fig. 3. The interaction analysis revealed no interactive role in the association between treatment and these variables.

after tilted left lateral to 15°. It showed that using left lateral tilted position alone did have some effect to prevent the maternal hypotension though just had limited effective. Therefore the key focus should be on the drug therapy. Ephedrine norepinephrine prophylactic bolus injection has the least impact on maternal and neonatal outcomes and intravenous ondansetron before spinal anesthesia significantly reduced the dose requirement of prophylactic norepinephrine infusion [17,18].

In this study, we found that the increasing in gestational age may decrease the hypotension risk, but we found no significant differences in other obstetrical elements. Thus, we performed stratified analyses and found that there were no significant difference in maternal age, gravidity and BMI before cesarean between the two treatments. It was reported that sensory height block anesthesia-to-incision time interval and anesthetist experience may be the identified risk factors for hypotension after spinal anesthesia [19]. Those factors need further elaboration.

There were some strengths of our study. Though this study was designed as retrospective case control study, there were no similar studies in the literature on this subject. We believed that the result and finding was sufficient and actual. However, there were some limitations in this study. Firstly, this study was a retrospective study which may be influenced by unmeasured, unnoticed and unaccounted bias and confounding, and then, may make it underpowered. Secondely, the sample size may be not large enough to identify a true difference. Thirdly, though it was not the single center setting, the combined spinal epidural anesthesia was performed with ropivacaine and bupivacaine and the effect may do not equipotent.

5. Conclusion

In conclusion, the incidence of hypotension was 65.4 % and only 11.3 % achieved complete anesis after left-lateral position, significantly higher than 17.4 % in left-lateral position combined phenylephrine prophylactic treatment. Single use of left-lateral position had limited effective and left-lateral position combined prophylactic phenylephrine used may be much better to prevent or treat hypetension. The effect of treatment was not moderated by maternal age, grabivity and BMI before cesarean section. But larger studies with more robust data are needed to confirm these findings.

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Ethics approval and consent to participate

This study was reviewed and approved by Ethics Committee of Shandong Province Maternal and Child Health Care Hospital, with

the approval number: SFYLL2020022 and Ethics Committee of Qingdao Central Hospital, with the approval number: KY202104301. Informed consent was not required for this study because this was a retrospective case control study and the data are anonymous.

Data availability statement

Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Songyuan Liu: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Shuzhi Luo:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Runzhi Jiang:** Investigation, Formal analysis, Data curation. **Shili Su:** Writing – review & editing, Visualization, Supervision, Software, Project administration, Methodology, Formal analysis, Conceptualization. **Mingqiang Zhao:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Project administration, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] N. Al-Husban, M.S. Elmuhtaseb, H. Al-Husban, et al., Anesthesia for cesarean section: retrospective comparative study, Int J Womens Health 13 (2021) 141–152.
[2] S.M. Kinsella, B. Carvalho, R.A. Dyer, et al., International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia, Anaesthesia 73 (1) (2018) 71–92.
[3] F.J. Mercier, M. Augè, C. Hoffmann, C. Fischer, A. Le Gouez, Maternal hypotension during spinal anesthesia for caesarean delivery, Minerva Anestesiol. 79 (1) (2013) 62–73.
[4] D. Knigin, A. Avidan, C.F. Weiniger, The effect of spinal hypotension and anesthesia-to-delivery time interval on neonatal outcomes in planned cesarean delivery, Am. J. Obstet. Gynecol. 223 (5) (2020) 747.e1–747.e13.
[5] B.I. Obasuyi, S. Fyneface-Ogan, C.N. Mato, A comparison of the haemodynamic effects of lateral and sitting positions during induction of spinal anaesthesia for caesarean section, Int. J. Obstet. Anesth. 22 (2) (2013) 124–128.
[6] M. Mohta, A. Garg, G.T. Chilkoti, et al., A randomised controlled trial of phenylephrine and noradrenaline boluses for treatment of postspinal hypotension during elective caesarean section, Anaesthesia 74 (7) (2019) 850–855.
[7] S. Xu, M. Mao, S. Zhang, et al., A randomized double-blind study comparing prophylactic norepinephrine and ephedrine infusion for preventing maternal spinal hypotension during elective cesarean section under spinal anesthesia: a CONSORT-compliant article, Medicine (Baltim.) 98 (51) (2019) e18311.
[8] M. Heesen, N. Hilber, K. Rijs, et al., A systematic review of phenylephrine vs. noradrenaline for the management of hypotension associated with neuraxial anaesthesia in women undergoing caesarean section, Anaesthesia 75 (6) (2020) 800–808.
[9] C. Cluver, N. Novikova, G.J. Hofmeyr, et al., Maternal position during caesarean section for preventing maternal and neonatal complications, Cochrane Database Syst. Rev. (3) (2013) CD007623.
[10] J.K. Mitra, J. Roy, P. Bhattacharyya, et al., Changing trends in the management of hypotension following spinal anesthesia in cesarean section, J. Postgrad. Med. 59 (2) (2013) 121–126.
[11] S.J. Jones, S.M. Kinsella, F.A. Donald, Comparison of measured and estimated angles of table tilt at Caesarean section, Br. J. Anaesth. 90 (1) (2003) 86–87.
[12] J.P. Fitzgerald, K.A. Fedoruk, S.M. Jadin, et al., Prevention of hypotension after spinal anaesthesia for caesarean section: a systematic review and network meta-analysis of randomised controlled trials, Anaesthesia 75 (1) (2020) 109–121.
[13] J.L. Fichter, K.E. Nelson, Optimal management of hypotension during cesarean delivery under spinal anesthesia, Adv. Anesth. 37 (2019) 207–228.
[14] W.D. Ngan Kee, S.W.Y. Lee, F.F. Ng, et al., Prophylactic norepinephrine infusion for preventing hypotension during spinal anesthesia for cesarean delivery, Anesth. Analg. 126 (6) (2018) 1989–1994.
[15] W.D. Ngan Kee, S.W. Lee, F.F. Ng, et al., Randomized double-blinded comparison of norepinephrine and phenylephrine for maintenance of blood pressure during spinal anesthesia for cesarean delivery, Anesthesiology 122 (4) (2015) 736–745.
[16] A. Doherty, Y. Ohashi, K. Downey, et al., Phenylephrine infusion versus bolus regimens during cesarean delivery under spinal anesthesia: a double-blind randomized clinical trial to assess hemodynamic changes, Anesth. Analg. 115 (6) (2012) 1343–1350.
[17] X. Xue, X. Lv, X. Ma, et al., Prevention of spinal hypotension during cesarean section: a systematic review and Bayesian network meta-analysis based on ephedrine, phenylephrine, and norepinephrine, J. Obstet. Gynaecol. Res. 49 (7) (2023) 1651–1662.
[18] Z.M. Sheng, H.Q. Sun, J.Q. Mao, et al., Comparative dose-response study on the infusion of norepinephrine combined with intravenous ondansetron versus placebo for preventing hypotension during spinal anesthesia for cesarean section: a randomised controlled trial, Int. J. Surg. 110 (2) (2024) 832–838.
[19] T. Shitemaw, B. Jemal, T. Mamo, L. Akalu, Incidence and associated factors for hypotension after spinal anesthesia during cesarean section at Gandhi Memorial Hospital Addis Ababa, Ethiopia, PLoS One 15 (8) (2020) e0236755.