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Special maternal care bundle to attenuate post-spinal hypotension in cesarean section: A randomized controlled clinical trial

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ABSTRACT

Background: This study aimed to assess the safety and efficacy of a special maternal care bundle as an alternative technique for the attenuation of hypotension following spinal anesthesia in parturients scheduled for CS.

Methods: This double-blinded, parallel-group, randomized trial enrolled 138 adult parturients who were scheduled for CS under spinal anesthesia. The patients were randomly allocated to two groups. In the care bundle group, 68 participants received a co-load of lactated Ringer's solution and ondansetron infusion during administration of spinal anesthesia with a slow rate intrathecal bupivacaine injection and a V-shaped supine position. While in the best practice group, 70 participants received a co-loaded lactated Ringer's solution during spinal anesthesia with early use of vasopressors and a left uterine tilting position. The primary outcome was the total ephedrine consumption. Secondary outcomes included the mean arterial blood pressure, heart rate, atropine usage, complications such as dizziness, nausea, and vomiting, as well as the baby's Apgar score.

Results: Special maternal care bundle significantly reduced the need and the total dose of ephedrine ($P = 0.042$). The mean arterial blood pressure was significantly less affected by maternal bundle care, but the reduction in heart rate, the need for atropine, the incidence of dizziness, nausea, vomiting, and the Apgar score were comparable in both groups.

Conclusion: The special maternal care bundle including co-load of lactated ringer, ondansetron 4 mg IV infusion, slow intrathecal injection and v-shaped positions can reduce the incidence of hypotension resulting from spinal anesthesia and ephedrine usage during CS.

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Care bundle; ephedrine; hypotension; multimodal; spinal anesthesia

1. Introduction

Spinal anesthesia carries a great risk of maternal hypotension. The prevalence of hypotension following spinal anesthesia during a cesarean section (CS) range from 7.4% to 74.1% [1,2]. Maternal hypotension not only causes unpleasant side effects, such as nausea and vomiting, but it also reduces the blood supply to the placenta, which results in a low Apgar score and fetal acidosis [3].

Spinal anesthesia-induced hypotension is the pathophysiological response to sympathectomy caused by the neuro-axial blockade. Peripheral vasodilatation and parasympathetic activation predominate. A pregnant uterus compresses the vena cava, and lower leg venous blood accumulation reduces cardiac output and venous return [2]. Furthermore, higher sympathetic block inversely decreases the compensatory mechanisms via baroreceptors resulting in cardioinhibitory reflexes, such as the Bezold-Jarisch reflex. Chemoreceptors located on cardiac vagal afferents are the site of this reflex, which is mediated by 5-HT or 5-HT3 agonists. As a result, hypotension, dizziness, vomiting, nausea, and bradycardia commonly occur with spinal anesthesia [4].

To avoid or lessen hypotension, many preventive strategies are performed, such as crystalloids, colloid pre-loading or co-loading, and vasopressor administration. Since then, numerous positioning techniques, including delayed supine positioning, left lateral tilting, lateral positioning during and after spinal blocks and head up and head down position after spinal blocks, have been studied [5,6]. However, the Cochrane database reviews [7,8] did not favor any positioning protocol over the other and no single best maneuver could be considered as the optimum approach to prevent hypotension induced by spinal anesthesia. Using the multimodal technique measure is supposed to prevent and treat spinal anesthesia-induced hypotension [2].

Care bundles are a collection of three to five practices that are supported by evidence. They have been consistently applied to raise the standard of care and have commonly been employed in healthcare settings to prevent and treat various medical diseases [9]. Ventilator-associated pneumonia, sepsis, and central

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line-associated bloodstream infection care bundles are well known in the field of critical care medicine [10,11]. Very few studies have yet looked at a particular care bundle in post-spinal hypotension during CS. This study aimed to assess the safety and efficacy of a special maternal care bundle as an alternative technique for the reduction of hypotension in parturients scheduled for CS under spinal anesthesia.

2. Methods

2.1. Ethical considerations

The ethical approval was obtained from the Ethical Committee of the Faculty of Medicine, Suez Canal University, Egypt (ID: 4876). Each participant was given signed consent after being informed of the study's objectives and methods. The information of each participant was kept private.

2.2. Study design, setting, and date

The study was carried out at the obstetric operating room (OR) of Suez Canal University Hospital, Egypt, between August and November 2022. This was a parallel-group, randomized, double-blinded trial with a registration number (Trial ID: NCT05468125) at the ClinicalTrials.gov.

2.3. Eligibility criteria

The present study included 138 adult parturients, aged from 21 to 40 years, with heights of 150–180 cm, body mass index not more than 35 kg/m^2, who had singleton uncomplicated pregnancies with the American Society of Anesthesiology physical status (ASA) grades I or II and were scheduled for elective CS under spinal anesthesia. We excluded patients refusing spinal anesthesia or participation in the study or suffering from an allergic history to the medications being utilized, diabetes mellitus, chronic hypertension, cardiac diseases, bronchial asthma, bleeding disorders, as well as those with body mass index more than 35 kg/m^2. Patients with marked deformities or infections at the site of spinal injection were also excluded.

2.4. Randomization, allocation concealment, and blinding

The participants were divided into two groups at random using computer-generated randomization software. The allocation concealment was ensured by codes contained in sequentially numbered sealed opaque envelopes. The allocation sequence was kept from the physician evaluating and enrolling subjects, and the envelopes were impermeable to bright light. The participant's name and hospital admission numbers were written on the envelope to prevent interfering with the allocation sequence. The information was written on the allocation card inside the envelope using carbon paper. Only after all baseline tests had been completed by the registered subjects. The corresponding envelopes were opened. The anesthesiologist who collected the data and the outcome evaluator were kept ignorant of the intervention allocation.

2.5. Interventions

2.5.1. Preoperative management

All participants underwent in-depth history taking, complete physical examinations and routine laboratory investigations. Complete blood count, random blood sugar, bleeding profiles, renal, and liver function tests were performed preoperatively.

A total of 138 parturients were randomly allocated to two groups. The bundle care group enrolled 68 participants who received four elements including rapid intravenous (IV) infusion of 15 mL/kg of lactated Ringer's solution that was co-loaded during spinal anesthesia, an IV infusion of 4 mg of ondansetron (ZOFATRONE®, 4 mg/2 mL, EVA Pharma, Egypt) over 100 ml of normal saline solution, the parturients were placed in the supine V-shaped posture of 15° head up and 15° leg up with 15° left tilting, and slow intrathecal injection rate of 2.5 mL of 0.5% bupivacaine over 25 seconds, approximately 0.05 mL/sec.

The best-practice group enrolled 70 participants who received a normal IV infusion of 15 mL/kg of lactated Ringer's solution that was co-loaded during spinal anesthesia, early use of vasopressors defined as use of ephedrine as early as decrease of mean arterial pressure was more than 10%, and placement of the patient's suitable position with left uterine tilting.

2.5.2. Intraoperative management

Prior to spinal anesthesia, baseline heart rate (HR) and mean arterial blood pressure (MABP) values were taken when the patient arrived at the operating room. While the patient was seated, a 25-gauge spinal needle was used to provide a dose of 2.5 mL of hyperbaric bupivacaine at 0.5% concentration (Bupivacaine ZOFATRONE®, Mylan medical SAS, Ramco, Paris, France) into the interspace of L3-L4 or L4-L5.

A nasal cannula was used to administer additional oxygen at a rate of 2 L per minute following spinal anaesthesia. After 5 min of spinal anesthesia, the sensory level was evaluated by feeling for cold sensation and again right before a skin incision with a forceps bite. The motor block was evaluated using the Bromage's scale [12], where 0 indicates no movement, 1 indicates knee but not hip movement, 2 indicates foot movement alone, and 3 indicates no knee or foot movement.

Heart rate and MABP were recorded every 3 min until the end of surgery till the end of surgery (45 min) and continued till the conclusion of the first hour after spinal anesthesia. Hypotension was diagnosed when the MABP dropped below 60 mmHg. For each episode of hypotension, lactated Ringer's solution (200 mL/5 min) was infused at a fast rate. If the hypotension continued for 5 min or returned, 6 mg of ephedrine as bolus doses were administered and repeated every 3 min. Bradycardia was diagnosed when HR decreased to 60 bpm. If bradycardia was not accompanied by hypotension, an intravenous (IV) 0.5 mg of atropine was administered.

The total doses and the necessity for ephedrine and atropine boluses were noted. Based on the standard protocols, the incidence of post-spinal hypotension, bradycardia, nausea, vomiting, and dizziness were managed. The baby's Apgar score were also recorded.

2.6. Outcomes

The primary outcome was the overall amount of the consumed ephedrine. Secondary outcomes included the mean arterial blood pressure, heart rate, atropine usage, complications such as dizziness, nausea, and vomiting, as well as the baby's Apgar score.

2.7. Sample size

According to Helmy et al. [13] and French et al. [14] and using the software program MedCalc version 20.118 © 2022 MedCalc Software Ltd, the mean value of the total doses of the consumed ephedrine was 3.21 mg in the care bundle. Meanwhile, in the control group, the mean value of the total doses of the consumed ephedrine was 8.35 mg. Hence, the difference in means of the overall amount of the consumed ephedrine would be 5.14 mg. Thus, for 80% power for independent populations, and a unilateral α of 0.05, a predicted 59 parturients per group was required for each group. We added 15% to compensate for the follow-up loss. One hundred and thirty-eight patients made up the entire sample as a result (69 parturients for each group).

2.8. Statistical analysis

The Statistical Package for Social Sciences (IBM SPSS Statistics) for Windows, version 24 (IBM Corp., Armonk, NY, USA) was used to conduct the statistical analysis. The Shapiro–Wilk test for normality was carried out on quantitative data. Data that were normally distributed were presented as mean standard deviation (SD). The Mann–Whitney U-test or independent t-test was used to compare the study groups. Frequencies were used to summarize the qualitative data, and the correlations between them were examined utilizing the Pearson's Chi-square test or the Fisher's exact test. There were two tails on each exam. A p-value<0.05 was considered significant.

3. Results

One hundred-forty patients were recruited, and two patients declined participation in the study. The study included 138 patients in total, who were divided into two groups at random. Sixty-eight participants were enrolled in a special maternal care bundle group and received rapidly infused co-loads of Ringer lactate, ondansetron, slow rate of intrathecal bupivacaine and were put on V-shaped supine position. Seventy participants were enrolled for best practice group and received normally infused co-load of Ringer's lactate with early use of vasopressors, and they were put on the left tilt position (Figure 1).

Patients' characteristic including the age, body mass index, and ASA were comparable in the study groups (Table 1).

The need for additional ephedrine bolus doses and the overall amount of ephedrine were significantly diminished in the care bundle group (0.24 ± 0.55 mg) compared to the best practice group (0.44 ± 0.69 mg; p = 0.042). However, the need for additional atropine bolus doses was comparable in both groups (p = 0.765). The incidence of dizziness, intraoperative and postoperative nausea and vomiting were also comparable in both groups. Concerning the neonatal outcomes after 1 min and 5 min following delivery, the baby's Apgar score did not statistically differ in both groups (p = 1.77 and 0.186, Table 2).

When comparing the MABP in the study groups, there were no detectable differences at the baseline. While between 2 and 60 min following the administration of spinal anesthetic, the MABP was considerably lowered in the best practice group (Figure 2).

Before the spinal anesthesia and from 2 min to 40-min intraoperative, HR did not differ statistically between both groups. Transient HR fluctuations were significantly diminished in the care bundle group at 40 min after anesthesia (Figure 3).

4. Discussion

Spinal-induced hypotension is a common problem during CS. Fluid co-loading, pharmacological agents, and positioning protocols are the three main components of the management of hypotension after spinal anesthesia [15]. However, there is no single ideal treatment option for hypotension following spinal anesthesia. It is hypothesized that using a multimodal combination of the existing evidence-based techniques could reduce the incidence of hypotension. This study aimed to assess the safety and efficacy of special

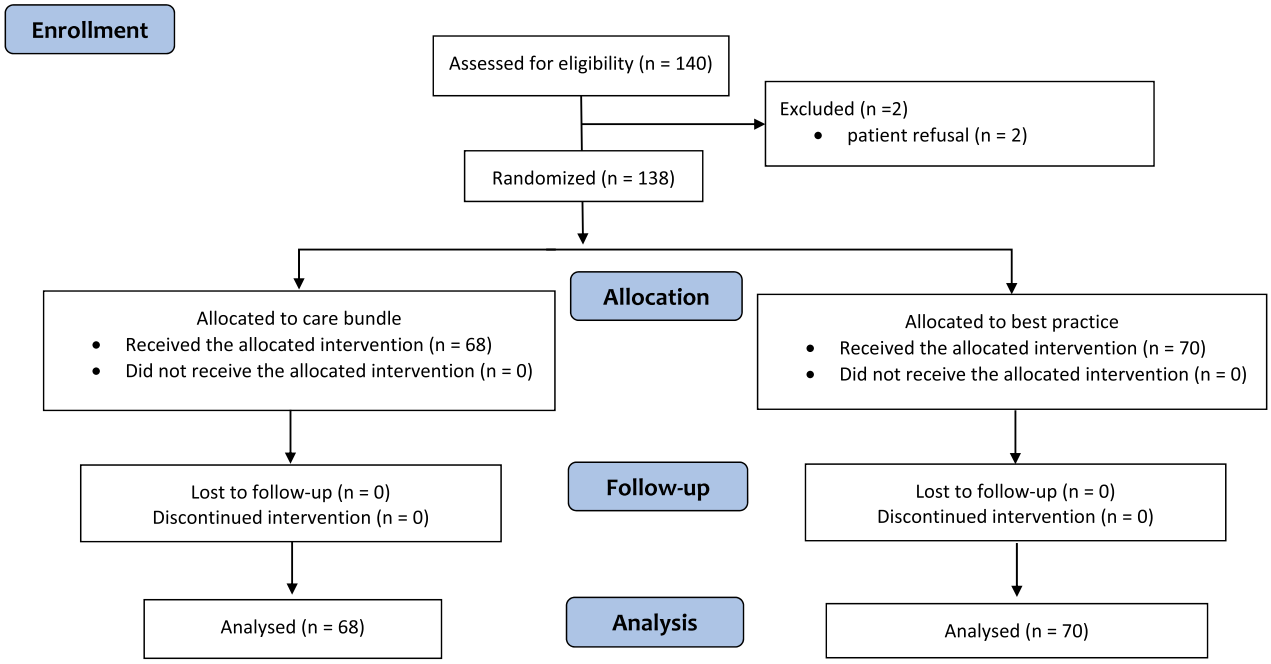

Figure 1. The trial flow chart.

Table 1. The patients' baseline and clinical characteristics (total n = 138).

Variable (mean ± SD)	Care bundle Group (*n* = 68)	Best practice Group (*n* = 70)	P value
Age, years	25.9 ± 2.9	26.3 ± 2.7	0. 397
Height, cm	164.1 ± 3.5	164.6 ± 3.7	0.443
Weight, kg	86.9 ± 4.6	86.4 ± 4.2	0.584
BMI	32.3 ± 2.3	32.0 ± 2.0	0.342
ASA	2.1 ± 0.3	2.1 ± 0.3	0.239
I (n, %)	59 (42.8%)	65 (47.1%)	0.239
II (n, %)	9 (6.5%)	5 (3.6%)	

Data are presented as mean ± SD. SD: standard deviation; n: number; ASA: American Association of Anesthesiologists; cm: centimeter; kg: kilogram; BMI: body mass index. The p-values are based on the independent t-test.

Table 2. Primary and secondary outcomes in the studied groups.

		Care bundle Group (*n*= 68)	Best practice Group (*n*= 70)	P value
Total ephedrine dose, mg, mean ± SD		0.24 ± 0.55	0.44 ± 0.69	0.042*
Need for ephedrine boluses, n (%)	None	56 (82.3%)	47 (67.1%)	
	One (6 mg)	8 (11.8%)	15 (21.4%)	
	Two (12 mg)	4 (5.9%)	8 (11.4%)	
Total atropine (mg), (mean ± SD)		0.06 ± 0.24	0.07 ± 0.26	0.765
Need for atropine boluses, n (%)	None	64 (94.1%)	65 (92.9%)	
	One (0.5 mg)	4 (5.9%)	5 (7.1%)	
Intraoperative dizziness, n (%)	None	55 (80.9%)	52 (74.3%)	0.355
	Yes	13 (19.1%)	18 (25.7%)	
Intraoperative nausea, n (%)	None	60 (88.2%)	55 (78.6%)	0.129
	Yes	8 (11.8%)	15 (21.4%)	
Postoperative nausea, n (%)	None	64 (94.1%)	63 (90%)	0.374
	Yes	4 (5.9%)	7 (10%)	
Intraoperative vomiting, n (%)	None	64 (94.1%)	59 (84.3%)	0.065
	Once	4 (5.9%)	11 (15.7%)	
Postoperative vomiting, n (%)	None	66 (97%)	65 (92.9%)	0.263
	Once	2 (3%)	5 (7.1%)	
Apgar score at 1 min, mean ± SD		8.5 ± 0.5	8.4 ± 0.5	1.77
Apgar score at 5 min, mean ± SD		9.7 ± 0.5	9.6 ± 0.5	0.186

Data are presented as mean ± SD or number (%). SD: standard deviation; n: number; min: minutes; mg: milligram. P-values are based on the Mann-Whitney U-test or the independent t-test. * Significant at $p < 0.05$.

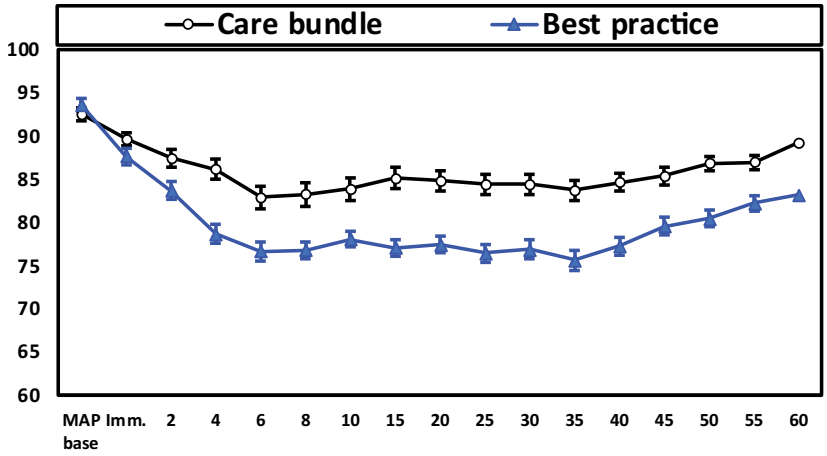

Figure 2. Mean arterial blood pressure (mmHg) intraoperatively.
Independent sample t-test; * significant at $p < 0.05$; m: minutes.

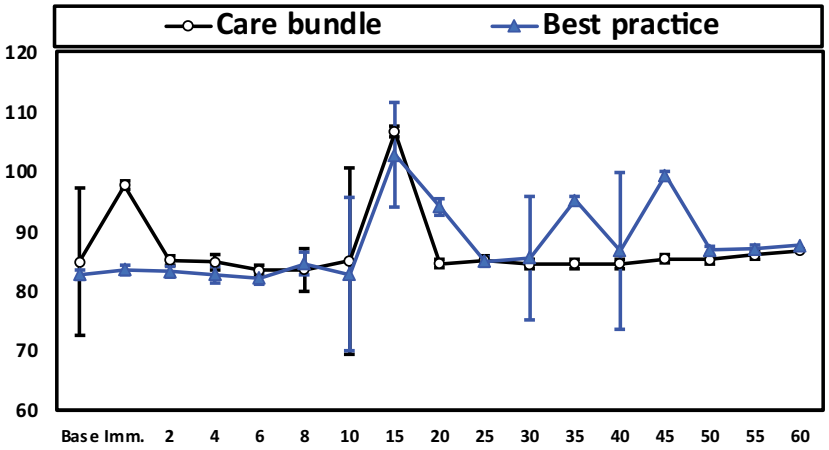

Figure 3. Intraoperative heart rate.
Independent sample t-test; * significant at $p < 0.05$; m: minutes.

maternal care bundles as an alternative technique for the reduction of hypotension brought on by spinal anesthetic in pregnant patients going for CS.

The baseline characteristics including age, body mass index and ASA were comparable in both groups. The total ephedrine consumption, need of ephedrine boluses and hypotension were significantly reduced with the maternal bundle care. Meanwhile, the need of atropine, heart rate, the incidence of dizziness, nausea, vomiting, and Apgar score were comparable in both groups.

Helmy et al. [13] investigated the efficacy of 7.5 mg of bupivacaine and fentanyl as fixed low doses, Ringer's lactate as co-loading, ephedrine administration after spinal anesthesia, the supine wedged position with the elevated leg position >45° and keeping leg elevation at 20° after using graduated compression stockings. Post-spinal hypotension dramatically decreased with the maternal care bundle. However, this case series did not include comparable groups to demonstrate the impact of using the whole bundle of care on spinal hypotension. Furthermore, the neonatal outcomes were not evaluated.

A randomized controlled trial was conducted by Vercauteren et al. [16]. In order to avoid spinal-induced hypotension during Caesarean birth, they adopted a multi-modal method. Low dose ephedrine, 1000 mL lactated Ringer's solution, 500 mL hydroxyethyl starch 6%, and low dose hyperbaric bupivacaine with sufentanil were given to all participants before the spinal injection. Administration of 5 mg of ephedrine was compared to saline. The incidence of hypotension was significantly reduced with the ephedrine use. V-shaped position and co-loading infusion of crystalloids were used in our study rather than preloading technique.

In addition, Mohammed et al. [17] reported the effectiveness of left displacement of the pregnant uterus as an adjuvant to a bundle of care including ondansetron administration, a constant dose of 10 mg

of hyperbaric bupivacaine, and administration of ephedrine after spinal anesthesia. The mean arterial blood pressure was comparable in both groups. However, the neonatal outcomes and Apgar score were not evaluated.

Concerning fluid administration, crystalloid co-loading was effective in preventing spinal anesthesia-induced hypotension [8,18,19]. Dyer et al. [18] recommended a quick co-loading with 20 mL/kg of Ringer's lactate solution over 10 min to reduce ephedrine requirement and occurrence of hypotension. Crystalloid infusions are not restricted to the intravascular region and quickly diffuse into the extracellular space. Thus, infusing crystalloids at the time of vasodilation is effective in reducing hypotension resulting from the spinal anesthesia-induced vasodilation [20]. Xu et al. [21] recommended an infusion rate of 100–150 mL/min of crystalloid, which ensured a quick infusion of the fluid and resulted in a median period of fluid administration of 6.3 min.

Regarding pharmacological administration, Šklebar et al. [2] suggested prophylactic administration of phenylephrine by continuous infusion immediately after intrathecal administration of the local anesthetic. Phenylephrine could be considered one of the safest and most effective vasopressors for spinal anesthesia-induced hypotension. Unfortunately, phenylephrine is not available in some countries [17]. In our study, ephedrine was used; however, it has many disadvantages and is a much less effective vasopressor [22]. Thus, other pharmacological drugs were needed to reduce the use of ephedrine. An earlier meta-analysis [23] reported that 5-HT3 receptor antagonists is effective in reducing the incidence of hypotension in women undergoing cesarean delivery. Tubog et al. [24] postulated that ondansetron might reduce the chances of spinal-induced hypotension and bradycardia. In addition, a previous systematic review [25] reported on the effectiveness of ondansetron in preventing spinal-induced hypotension, bradycardia, and nausea and/or vomiting, while the rates of neonatal acidosis or Apgar scores of less than 8 at 5 min were not affected by ondansetron. Ondansetron's action ascribed to the inhibition of the cardioinhibitory Bezold-Jarisch response from chemoreceptors via blocking serotonin receptors (5-HT3). The reflex manifests as a contradictory response to an abrupt drop in blood pressure, further impairing the circulatory system's compensatory processes [26]. The exact doses of ondansetron that could prevent post-spinal hypotension in the obstetric population are debatable [23]. Wang et al. [27] reported that 4 mg could be an optimal dose to prevent maternal hypotension during cesarean delivery. A more recent randomized trial [28] reported a marked decrease in the ephedrine consumption with higher doses (8 mg) of ondansetron.

The current study shows that the slow injection rate of intrathecal bupivacaine of 0.05 mL/sec as part of maternal care bundle could reduce the incidence of hypotension more than the normal infusion rate. The effect of slow rate injection of local anesthetics during spinal anesthesia of parteriunts undergoing CS is controversial. Bouchnak et al. [29] compared the slow (0.06 mL/sec) and the fast (0.18 mL/sec) rates and concluded that the slow rate significantly reduced the incidence of hypotension. Simon et al. [30] reported that a slow injection rate of bupivacaine, sufentanil, and morphine was a simple, effective way to reduce the incidence and severity of hypotension during CS under spinal anesthesia. Another recent study [31], found that 120-s injection duration during spinal anesthesia was associated with slower onset of hypotension. At the same time, Singh et al. [32] found that the incidence of hypotension and nausea in parturients, as well as the distribution of spinal anesthesia, were unaffected by a quick intrathecal injection of hyperbaric bupivacaine. According to Tugcugil and Besir [31], the fast and turbulent bupivacaine flow can reach the sympathetic efferent fibers arising from the anterior motor neurons, which induced vasoconstriction, preventing the local anesthetic from spreading cephalad. Additionally, it was believed that the quick injection rate did not give the patients enough time to adjust their hemodynamics following the sudden beginning of sympathetic block.

Hypotension following spinal block in pregnant women may be attributable to a reduction in the systemic vascular resistance because of arterial vasodilation secondary to a minor degree of venodilation [33]. Thoracolumbar sympathetic fiber is blocked by spinal block, which causes a significant vasodilatation [34]. Vasodilation lowers venous return and lowers arterial blood pressure, both of which worsen hypotension. An old theory suggested that the solution that was previously injected at ambient temperature may become warmed as it travels through the needle. Variations in the rate of injection may alter the baricity and, consequently, the spread of the local anesthetic solution, since temperature affects the baricity of the solution [35].

Concerning the maternal position, using a combined supine V-shaped position with 15° head up and 15° leg up with 15° left tilting as a part of maternal care bundle was effective in reducing hypotension with little adverse effect. Lewis et al. [36] reported that the supine wedge position was associated with a relatively faster block onset, but it produced a spinal block with similar characteristics to that obtained in the left lateral position. The cardiac output and mean arterial pressure also increased

when the position was changed from supine to the tilted left lateral position. The two tilt angles (15° and 30°) were comparable to each other [15]. Leg elevation would be useful in the prevention and treatment of profound spinal-induced hypotension, especially when combined with other measures [5]. Head elevation during CS was superior to positioning without head elevation in the lateral to supine position because it resulted in a more gradual onset, an optimal block height and enhanced hemodynamics [6]. A modest (5–10°) head-up position does not influence the occurrence of venous air embolism in patients having CS. An et al. [37] found that the incidence and grade of venous air embolism in the head-up tilt group were statistically lower compared to those in the supine group during abdominal myomectomy.

The current study is the first research work evaluating multimodal technique in prevention of spinal anesthesia-induced hypotension during CS, including the co-load of crystalloid, ondansetron administration, slow intrathecal bupivacaine injection, and multiple supine V-shaped position.

4.1. Limitation

This is a single-center study. Furthermore, the study did not indicate which element in this multimodal methodology was better in preventing hypotension in a small number of participants. Larger, multicenter randomized trials are therefore required.

5. Conclusions

The described maternal care bundle can reduce the incidence of spinal anesthesia-induced hypotension and the usage of ephedrine during CS.

Disclosure statement

The authors note that they have no conflicting interests.

References

[1] Lee JE, George RB, Habib AS. Spinal-induced hypotension: incidence, mechanisms, prophylaxis, and management: summarizing 20 years of research. Best Pract Res Clin Anaesthesiol. 2017;31(1):57–68.
[2] Šklebar I, Bujas T, Habek D. Spinal anaesthesia-induced hypotension in obstetrics: prevention and therapy. Acta Clin Croat. 2019;58:90–95.
[3] Ryu C, Choi GJ, Park YH, et al. Vasopressors for the management of maternal hypotension during cesarean section under spinal anesthesia: a systematic review and network meta-analysis protocol. Medicine (Baltimore). 2019;98(1):e13947. DOI:10.1097/MD.0000000000013947
[4] Simmons SW, Dennis AT, Cyna AM, et al. Combined spinal-epidural versus spinal anaesthesia for Caesarean section. Cochrane Database Syst Rev. 2019;10 10 :CD008100.
[5] Hasanin A, Soryal R, Kaddah T, et al. Hemodynamic effects of lateral tilt before and after spinal anesthesia during cesarean delivery: an observational study. BMC Anesthesiol. 2018;18(1):8. DOI:10.1186/s12871-018-0473-0
[6] Lee MH, Kim EM, Bae JH, et al. Head elevation in spinal-epidural anesthesia provides improved hemodynamics and appropriate sensory block height at Caesarean section. Yonsei Med J. 2015;56(4):1122–1127. DOI:10.3349/ymj.2015.56.4.1122
[7] Cyna AM, Andrew M, Emmett RS, et al. Techniques for preventing hypotension during spinal anaesthesia for Caesarean section. Cochrane Database Syst Rev. 2006 4 ;CD002251.
[8] Chooi C, Cox JJ, Lumb RS, et al. Techniques for preventing hypotension during spinal anaesthesia for Caesarean section. Cochrane Database Syst Rev. 2020;7(7 CD002251).
[9] Lavallée JF, Gray TA, Dumville J, et al. The effects of care bundles on patient outcomes: a systematic review and meta-analysis. Implement Sci. 2017;12(1):142. DOI:10.1186/s13012-017-0670-0
[10] Smulders CA, van Gestel JP, Bos AP. Are central line bundles and ventilator bundles effective in critically ill neonates and children? Intensive care Med. 2013;39(8):1352–1358.
[11] Sahni N, Biswal M, Gandhi K, et al. Effect of intensive education and training of nurses on ventilator-associated pneumonia and central line-associated bloodstream infection incidence in intensive care unit at a tertiary care center in North India. Indian J Crit Care Med. 2017;21(11):779. DOI:10.4103/ijccm.IJCCM_259_17
[12] Bromage PR. Epidural analgesia. Philadelphia: WB Saunders Company; 1978.
[13] Helmy NY, Ibrahim JH, Salama AK, et al. Maternal care bundle: the effect of a multimodal approach on the prevention of maternal hypotension following spinal anesthesia in parturients undergoing elective or urgent cesarean section. Egypt J Anaesth. 2017;33(2):171–174. DOI:10.1016/j.egja.2017.01.001
[14] French GW, White JB, Howell SJ, et al. Comparison of pentastarch and Hartmann's solution for volume preloading in spinal anaesthesia for elective Caesarean section. Br J Anaesth. 1999;83(3):475–477. DOI:10.1093/bja/83.3.475
[15] Hasanin A, Mokhtar AM, Badawy AA, et al. Post-spinal anesthesia hypotension during cesarean delivery, a review article. Egypt J Anaesth. 2017;33(2):189–193. DOI:10.1016/j.egja.2017.03.003
[16] Vercauteren MP, Coppejans HC, Hoffmann VH, et al. Prevention of hypotension by a single 5-mg dose of ephedrine during small-dose spinal anesthesia in prehydrated cesarean delivery patients. Anesth Analg. 2000;90(2):324–327. DOI:10.1213/00000539-200002000-00016
[17] Mohammed AAEF, Salem E, Alshawadfy A. Role of left uterine placement in maternal care bundle for the prevention of spinal anesthesia-induced hypotension in cesarean section. Al-Azhar Assiut Med J. 2021;19(2):287–292.
[18] Dyer RA, Farina Z, Joubert IA, et al. Crystalloid preload versus rapid crystalloid administration after induction of spinal anaesthesia (coload) for elective Caesarean

section. Anaesth Intensive Care. 2004;32(3):351–357. DOI:10.1177/0310057X0403200308

[19] Oh AY, Hwang JW, Song IA, et al. Influence of the timing of administration of crystalloid on maternal hypotension during spinal anesthesia for cesarean delivery: preload versus coload. BMC Anesthesiol. 2014;14(1):36. DOI:10.1186/1471-2253-14-36

[20] Loubert C. La prise en charge des liquides et des vasopresseurs pour la césarienne effectuée sous rachianesthésie. Can J Anesthesia. 2012;59(6):604–619.

[21] Xu S, Wu H, Zhao Q, et al. The median effective volume of crystalloid in preventing hypotension in patients undergoing cesarean delivery with spinal anesthesia. Rev Bras Anestesiol. 2012;62(3):312–324. DOI:10.1016/S0034-7094(12)70132-0

[22] Fitzgerald JP, Fedoruk KA, Jadin SM, et al. Prevention of hypotension after spinal anaesthesia for Caesarean section: a systematic review and network meta-analysis of randomised controlled trials. Anaesthesia. 2020;75(1):109–121. DOI:10.1111/anae.14841

[23] Heesen M, Klimek M, Hoeks SE, et al. Prevention of spinal anesthesia-induced hypotension during cesarean delivery by 5-hydroxytryptamine-3 receptor antagonists: a systematic review and meta-analysis and meta-regression. Anesth Analg. 2016;123(4):977–988. DOI:10.1213/ANE.0000000000001511

[24] Tubog TD, Kane TD, Pugh MA. Effects of ondansetron on attenuating spinal anesthesia–induced hypotension and bradycardia in obstetric and nonobstetric subjects: a systematic review and meta-analysis. Aana j. 2017;85(2):113–122.

[25] Chooi C, Cox JJ, Lumb RS, et al. Techniques for preventing hypotension during spinal anaesthesia for Caesarean section. Cochrane Database Syst Rev. 2017;8 8 :CD002251.

[26] Sahoo T, Sen Dasgupta C, Goswami A, et al. Reduction in spinal-induced hypotension with ondansetron in parturients undergoing Caesarean section: a double-blind randomised, placebo-controlled study. Int J Obstet Anesth. 2012;21(1):24–28. DOI:10.1016/j.ijoa.2011.08.002

[27] Wang M, Zhuo L, Wang Q, et al. Efficacy of prophylactic intravenous ondansetron on the prevention of hypotension during cesarean delivery: a dose-dependent study. Int J Clin Exp Med. 2014;7(12):5210–5216.

[28] Aksoy M, Dostbil A, Aksoy AN, et al. Granisetron or ondansentron to prevent hypotension after spinal anesthesia for elective cesarean delivery: a randomized placebo-controlled trial. J Clin Anesth. 2021;75:110469.

[29] Bouchnak M, Belhadj N, Chaaoua T, et al. Rachianesthésie pour césarienne : la vitesse d'injection a-t-elle une influence sur l'incidence de l'hypotension ? Ann Fr d'Anesth et de Réanimation. 2006;25(1):17–19. DOI:10.1016/j.annfar.2005.07.078

[30] Simon L, Boulay G, Ziane AF, et al. Effect of injection rate on hypotension associated with spinal anaesthesia for Caesarean section. Int J Obstet Anesth. 2000;9(1):10–14. DOI:10.1054/ijoa.1999.0348

[31] Tugcugil E, Besir A. A comparison of the injection rate of local anesthetic during spinal anesthesia on the onset of sensory block and incidence of hypotension in Caesarean section. Clin Exp Obstet Gynecol. 2022;49(7):152.

[32] Singh I, Morley-Forster P, Shamsah M, et al. L'influence de la vitesse d'injection de bupivacaïne hyperbare sur la rachianesthésie chez les parturientes : une étude randomisée. Can J Anesthesia. 2007;54(4):290–295. DOI:10.1007/BF03022774

[33] Kuhn JC, Hauge TH, Rosseland LA, et al. Hemodynamics of phenylephrine infusion versus lower extremity compression during spinal anesthesia for cesarean delivery: a randomized, double-blind, placebo-controlled study. Anesth Analg. 2016;122(4):1120–1129. DOI:10.1213/ANE.0000000000001174

[34] Hofhuizen C, Lemson J, Snoeck M, et al. Spinal anesthesia-induced hypotension is caused by a decrease in stroke volume in elderly patients. Local Reg Anesth. 2019;12:19–26.

[35] Bucx MJ, Kroon JW, Stienstra R. Effect of speed of injection on the maximum sensory level for spinal anesthesia using plain bupivacaine 0.5% at room temperature. Reg Anesth. 1993;18(6):103–105.

[36] Lewis NL, Ritchie EL, Downer JP, et al. Left lateral vs. supine, wedged position for development of block after combined spinal-epidural anaesthesia for Caesarean section*. Anaesthesia. 2004;59(9):894–898. DOI:10.1111/j.1365-2044.2004.03752.x

[37] An J, Shin SK, Kwon JY, et al. Incidence of venous air embolism during myomectomy: the effect of patient position. Yonsei Med J. 2013;54(1):209–214. DOI:10.3349/ymj.2013.54.1.209