How to handle hypotension following spinal anesthesia for a cesarean section

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Spinal block is the chosen anesthetic technique for cesarean sections because it poses less hazards to the mother and fetus than general anesthesia. The most frequent adverse effect of spinal block is hypotension owing to sympatholysis, which can reduce preload and afterload and cause arterial and venous vasodilation. This leads to maternal hypotension, which can affect uterine blood flow and fetal circulation and result in fetal hypoxia, acidosis, and bradycardia. Since then, a number of research studies on various medications, techniques, and regimens have been published, and neuraxial anesthesia methods in obstetrics are becoming more and more common. Clinical practice employs a variety of strategies for the prevention and management of spinal block-induced hypotension, including intravenous colloid preloading or crystalloid coloading, compression bandages or stockings for the lower limbs, left tilt positioning, administering the ideal local anesthetic dose and attaining the ideal spinal block level, as well as the administration of inotropes and vasopressors as constriction of the arterial vessels is currently emerging as the ideal strategy. The most recent algorithms advocate giving vasopressor infusions as a preventative measure rather than when hypotension has already occurred.

Keywords:
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Introduction

The majority of elective cesarean sections (78% of cases) are performed under spinal anesthesia [1]. As surgical delivery requires cephalad block distributions up to T4 and parturients exhibit higher susceptibility to the effects of local anesthetics, minimizing neuraxial block adverse effects may prove to be relatively difficult.

Iatrogenic sympathetic block, which reduces preload and afterload and produces arterial and venous vasodilation, is widely recognized to lower systemic vascular resistance. By inhibiting the acceleration of sympathetic cardiac fibers, high spinal distribution levels can result in bradycardia and a reduction in stroke volume. Reduced right ventricular filling may also activate heart wall mechanoreceptors, causing a vasovagal Bezold-Jarisch reaction [2].

It is interesting to note that cardiovascular and physiologic hemodynamic changes brought on by pregnancy enhance the risk of hypotensive episodes after neuraxial sympathetic inhibition. In late pregnancy, the pregnant woman's body may compress the inferior vena cava in the supine position, resulting in a sharp drop in preload and consequent drop in cardiac output. The prevalence and management of spinal-induced hypotension are greatly influenced by a physiological decrease in systemic vascular resistance and its effects, which is more significant but less well documented [2].

Owing to the higher amounts of prostaglandins, progesterone, and estrogen in the early stages of pregnancy, peripheral arterial vasodilation already occurs. Strong vasodilatory mediators include the circulating peptide hormone relaxin and elevated nitric oxide levels in uterine arteries, which support better uterine perfusion. Relative arterial underfilling induces renal sodium and water retention and promotes plasma volume expansion and total body water because it activates the renin–angiotensin–aldosterone pathway. Dilutional anemia stimulates a permanent increase in the heart rate. Additionally, atrial stretch brought on by volume overload not only results in an increased stroke volume but also causes remodeling processes in the cardiac wall and a further release of natriuretic peptides, which have additional vasodilatory effects [2].

The increase in plasma volume and the increase in cardiac output are insufficient to counteract the decrease in vascular resistance, which may reach up to 40%, as mean arterial pressures are continuously compared with the nonpregnant state, throughout normal pregnancies [3]. This highlights the fact that maternal hemodynamic maintenance already depends

on insufficient compensation. A further decrease in peripheral vascular resistance, such as that brought on by iatrogenic sympathectomy caused by spinal anesthesia, could rapidly surpass compensatory limits and finally result in a significant hemodynamic impairment [2]. It is not a surprising result that arterial hypotension is one of the most common complications of spinal anesthetic for cesarean section and appears to significantly overshoot when compared with the nonpregnant patients.

Common accompanying symptoms of maternal hypotension include nausea and vomiting. Many theories regarding its pathogenesis have been put forth, including the possibility that gastrointestinal ischemia due to decreased splanchnic perfusion might result in the release of pro-emetic chemicals like serotonin [4], in addition cerebral hypoperfusion resulting in ischemia of the vomiting center in the brain stem [5].

Untreated hypotension leads to adverse fetal outcomes in addition to being a significant maternal risk factor. It may eventually lead to loss of consciousness and aspiration. Fetal hypoxia, low Apgar scores, and acidosis result from maternal hypotension, as there is no vascular autoregulation. These outcomes are associated with the severity and length of hypotensive events. Since then, several studies on various drugs, strategies, and regimens have been published along with the rising popularity of neuraxial anesthetic procedures in obstetrics [2].

The best vasopressor to use, timing (prophylaxis vs. treatment), and administration technique are all crucial considerations (bolus versus continuous administration). Owing to this, this study emphasizes the most recent evidence while also highlighting current recommendations.

Vasopressors

The continued high level of interest in obstetric anesthetic research, with a focus on various substances and administration methods, likely reflects the importance of treating maternal hypotension with vasopressors. Phenylephrine and ephedrine are now the drugs that have undergone the most research in this area and have a lengthy history of use.

Ephedrine

Although ephedrine was once the most often used vasopressor in obstetrics, being used as the sole vasoconstrictor by 95% of clinicians in 1999 [6], it is currently almost nonexistent in current suggestions. Ephedrine has a direct sympathomimetic effect at the receptors (alpha and beta) and indirectly through the endogenous release of norepinephrine.

During a cesarean section under spinal anesthesia, the international consensus statement on the management of hypotension using vasopressors in 2018 advised that ‘œ-agonist drugs are the most appropriate agents to prevent or treat hypotension after spinal anesthesia and further that the highly selective alpha1-agonist phenylephrine is advised based on the available data’ [7].

In 2002, Lee and colleagues advocated this change of course after publishing a meta-analysis of eight randomized-controlled studies. When contrasting the usage of ephedrine and phenylephrine during cesarean sections, they discovered that women who received phenylephrine had significantly higher umbilical cord pH values [weighted mean difference was 0.03 (95% confidence interval (CI) 0.02–0.04)] [8]. Despite the fact that formerly ephedrine was preferred due to findings from animal research showing that it caused less uteroplacental vasoconstriction [9], ephedrine transferred to the placenta more readily than phenylephrine according to an analysis of plasma concentrations in maternal and venous umbilical blood (median umbilical venous/mother arterial plasma concentration ratio = 1.13 vs. 0.17).

Moreover, the analysis by Lee *et al*. [8] revealed that ephedrine was neither linked to real fetal acidosis, which is defined at a pH lower than 7.2 (RR = 0.78, 95% CI 0.16–3.92), nor had any discernible variations in APGAR scores at 1 min (RR = 0.77, 95% CI 0.17–3.51) or 5 min (RR = 1.00, 95% CI 0.21–4.83).

There was no conclusive evidence to support a higher risk of fetal acidosis in a Cochrane review on preventing hypotension during spinal anesthesia for cesarean section [incidence with phenylephrine 11/1000 vs. ephedrine 10 (1–131)/1000; (RR = 0.89, 95% CI 0.07–12.00); three studies (175 babies) with low-quality evidence] [10].

However, Veeser and colleagues showed in another systematic analysis that ephedrine was significantly more likely to cause umbilical cord pH readings to fall below 7.2. Only two of the five included trials – which is noteworthy – reported substantial occurrences of fetal acidosis [11] (, 12/25 vs. 0/24; 20/50 vs. 1/48), in contrast to other trials, which showed zero to one cases of fetal acidosis in each group. This result’s external validity is questioned. It is interesting to note that ephedrine was continually administered in both studies with high incidence outcomes, yet bolus injections were the focus of the other trials [12]. This could explain

that it is not the ephedrine administration that raises the risk of a true fetal acidosis and it should be avoided, but it is the continuous ephedrine administration that causes potential harm [2].

Phenylephrine

Although phenylephrine is still the preferred and popular vasopressor, attention is now shifted to other substitute drugs such as norepinephrine. This is because of the occasional bradycardia that is associated with phenylephrine use, which is usually treated with a second anticholinergic or vasopressor substance such as atropine or glycopyrrolate. This is demonstrated by the pooled incidence of maternal bradycardia necessitating intervention after phenylephrine administration, which reaches about 243 every 1000 [10] with an increasing likelihood in a dose-dependent way [50 mg/min 1/54 (0.5%) vs. 100 mg/min 11/63 (17.4%)] [13].

The question of which is a better regimen for maintaining maternal hemodynamic stability whether repeated boluses or a continuous fixed infusion rates has been so roughly investigated. The current consensus recommendation favors preventive infusions of vasopressors rather than repeated boluses technique [7].

In a randomized-controlled experiment, closed loop vasopressor systems, which automatically deliver ephedrine or phenylephrine based on continuous blood pressure monitoring, have been linked with reduction of nausea and maintaining stability of maternal hemodynamic [14]. The cost and necessity of such devices in clinical practice, however, remain debatable because there were no differences in fetal fate that could be detected.

Norepinephrine

The catecholamine norepinephrine, which has more alpha than beta agonistic activity, is arguably the most commonly used vasopressor in critical care environments globally. However, its emerging use in obstetric anesthesia has the potential benefit of being a mild beta adrenergic receptor agonist as well. The body of evidence of its use is still growing as norepinephrine is extensively subjected to ongoing research. Without any discernible alterations in the fetal acid–base balance, lower incidences of bradycardia were recorded when phenylephrine was used [(Ngan Kee *et al.* 18.4 vs. 55.8% (P = 0.001), and Sharkey *et al.* 10.9 vs. 37.5% (P = 0.001)] [15,16]. However, Mohta *et al.* [17] found significantly lower fetal pH values in the norepinephrine group (7.29 ± 0.07 vs. 7.25 ± 0.10, P = 0.03); however, there was no difference in the development of true fetal acidosis between the groups. They found no differences regarding maternal bradycardia (6.6 vs. 2.2%, P = 140.1) but significant differences regarding fetal pH.

To evaluate the technique of delivery, prophylactic manually controlled continuous infusions were contrasted in a double-blinded randomized-controlled experiment (0–5 g/min) with bolus administrations (5 g). The amount of norepinephrine administered overall was noticeably higher with the continuous infusion [continuous 61.0 mg (interquartile range = 47.0–72.5 mg) vs. bolus 5.0 mg (interquartile range 0–18.1 mg, P < 0.001)], and it also improved maternal hemodynamic stability. Umbilical cord pH measurements and APGAR scores were comparable between the two groups [18].

Based on further evidence, norepinephrine appears to be well tolerated and effective, with more advantageous for mothers and newborn safety in parturients with preeclampsia [19].

5-Hydroxytryptamine-3 receptor antagonists

A potential additional pharmaceutical strategy to support hemodynamic stability during spinal anesthesia is the 5-hydroxytryptamine-3 receptor (5HT3) antagonist. As serotonin-sensitive chemoreceptors and mechanoreceptors trigger the Bezold-Jarisch reaction, it has the potential to aggravate hypotension. 5HT3 antagonists were first discovered to stop reflex responses in animal models, and multiple clinical trials have since shown their effectiveness [20]. A meta-analysis of 17 trials that examined the prophylactic double-blind administration of 5HT3 antagonists for spinal anesthesia comprised 1604 people. Despite the lack of any discernible effects in nonobstetric cohorts, the RR for cesarean section patients was 0.52 (95% CI 0.30–0.88) [21].

Volume therapy

Although fluid treatment alone is frequently insufficient to avoid maternal hypotension, it is an important step in preventing the decline in blood pressure and minimizing the total need for vasopressors [2].

Preload versus coload

Rapid crystalloid coloading, as opposed to crystalloid preload, was found to be a more effective method of reducing the incidence of hypotension, according to an analysis of five clinical trials including 384 parturients. Yet, neither ‘fast’ nor ‘coloading’ was specified. The majority of studies found that ‘coloading’ started with the positive detection of cerebrospinal fluid/intrathecal injection at the latest with a total volume ranging between 15 and 20 ml/kg; the concept of rapid

infusion varied widely. Some claimed to have given the drug for 20 min at the 'maximum feasible tempo,' or without giving any details at all [10], whereas others used a pressured giving set.

Colloids versus crystalloids

Colloidal solutions appear to have at least a slight benefit over crystalloids in terms of lowering the frequency of hypotension. Doherty and colleagues used a wide-bore 14-G intravenous catheter to infuse 1 l of a colloid solution and 1 l of a crystalloid co-load solution at a flow rate of 200 ml/min while measuring cardiac output using suprasternal Doppler in a randomized-controlled double-blinded experiment. Regarding cardiac output factors and the need for vasopressors, they discovered no overall differences between the groups. They also noted that the administration of crystalloids by pressured infusion at a high flow rate has been shown to be equal to colloids [22].

Moreover, because there are so few studies, it is impossible to draw any conclusions about the long-term safety of colloids owing to their unfavorable adverse effect profile and the need to balance their advantages against their inherent risks while using them.

Lateral tilt position

Doing cesarean sections in a 158 lateral tilt position can frequently be seen as a regular technique in clinical routine, taking into consideration that aortocaval compression in the supine position is a key contributing element to maternal hypotension. Left lateral tilt position was first brought up by several authors in the 1970s, such as Crawford *et al.* [23], who reported a correlation between higher umbilical pH values in this position. Since then, it has become one of the most persistent beliefs in obstetric practice, and the current international consensus statement continues to recommend it [7]. However, this lateral tilt may hinder or result in unilateral intrathecal anesthetic spread, which would be uncomfortable for the mother during surgery.

A left lateral tilt of at least 30° is required to relieve partially vena cava compression, but this is almost never achieved in clinical practice because most practitioners overestimate the set tilt [24]. Furthermore, implementing a 30° lateral tilt necessitates the addition of an additional barrier to prevent the parturient from falling off the operating table.

Conclusion

In obstetrics, a multimodal approach should be used to treat spinal-induced hypotension that includes both preventive and therapeutic interventions. Implementing spinal anesthesia using opioid adjuvants and low-dose local anesthetics prevents the subsequent drop in blood pressure. Ondansetron 4 mg used as a preventative measure may lower the frequency of hypotensive events necessitating intervention. The first step in fluid treatment administration should be rapid coloading with pressurized crystalloid infusions to achieve flow rates of up to 200 ml/min. Continuous phenylephrine or norepinephrine administration causes less maternal hypotension but has equivalent effects on the fetus.

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Conflicts of interest

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