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Update on Vasopressors for Cesarean Delivery

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Abstract

Purpose of Review The aim of this article is to provide an overview of the current strategies for managing spinal-induced hypotension during cesarean delivery with a particular focus on the evidence guiding the use of vasopressors.

Recent Findings Phenylephrine is currently regarded as the first-line vasopressor in the prevention and treatment of spinal-induced hypotension following evidence that supports a favorable effect on neonatal acid-base status as well as reduced incidences of nausea and vomiting when compared with ephedrine. Norepinephrine and metaraminol are also effective in the prevention and treatment of hypotension.

Summary The current consensus for vasopressor use in the treatment of spinal-induced hypotension has been shaped by data gathered from studies involving healthy parturients undergoing elective cesarean deliveries. While these results cannot necessarily be extrapolated to high-risk patients with impaired cardiovascular function or evidence of fetal compromise, these studies may help inform vasopressor choice and establish recommendations for clinical practice.

Keywords Vasopressor · Spinal anesthesia · Hypotension · Cesarean delivery · Aortocaval compression

Introduction

In the UK, the adoption of spinal anesthesia as the preferred technique for cesarean delivery has accompanied a fall in mortality directly attributed to the increased use of neuraxial anesthesia [1]. While general anesthesia may still be required, it carries risks of failed tracheal intubation, aspiration, and accidental awareness, all of which are major contributing factors to patient mortality and morbidity associated with obstetric anesthesia. In the UK, fewer than 5% of elective cesarean deliveries are performed under general anesthesia although this varies internationally depending on resources and experience [2]. The rate of general anesthesia for emergency cesarean delivery is higher, between 10 and 20% in most nations [3].

Neuraxial anesthesia conveys a number of benefits to the mother, allowing her to participate in the birth of her newborn as well as providing superior postoperative analgesia, increasing maternal satisfaction. However, hypotension following spinal anesthesia is common and may result in significant maternal distress and potentially in fetal compromise. A number of preventive and therapeutic approaches have been studied, most notably fluid loading and vasopressors, yet there is limited evidence to support one specific intervention and this is reflected in the considerable variation in practice amongst clinicians.

An understanding of the causes and management of hemodynamic instability during cesarean delivery under spinal anesthesia will not only improve both maternal and neonatal safety but also maternal comfort. As a result, the prevention of spinal-induced hypotension remains a key area of research within the field of obstetric anesthesia.

Spinal-Induced Hypotension

Hypotension resulting from spinal anesthesia is common in the maternal population; the incidence often being quoted as between 70 and 80% [4, 5]. Hypotension results in both maternal and fetal effects by means of reduced cerebral and uteroplacental blood flow, respectively. Maternal symptoms can be distressing and include dizziness, nausea, and vomiting. In rare cases of

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sustained or refractory hypotension, cardiovascular collapse may result. The absence of uteroplacental autoregulation exposes the fetus to reduced blood flow. Fetal bradycardia may be the first sign of hypoperfusion, which risks subsequent fetal hypoxia, metabolic acidosis, and neurological injury.

The etiology of hypotension following spinal anesthesia is multi-factorial but is predominantly due to a combination of aortocaval compression and the relative sympathectomy caused by the cephalad spread of intrathecal local anesthetic. Hypotension resulting from the extension of an existing epidural block previously established for labor analgesia is usually less profound; the relatively slower onset of epidural anesthesia causes a partial sympathectomy and permits compensatory physiological mechanisms to become established. Hypotension is also less common in laboring mothers and possibly reflects the autotransfusion of blood entering the central circulation during uterine contractions [6].

Hypotension in this context is frequently defined as < 80% of a baseline systolic blood pressure measured before spinal anesthesia. This helps to define the severity of hypotension as well as establishing thresholds for intervention such as a systolic blood pressure less than 90% or 100% of the baseline [7]. This definition of hypotension is favored as patient variability means using absolute values (e.g., a SBP < 90 mmHg) to describe hypotension would be less helpful. Identifying an accurate baseline measurement is important; however, a falsely high baseline may be recorded in an anxious patient and targeting this with vasopressors might unwittingly precipitate reactive hypertension or trigger a reflex bradycardia with significant attenuation of the cardiac output as a result.

Prediction of those at risk of hypotension may allow a more targeted management strategy. There are a number of studies utilizing various methods but there remains a lack of consensus on the most appropriate techniques; the calculation of complex cardiac variables by echocardiography is not only time-consuming but is also beyond the skill of most anesthesiologists. The performance of more accessible bedside assessments including baseline heart rate and postural variations in blood pressure has proved inconsistent in predicting patient susceptibility to spinal-induced hypotension [8–10].

Prevention and Management of Hypotension

Patient Positioning

In the supine position from about 20-week gestation, compression of the inferior vena cava (IVC) by the gravid uterus impedes venous return to the heart, reducing the stroke volume, thereby lowering the cardiac output. For these reasons, a key component of maternal and fetal resuscitation is to place the mother in the full left lateral position or, in cases of trauma or cardiac arrest, to manually displace the uterus. MRI imaging in the supine mother has demonstrated near-complete occlusion of the IVC by term pregnancy [11•, 12•]. Similarly, compression of the abdominal aorta near term was thought to cause reduced distal perfusion involving the uteroplacental circulation resulting in fetal compromise; however, evidence supporting this physiological process is questionable [11•]. The potentially harmful effects of aortocaval compression on the mother and fetus are such that it is a standard clinical practice to provide lateral pelvic tilt to mothers during cesarean delivery, displacing the gravid uterus from the aorta and IVC. Although a tilt of 15° is regularly used, studies have demonstrated that as much as 34° is required to overcome the complete compression of the IVC and indeed there is a subset of patients in whom aortocaval compression is still significant beyond this level [12•, 13]. One study was able to demonstrate a 5% increase in cardiac output when non-laboring patients were tilted more than 15°; however, excessive degrees of tilt might be poorly tolerated by the patient and may complicate the surgical approach to the abdomen and pelvis [14]. Lee and colleagues demonstrated that in the presence of crystalloid co-loading and a phenylephrine vasopressor infusion, these effects can be overcome regardless of whether the patient is supine or at 15° of tilt, with no difference observed in neonatal outcome in a healthy obstetric population undergoing cesarean delivery [15•]. Although some may argue that the results of this study might call into question whether left uterine displacement is necessary when using vasopressors, the study noted a significantly greater phenylephrine requirement and fall in cardiac output in the supine group. Although this did not appear to translate to a discernible effect on the healthy parturient or fetus, the improvement in cardiac output and reduction in vasopressor requirements associated with left lateral tilt may be of significant clinical benefit in cases of impaired placental perfusion or fetal compromise.

Despite the hemodynamic changes observed as a result of aortocaval compression, fewer than 20% of mothers experience symptoms of this "supine hypotension syndrome." This is likely to be explained by sympathetic-driven compensatory mechanisms correcting the cardiac output; firstly, an increase in systemic vascular resistance (SVR) and heart rate (HR) and, secondly, *veno*constriction and subsequent venous return via collateral venous plexi formed during pregnancy which bypass the IVC [16]. Under spinal anesthesia, these compensatory mechanisms are lost secondarily to what is effectively a pharmacological denervation of the sympathetic chain. The block height will determine the extent of this sympathetic blockade; however, the degree of hemodynamic change is unpredictable requiring vigilance and additional management strategies immediately to hand.

Intravenous Fluids

Intravenous fluid therapy regimens seem to attract contention in most corners of anesthesia and obstetric anesthesia and the delivery theater is no exception. Fluid is traditionally the

mainstay of hypotension prophylaxis and a number of studies have assessed both the type (colloid or crystalloid) and the timing of administration. When given solely as a preload prior to spinal anesthesia, colloids have demonstrated efficacy in treating hypotension whereas crystalloids are largely ineffective and are no longer recommended, most likely a result of their rapid redistribution from the intravascular compartment into the interstitial space [17]. Co-loading intravenous fluids with spinal anesthesia to overcome this redistribution showed both crystalloids and colloids were effective in reducing the vasopressor doses required to treat hypotension [18]. The timing of intravenous fluid co-loading is critical and dependent on immediate and rapid infusion as soon as the spinal anesthetic has been sited. Crystalloid co-loading is generally favored, possibly reflecting the relative expense of colloids and the, albeit small, association with adverse effects such as anaphylaxis. Importantly, despite the clinical application of these findings, no study has demonstrated an intravenous fluid regimen that is 100% effective in reducing the incidence of hypotension [19, 20]. It is possible that some parturients will benefit from fluid loading more than others, for example, in women with existing volume deficits or a higher resting sympathetic tone in whom one may expect to see a greater fall in blood pressure following spinal anesthesia.

Local Anesthetic Dose

The efficacy of intrathecal local anesthesia is affected by the dose and the baricity of the solutions used. A recent study has also demonstrated that the ED_{50} and ED_{95} for hyperbaric bupivacaine are higher in the presence of a phenylephrine infusion. The mechanisms are unclear but reduced rostral spread may be attributable to attenuating the relative reduction in lumbar CSF volume that is observed in pregnancy secondary to epidural venous plexus engorgement [21]. Many anesthetists have adopted the use of hyperbaric (8% glucose) 0.5% or 0.75% bupivacaine for spinal anesthesia in cesarean delivery with the addition of opioids to augment the quality of both surgical anesthesia and postoperative analgesia. Hypobaric bupivacaine solutions have been shown to be associated with a higher incidence of hypotension when compared with hyperbaric equivalents although interestingly, the use of marginally hyperbaric solutions (with the addition of 0.5% or 0.33% glucose) demonstrated a reduced incidence of hypotension without compromising the efficacy of the spinal block [22, 23]. The risk of hemodynamic instability increases with the dose of local anesthetic administered; most doses used are in the range of 7.5 to 15 mg (1.5 to 3 mL of 0.5% solution) with those less than 8 mg (1.6 mL) considered "low dose" [24]. Low-dose spinal anesthesia techniques significantly reduce vasopressor requirements but at the risk of increasing the incidence of patient discomfort should the anesthesia become inadequate during surgery [25]. A meta-analysis of 12 randomized controlled trials comparing low-dose (< 8 mg) bupivacaine with a dose of > 8 mg showed a threefold increase in the incidence of breakthrough pain requiring intraoperative supplemental analgesia [26]. It is generally considered that patient experience should not be compromised for a more hemodynamically stable spinal block. For this reason, it is recommended that low-dose spinal anesthesia should only be administered as part of a CSE technique permitting epidural supplementation if required to rescue inadequate intraoperative analgesia [24].

Vasopressors

As the understanding of the pathophysiology of spinal-induced hypotension has evolved, so have our interventions to manage it. Addressing the effects of aortocaval compression with intravenous fluid therapy and left lateral tilt does not compensate for the sympathectomy-driven reduction in systemic vascular resistance resulting from neuraxial blockade and therefore attention has turned to the use of vasopressors to attenuate this response.

Vasopressors mediate their vasoactive effects via alpha-1 adrenoreceptor-induced smooth-muscle contraction within the vessel walls which increases systemic vascular resistance and mean arterial blood pressure. Direct-acting alpha-1 adrenoreceptor agonists such as phenylephrine are very effective agents to increase the blood pressure, but their use may cause a baroreceptor-mediated fall in heart rate and corresponding reduction in cardiac output, which is key to oxygen delivery. Some vasopressors additionally exhibit beta-1 receptor–mediated positive inotropy and chronotropy. These may confer benefit over pure alpha-adrenoreceptor agonists by overcoming these bradycardic reflexes.

Ephedrine

Historically, ephedrine was considered the first-line vasopressor in the management of spinal-induced hypotension following animal studies in which it was demonstrated to preserve uterine blood flow in arteries from pregnant ewes when compared with other alpha-agonists [27]. The subsequent description of ephedrine-induced local release of nitric oxide synthase within the uterine arteries of ewes further cemented the view that this rendered the vessel smooth muscle less susceptible to ephedrine when compared with other vasopressors leading to its historical position as the vasopressor of choice [28].

The exact mechanism of action of ephedrine is not fully understood but it is believed that it acts indirectly, increasing the availability of norepinephrine within the synaptic cleft to exert effects on the postsynaptic alpha-1 adrenoreceptors. It is possible that it achieves this either by promoting norepinephrine release from presynaptic vesicles or by competing with the

site of norepinephrine reuptake [29]. Both these mechanisms may explain its slow onset, relatively prolonged duration of action and the tachyphylaxis observed as a result of presynaptic depletion of available norepinephrine. Importantly, ephedrine also exerts direct beta-agonist properties with a notable tachycardia observed following its administration.

Unfortunately, the benefits of ephedrine observed in the laboratory environment have not translated well to clinical practice. When compared with phenylephrine or a combination of these vasopressors, ephedrine use was associated with an increased incidence of fetal acidosis [30]. This is thought to be secondary to the placental transfer of ephedrine and subsequent direct simulation of fetal beta-receptors resulting in an increased fetal metabolic rate and oxygen demand [31]. While fetal acidosis observed in low-risk cases is unlikely to be clinically significant, it could be inferred that in high-risk cases associated with placental insufficiency or fetal distress, a compromised fetus might not be able to cope with the increased oxygen demand generated by an increased metabolic rate following ephedrine administration.

Phenylephrine

The association of ephedrine with reduced fetal pH has led to the promotion of phenylephrine (a direct-acting alpha-1 adrenoreceptor agonist) in the treatment of hypotension due to its more favorable effect on fetal acid-base status. Studies comparing phenylephrine and ephedrine use in low-risk, elective cesarean deliveries have consistently described not only a lower umbilical artery pH in the ephedrine group but also an increased base deficit and higher umbilical plasma concentrations of lactate, glucose, epinephrine, and norepinephrine. In a study of 104 parturients undergoing elective cesarean delivery, Ngan Kee and colleagues compared ephedrine with phenylephrine by intravenous infusion, the latter resulting in more favorable fetal blood gases (median umbilical artery pH 7.25 vs. 7.33, median base deficit −4.8 vs. −1.9 mmol/L, and median lactate 4.2 vs. 2.2 mmol/L) [31].

In comparison to ephedrine, phenylephrine has a faster onset and shorter duration of action lending itself to easier titration [32]. Phenylephrine can be given by intravenous bolus but recent evidence supports the view that administration using a continuous intravenous infusion is superior [33–35]. Most recently, a study by Choudhary and colleagues compared a 50-mcg/min infusion of phenylephrine with 50 mcg boluses of phenylephrine administered if the systolic blood pressure fell below 20% of the baseline [36•]. The results confirmed the hypothesis that a phenylephrine infusion is associated with a tighter control of blood pressure around the baseline and additionally demonstrated lower rates of nausea and vomiting. There was no appreciable difference in the secondary outcome measures of APGAR score or fetal pH. Prolonged administration may be associated with tachyphylaxis possibly secondary to alpha-receptor downregulation but is unlikely to be of significance considering the relatively short duration of exposure to the drug during cesarean deliveries.

While phenylephrine is effective in the treatment of hypotension, the risk of associated reflex bradycardias and the corresponding fall in cardiac output is of concern [37]. While these effects are normally transient, well tolerated in the healthy parturient and easily reversible pharmacologically, the impact on those with existing cardiovascular dysfunction or evidence of fetal compromise may be deleterious. To date, there is a paucity of studies comparing vasopressors in non-elective or emergent cesarean deliveries [38]; one such study compared ephedrine and phenylephrine boluses in non-elective cesarean delivery but found no differences in pH or fetal outcomes [39]. Dosing regimens that address hypotension associated with spinal anesthesia while avoiding both reactive hypertension and bradycardias are therefore desirable. The ED_{95} of phenylephrine to prevent spinal-induced hypotension has been identified as 159 mcg (95% confidence interval, 122–371 mcg) although it is common clinical practice to use doses between 50 and 100 mcg, avoiding the hemodynamic effects of the larger doses [40]. Similarly, different rates of phenylephrine intravenous infusion in the range of 25 to 100 mcg/min have also been studied; those receiving the lower infusion rates of 25 to 50 mcg/min are found to require fewer interventions to maintain the target blood pressure and fewer incidences of both reactive hypertension and bradycardias when compared with those receiving the high infusion rates of 75 to 100 mcg/min [41].

Norepinephrine

Norepinephrine, a potent vasopressor, has potential advantages over both ephedrine and phenylephrine and, in theory, may represent an effective alternative agent in the management of spinal-induced hypotension, its use being advocated in a growing number of articles [42•, 43•, 44–47]. Firstly, norepinephrine is a potent alpha-receptor agonist but additionally confers efficacy at the beta-receptors counteracting a reflex bradycardia; in comparison to phenylephrine, this potentially more stable hemodynamic profile of norepinephrine may negate the need for rescue anticholinergics or ephedrine boluses to correct falls in heart rate. Norepinephrine has an advantage over ephedrine by exhibiting a quicker onset and shorter duration of action. Placental transfer of norepinephrine and any subsequent detection of neonatal acidosis has not been demonstrated. Comparison of both norepinephrine and phenylephrine delivered by bolus and infusion has demonstrated fewer fluctuations in heart rate in the norepinephrine groups but differences in maternal and fetal outcomes have not been shown [42•, 43•]. This suggests that although an overall benefit of norepinephrine when compared with phenylephrine is not observed in the healthy mother; further studies in those with placental

insufficiency or signs of fetal compromise may be required to identify any benefit of norepinephrine in higher risk groups. Many centers only administer norepinephrine via the central venous access together with direct arterial pressure monitoring and may be reluctant to consider peripheral administration with only intermittent non-invasive blood pressure monitoring. While there are concerns that peripheral administration of norepinephrine risks ischemic injury to the limb, there are no cases to support this theory when administering bolus doses of 6–8 mcg, equipotent to 100 mcg of phenylephrine [45•]. Similarly, norepinephrine infusion rates of ≤ 5 mcg/min have been shown to be effective at maintaining maternal blood pressure without affecting neonatal outcome [48].

Metaraminol

Like norepinephrine and ephedrine, metaraminol is an alpha-agonist with mild beta activity and may also be considered to treat spinal-induced hypotension. One study compared an intravenous infusion of metaraminol with one of phenylephrine, both titrated to achieve a systolic blood pressure of > 90% of baseline, the primary outcome being a difference in umbilical pH [49•]. Although a more favorable umbilical pH was observed in the metaraminol group (the mean umbilical arterial pH was 7.31 in the metaraminol group and 7.28 in the phenylephrine group [$p = 0.0002$]), the authors advised caution when interpreting the significance of this finding given the small effect size. Metaraminol was associated with a greater number of hypertensive episodes, defined as a systolic blood pressure of greater than 110% of baseline, though this was not felt to be clinically significant in the healthy, elective population concluding that metaraminol is likely a suitable alternative to phenylephrine. This study was designed as a "non-inferiority" study to establish whether metaraminol was at least as effective as phenylephrine. It was not powered as a "superiority" study therefore despite the findings; additional studies are warranted to further elucidate metaraminol's potential to be more favorable than phenylephrine in terms of neonatal acid-base status.

Alternative Pharmacological Strategies

In addition to vasopressors, other drugs have been described to manage spinal-induced hypotension, most notably glycopyrrolate and ondansetron. Glycopyrrolate, an anticholinergic, has been shown to reduce total vasopressor dose requirements for the treatment of hypotension when given prophylactically although its administration neither reduces the absolute incidence of spinal hypotension nor influences APGAR scores in terms of neonatal outcome [50, 51]. A meta-analysis did not support the routine use of glycopyrrolate in the prophylaxis of spinal-induced hypotension but it advocated consideration in those with a history of bradycardia or with high vasopressor requirements. Caution was advised, however, regarding the risk of increasing myocardial oxygen demand though positive chronotropy in those with cardiac disease or with susceptibility to ischemia [52•]. It should be remembered that it is a very effective anti-sialagogue causing a dry mouth and potential discomfort to the mother. Similarly, ondansetron given prior to spinal anesthesia has also been shown to reduce vasopressor requirements. Although earlier studies had been inconsistent at demonstrating a reduction in the incidence of hypotension following ondansetron, a recent meta-analysis by Heesen and colleagues was able to demonstrate a moderate effect [53–55, 56•]. Rigorous studies are still required to establish its efficacy as well as clarity regarding the placental transfer of ondansetron and subsequent effects on neonatal outcomes.

Vasopressor Use in Other High-Risk Groups

The relatively few studies in higher risk cohorts provide little in the way of evidence-based guidance as to appropriate vasopressor therapy in those with existing cardiac disease or preeclampsia. However, it seems sensible that ephedrine-driven increases in heart rate, and therefore myocardial oxygen demand, should be avoided in mothers with existing ischemic heart disease or aortic stenosis. Similarly, phenylephrine might be preferred in cases of hypertrophic cardiomyopathy, as beta stimulation and resulting inotropy by alternative agents may risk ventricular outflow tract obstruction. The reduction in heart rate associated with phenylephrine may, however, impede forward flow through regurgitant valves. In the same way that neuraxial anesthesia should be approached more cautiously in heart disease (using combined spinal epidural (CSE) or low-dose spinal techniques), the choice of vasopressor should be carefully considered and commenced at lower doses to allow a safer assessment of efficacy and hemodynamic response [57].

Unlike cardiac disease, which is more likely to be encountered in tertiary maternity centers, preeclampsia is found in even the most remote delivery areas. Spinal anesthesia in severe preeclampsia, when not contraindicated by coagulopathy or thrombocytopenia, has been shown to be associated with a lower incidence of hypotension when compared with healthy parturients. Epidural anesthesia is more hemodynamically stable than spinal anesthesia but the difference between these two methods of neuraxial blockade is not thought to be clinically significant [58]. A small degree of afterload reduction and increase in cardiac output might be beneficial to mothers with an increased vascular tone; however, any hypotension may be less tolerated by the fetus in cases of placental insufficiency [59, 60]. Regarding the treatment of hypotension in preeclampsia, phenylephrine would seem to return the systemic vascular resistance, heart rate, and cardiac output back to baseline more effectively than ephedrine; however, comparison of these two drugs has not demonstrated a difference in umbilical

pH, APGARs, or neonatal outcome in women with severe preeclampsia and fetal compromise [61, 62•]. Caution continues to be advised when treating hypotension in preeclampsia; fluid boluses risk pulmonary edema and acute left heart failure and a greater sensitivity to vasopressors necessitate extra vigilance and smaller doses.

Consensus

It is surprising that despite growing evidence to support the use of phenylephrine in the management of spinal-induced hypotension, the uptake of this practice remains considerably variable. A European survey conducted in 2012 showed that ephedrine remained the vasopressor of choice, though in the UK, there appeared to be a move towards a preference for phenylephrine [63–65]. A general consensus on the use of bolus vs. infusion or the proportion of baseline BP to be maintained remained elusive. Guidelines provided by both the National Institute for Health and Care Excellence (NICE) and the American Society of Anesthesiologists (ASA) recommend both ephedrine or phenylephrine although the latter recognizes the improved fetal acid-base status offered by phenylephrine in low-risk cases [66, 67].

In recognition that there is variability in the management of spinal-induced hypotension dependent on the different options available, an international consensus statement was published to provide clinicians with what is regarded as the current best-available practice [68••]. This statement decisively advocates the use of phenylephrine over ephedrine and supports delivery of the drug by intravenous infusion as opposed to reactive boluses while targeting a systolic blood pressure of greater than 90% of the baseline. This is substantiated by the findings of Ngan Kee and colleagues who demonstrated that maintaining a baseline systolic blood pressure was associated with lower incidences of maternal nausea, vomiting, and a higher umbilical cord pH [31]. Phenylephrine dose should also be targeted to heart rate reflecting the observation by Dyer and colleagues that heart rate closely correlates with cardiac output and may be a useful surrogate in the absence of routine cardiac output monitoring [69]. The consensus statement recommends that the use of ephedrine should be reserved for the management of hypotension in the presence of a low heart rate although other second-line agents to correct hypotension such as atropine or glycopyrrolate should also be considered in this scenario.

Conclusions

The literature exploring the use of vasopressors in the management of spinal-induced hypotension provides a relative framework upon which to establish best-practice recommendations to guide clinical practice. However, it is clear that the current evidence available is limited. The studies that describe benefits to a particular treatment, whether phenylephrine over ephedrine, norepinephrine over phenylephrine, or infusions over boluses, have all been carried out in low-risk, elective cases. The clinical impact of these findings is also relatively small owing to the fact that many physiological effects observed in these studies are likely to be well tolerated in this cohort of patients. Caution is advised so as not to misinterpret clinical findings; for example, the reduction in cardiac output following alpha-1 agonists may in fact be a return to the preoperative baseline rather than an absolute reduction given that spinal anesthesia is known to increase cardiac output [70].

The relatively small number of studies in higher risk groups have so far neither replicated findings seen in low-risk cohorts nor sufficiently demonstrated differences in maternal or fetal outcomes between the therapies being compared. A small number of studies comparing vasopressors in emergency cases found no difference in cord pH and *may* reflect a shorter time interval between spinal and delivery due to the time-critical nature of an emergency cesarean delivery. In comparison, studies of elective cases that positively identified a lower pH in umbilical cord samples also had longer intervals between the spinal injection and delivery, highlighting the potential of clinically unnecessary delays in order to gather data [71]. It is widely recognized that further studies investigating treatment strategies in high-risk patients are required, as it is in this group whom patients are most likely to benefit, but ethical considerations limit the design of such research.

While the international consensus appreciates the limitations of the evidence available, it also recognizes the benefit of addressing the variation amongst clinicians and seeks to consolidate current evidence into best-practice recommendations [68••]. Further well-conducted studies are required, and in the future, we may see the emergence of more accessible methods by which to predict hypotension and a more established use of cardiac output monitoring to facilitate a bespoke fluid and vasopressor regimen. The use of computer-controlled smart-pumps to deliver vasopressors might aid a tighter control of blood pressure and norepinephrine may even supersede phenylephrine as the recommended first-line vasopressors [72, 73].

In conclusion, spinal-induced hypotension during cesarean delivery remains a significant clinical challenge. Fluid loading has limited efficacy in the prevention hypotension and as such, the use of vasopressors has gained prominence. Despite the lack of studies performed in high-risk patient groups, a growing body of evidence within low-risk cohorts has helped inform vasopressor choice and establish firm recommendations for clinical practice.

Compliance with Ethical Standards

Conflict of Interest Stephen Ramage, Sarah Armstrong, and Roshan Fernando declare they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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