Anaesthesia 2018, 73, 71–92 doi:10.1111/anae.14080

# Guidelines

## International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia

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*Accepted: 23 August 2017*
*Keywords: blood pressure measurement; caesarean section; ephedrine; hypotension; intravenous fluid; phenylephrine; spinal anaesthesia; vasopressor*
*This article is accompanied by an editorial by Campbell and Stocks, Anaesthesia 2018; 73: 3-6, and the following articles by Zieleskiewicz et al., Anaesthesia 2018; 73: 15-22 and Dyer et al., Anaesthesia 2018; 73: 23-31.*

### *Why was this consensus statement developed?*

Advances in clinical practice are sometimes inhibited by a multitude of different options that need to be selected. There has been significant variation in the treatment of spinal anaesthesia-induced hypotension. These guidelines are designed to provide clinicians with specific best-practice plans that will cover a wide range of drug and equipment availability. Detailed recommendations are provided for the management of hypotension in resource-rich and resource-poor environments.

### *How does this consensus statement differ from other available guidelines?*

The American Society of Anesthesiologists/Society for Obstetric Anesthesia and Perinatology Task

Force, and the UK National Institute for Health and Care Excellence, have made generic recommendations on this topic [1, 2]. We are unaware of detailed guidelines from any organisations. We aim to offer independent, pragmatic advice that will be of benefit to clinicians and the women we treat.

## Recommendations for best clinical practice

1 Hypotension following spinal or combined spinal-epidural anaesthesia at caesarean section causes both maternal and fetal/neonatal adverse effects.
2 Hypotension is frequent and, therefore, vasopressors should be used routinely and preferably prophylactically.
3 α-agonist drugs are the most appropriate agents to treat or prevent hypotension following spinal anaesthesia. Although those with a small amount of β-agonist activity may have the best profile (noradrenaline (norepinephrine), metaraminol), phenylephrine is currently recommended due to the amount of supporting data. Single-dilution techniques, and/or prefilled syringes should be considered.
4 Left lateral uterine displacement and intravenous (i.v.) colloid pre-loading or crystalloid coloading, should be used in addition to vasopressors.
5 The aim should be to maintain systolic arterial pressure (SAP) at $\geq$ 90% of an accurate baseline obtained before spinal anaesthesia, and avoid a decrease to < 80% baseline. We recommend a variable rate prophylactic infusion of phenylephrine using a syringe pump. This should be started at 25–50 $\mu g.min^{-1}$ immediately after the intrathecal local anaesthetic injection, and titrated to blood pressure and pulse rate. Top-up boluses may be required.
6 Maternal heart rate can be used as a surrogate for cardiac output if the latter is not being monitored; both tachycardia and bradycardia should be avoided.
7 When using an α-agonist as the first-line vasopressor, small doses of ephedrine are suitable to manage SAP < 90% of baseline combined with a low heart rate. For bradycardia with hypotension, an anticholinergic drug (glycopyrronium (glycopyrrolate) or atropine) may be required. Adrenaline (epinephrine) should be used for circulatory collapse.
8 The use of smart pumps and double (two drug) vasopressor infusions can lead to greater cardiovascular stability than that achieved with physician-controlled infusions.
9 Women with pre-eclampsia develop less hypotension after spinal anaesthesia than healthy women. Abrupt decreases in blood pressure are undesirable because of the potential for decreased uteroplacental blood flow. A prophylactic vasopressor infusion may not be required but, if used, should be started at a lower rate than for healthy women.
10 Women with cardiac disease should be assessed on an individual basis; some conditions are best managed with phenylephrine (an arterial constrictor without positive inotropic effect), whereas others respond best to ephedrine (producing positive inotropic and chronotropic effect).

## Introduction

Hypotension is a very common consequence of the sympathetic vasomotor block caused by spinal anaesthesia for caesarean section. Maternal symptoms such as nausea, vomiting and dyspnoea frequently accompany severe hypotension, and adverse effects on the fetus, including depressed Apgar scores and umbilical acidosis, have been correlated with severity and duration of hypotension.

Ephedrine, a mixed α- and β-adrenergic agonist, became the drug of choice in obstetric anaesthesia following work that found that it was the best vasopressor for preservation of uterine blood flow in a sheep model of drug-induced hypertension. However, higher doses of ephedrine, used clinically in attempts to reduce hypotension, were found not to improve neonatal acidosis, but rather the reverse [3]; this is now acknowledged to be because ephedrine has a direct effect on fetal metabolism that negates any improvement in uterine blood flow produced by normalising blood pressure [4, 5]. Clinical work dating from the 2000s indicated that α-adrenergic agonists

are effective at reducing hypotension, and associated with less neonatal acidosis than ephedrine [6].

National practice guidelines suggest the use of both ephedrine and phenylephrine for the management of hypotension; UK guidelines from 2011 state that: '*Women who are having a caesarean section under regional anaesthesia should be offered intravenous ephedrine or phenylephrine, and volume preloading with crystalloid or colloid to reduce the risk of hypotension occurring during caesarean section*' [2]. American guidelines from 2016 provide more detail: '*Intravenous fluid preloading or co-loading: intravenous fluid preloading or co-loading may be used to reduce the frequency of maternal hypotension after spinal anesthesia for cesarean delivery; do not delay the initiation of spinal anesthesia in order to administer a fixed volume of intravenous fluid. Ephedrine or phenylephrine: either intravenous ephedrine or phenylephrine may be used for treating hypotension during neuraxial anesthesia; in the absence of maternal bradycardia, consider selecting phenylephrine because of improved fetal acid–base status in uncomplicated pregnancies*' [1].

Surveys of clinical practice indicate that there has been a shift away from what was the almost universal use of ephedrine as the vasopressor of choice. In the UK, a 1999 survey found that 95% of respondents used ephedrine alone during caesarean section [7]; in 2011, 89% of respondents used phenylephrine, and the remainder used metaraminol or ephedrine [8]. A survey carried out in the USA in 2007 noted that 32% of respondents used ephedrine for vasopressor prophylaxis and treatment of hypotension, 26% and 23%, respectively, used phenylephrine, and the remainder used either agent according to maternal heart rate [9].

## Definition of hypotension

Klöhr et al. found 15 different definitions of hypotension in 63 studies of hypotension following spinal or combined spinal-epidural anaesthesia for caesarean section, performed between 1999 and 2009 [10]. Definitions varied between those using an absolute blood pressure value, ranging from 80 mmHg to 100 mmHg, a decrease of 0–30% from a baseline or a combination of an absolute value and a percentage decrease. Some studies distinguished between severe hypotension and lesser (mild-moderate) degrees. All studies used the systolic arterial pressure (SAP) measured in the arm, in a variety of body positions; all but one [11] used the non-invasive oscillometric method. Baseline blood pressure readings were usually taken just before performing spinal anaesthesia, although occasionally at an earlier stage, such as on admission to the labour ward. The baseline was estimated from one, two or three replicate readings. Applying these different definitions to a cohort of women having elective caesarean section gave incidences for hypotension varying between 7.4% and 74.1% [10].

The most common definitions of hypotension used in research studies were either '< 80% baseline', or '< 100 mmHg OR < 80% baseline' [10]. A 1999 survey in the UK found that most consultant obstetric anaesthetists use a threshold of either 100 or 90 mmHg [7].

The SAP is a less important variable than mean arterial pressure (MAP) as a determinant of organ perfusion; however, because methods used to measure blood pressure in routine clinical practice did not include the mean until recent decades, it is unlikely to be adopted for the definition of obstetric hypotension without considerably more supportive data.

Most of the studies identified by Klohr et al. were at elective caesarean section; few included women in labour [12]. Arterial pressure increases during labour; using baseline values taken in the antenatal period or at the start of labour was shown to reduce the incidence of recorded hypotension, defined as a decrease < 80% baseline value, after epidural analgesia [13]. Many studies of hypotension at caesarean section did not include hypertensive women. The SAP threshold for pregnancy-induced hypertension or pre-eclampsia is > 140 mmHg [14].

## Consequences of hypotension and its pharmacological treatment

Nausea and vomiting are significantly more frequent during spinal anaesthesia for caesarean section than during non-obstetric surgery. The aetiology of this is multifactorial [15]. Acute hypotension reduces cerebral perfusion, induces transient brainstem ischaemia and activates the vomiting centre. Transient cerebral hypoxia may occur, as studies using near-infrared spectroscopy (NIRS) show that hypotension is accompanied by a significant decrease in maternal regional

 

cerebral blood volume, cerebral oxygen saturation and oxygenation [16]. This is consistent with the observation that supplemental oxygen may relieve this nausea [17, 18]. Spinal anaesthesia decreases splanchnic blood flow by approximately 20% [19], which may be accentuated by accompanying systemic hypotension. The resulting splanchnic hypoperfusion releases emetogenic factors such as serotonin from the gastro-intestinal tract. Finally, acute sympathetic blockade may cause unopposed vagal action and subsequent hyperactivity in the gastro-intestinal tract [20]. Regardless of the aetiology, the use of prophylactic vasopressors significantly reduces the incidence of intra-operative nausea and vomiting during caesarean section [21]. Dizziness and decreased levels of consciousness may follow severe and prolonged maternal hypotension, but are uncommon when blood pressure is treated promptly. The effect of postspinal hypotension on fetal physiology during caesarean section remains poorly characterised in humans, although animal research shows that a sustained decrease of > 60% in uterine blood flow results in bradycardia and acidaemia within 10 min in a previously uncompromised fetus [22]. Clinical data have largely come from observational studies that separated groups with and without hypotension, or assessed duration of hypotension. Neonates of women with spinal-induced hypotension had significant acidosis [23, 24], and hypotension of more than 2 min duration was associated with a significant increase in umbilical venous oxypurines and lipid peroxides, suggestive of ischaemia–reperfusion injury [25].

Duration of hypotension may be more important than severity. A transient ≥ 30% decrease in blood pressure did not affect neonatal Apgar scores, incidence of meconium-stained amniotic fluid or the need for oxygen therapy in the neonate [26]. Hypotension for less than 2 min did not affect neonatal neurobehavioral outcomes [23], whereas more than 4 min of maternal hypotension was associated with neurobehavioral changes at 4–7 days of life [27].

An important confounder in interpreting acid–base changes during spinal anaesthesia for caesarean delivery is the choice of vasopressor used to treat hypotension. Although results from early animal studies were conflicting, recent clinical trials clearly suggest that phenylephrine, given as an infusion, is associated with better neonatal acid–base balance than ephedrine [5, 28]. Ephedrine has higher transplacental transfer than phenylephrine, with median umbilical venous/maternal arterial ratios of 1.13 and 0.17, respectively; in large doses this is associated with lower neonatal pH, higher base deficit, and increased lactate and catecholamine levels [5]. These findings support activation of fetal sympathetic metabolism by ephedrine administration. Although the use of phenylephrine infusions for hemodynamic control during caesarean section results in optimum umbilical cord biochemical values, clinical differences in neonatal outcomes have not been demonstrated so far.

Whether these biochemical advantages of phenylephrine over ephedrine translate into improved clinical outcomes in the compromised fetus is unclear as yet. The available studies show no difference in the incidence of fetal acidosis when either ephedrine or phenylephrine infusion was used to maintain blood pressure during spinal anaesthesia for emergency caesarean delivery, both in unselected (i.e. non-elective) cases [12], or specifically those with acute fetal compromise [29].

## Comparative pharmacology of vasopressor agents

Vasopressor drugs mediate their cardiovascular effects primarily through their actions on α1-, β1- and β2-adrenergic receptors, the relative stimulation of each receptor resulting in differing physiological effects. In addition, further changes, such as bradycardia, may result from reflex cardiovascular responses. The major clinical considerations relate to relative α- and β-adrenergic effects, onset time and duration, and fetal effects (Table 1).

Ephedrine not only has mainly indirect adrenergic receptor activity but also exerts weak direct effects, which explains the comparatively slow onset and long duration of action. Ephedrine typically increases heart rate and contractility by cardiac β1-adrenergic receptor stimulation.

Phenylephrine has a potent direct α1-effect, with virtually no β-effects at clinical doses. When given at higher than required doses, it may induce baroreceptor-mediated bradycardia with a consequent reduction

 

**Table 1** Comparison of commonly used vasopressors.

| | Ephedrine | Phenylephrine | Metaraminol | Noradrenaline | Adrenaline | Mephentermine |
|---|---|---|---|---|---|---|
| **Receptor** | β1, β2, weak α | α1 | α1, weak β | α1, β | α1, β | α1, β |
| **Mechanism** | Indirect, weak direct | Direct | Direct and indirect | Direct | Direct | Indirect |
| **Onset** | Slow | Immediate | 1–2 min | Immediate | Immediate | Immediate |
| **Duration** | Prolonged | Intermediate | Prolonged | Short | Short | Prolonged |

in maternal cardiac output [11, 30, 31]. George et al., using up-down sequential allocation, found the $ED_{90}$ of a phenylephrine bolus to treat spinal hypotension to be 147 (95%CI 98–222) μg [32]. Using similar methodology, Tanaka et al. estimated the $ED_{95}$ to prevent spinal hypotension or nausea to be 159 (95%CI 122–371) μg [33]. However, doses of this magnitude may be associated with increases in systemic vascular resistance and bradycardia, and a bolus dose of 100 μg is more common [32, 34]. Supporting this conclusion, Mohta et al. found no benefit when using doses of 125 μg or 150 μg phenylephrine to treat hypotension, in comparison with doses of 100 μg [35]. The potency ratio of phenylephrine to ephedrine for infusions, established using up-down sequential allocation, is 81:1 [36].

Metaraminol is a mixed α- and β-agonist although, at doses used clinically, α-effects predominate. It has both direct and indirect effects; it undergoes uptake into postganglionic sympathetic nerve endings, where it substitutes for noradrenaline to act as a weak false neurotransmitter [37]. A recent comparative study used a dose ratio of 5:1 for metaraminol:phenylephrine [38].

Noradrenaline is the primary catecholamine released by postganglionic adrenergic nerves. It is a potent α1-adrenergic agonist, with comparatively modest β-agonist activity. It causes marked vasoconstriction with some direct inotropic effects. Administration results in higher heart rates than with comparable doses of phenylephrine [39, 40]. The $ED_{90}$ for prevention of hypotension is 5.8 μg [41]. Ngan Kee et al. found a dose ratio of 1:17 for noradrenaline:phenylephrine [39].

In comparison, adrenaline (epinephrine) has high affinity for α1-, β1- and β2-adrenergic receptors. β-effects predominate at low doses, while α1-effects are more significant at higher doses.

Mephentermine is a mixed α- and β-adrenergic receptor agonist that has both direct and indirect effects due to the release of noradrenaline and adrenaline. Limited information is available regarding placental transfer and fetal metabolic effects [42], although it is a popular agent in a number of low- and middle-income countries. An advantage of this drug is that it does not require multiple dilutions.

## Cardiovascular changes after spinal anaesthesia

The main focus of clinical management is the maintenance of maternal blood pressure, based on our understanding of the adverse effects of hypotension. However, evidence from research studies suggests that cardiac output is an important additional variable.

The primary effect of spinal anaesthesia in a healthy woman is a decrease in systemic vascular resistance secondary to small artery vasodilation [43, 44], with a modest degree of venodilation [45]. There is a compensatory baroreceptor-mediated increase in heart rate and stroke volume, which increases cardiac output [11, 31, 43, 46, 47]. With a high spinal block to cervical levels, the pre-ganglionic sympathetic cardiac accelerator fibres may be blocked resulting in a failure of compensatory tachycardia. However, heart rate does not correlate well with block height; a pattern of sudden bradycardia, secondary to vasovagal (also termed Bezold–Jarisch) reflex activation, is well recognised [48].

The aim of vasopressor treatment should be, therefore, to restore systemic vascular resistance, which is best achieved using agents with predominantly α-agonist activity. However, dependence on high doses of vasopressors to restore blood pressure, without other manoeuvres [49], may lead to low cardiac output.

 

### *Pharmacological treatment*

Dyer et al. used the calibrated LiDCOplus® monitor (LiDCO, Cambridge, UK) and transthoracic bioimpedance to measure cardiac output in a comparison of phenylephrine and ephedrine boluses used in elective caesarean section. Phenylephrine corrected the postspinal decrease in systemic vascular resistance and hypotension more effectively than ephedrine. Of note, there was good correlation between the percentage change in peak heart rate and peak cardiac output after the vasopressor bolus, independent of vasopressor type. They concluded that heart rate, not MAP, is the best surrogate for cardiac output when the latter is not being measured [31]. Stewart et al. found dose-dependent reductions in both maternal heart rate and cardiac output, measured with suprasternal Doppler, when comparing three different infusion regimens of phenylephrine. The highest infusion rate reduced both cardiac output and heart rate by > 20%. This study also supports the hypothesis that reduced heart rate may indicate excessive phenylephrine doses that are causing a reduced cardiac output [30].

### *Non-pharmacological measures and i.v. fluid administration*

Other measures to prevent or treat hypotension and haemodynamic instability include methods to reduce inferior vena cava compression and venous pooling in the legs, as well as intravascular fluid loading [45, 50–52]. Once the woman is positioned supine for surgery, left uterine displacement is routinely used to reduce inferior vena cava compression, with a recommended angle of 15° [53, 54]. This angle of table tilt is associated with higher maternal SAP and cardiac output and lower doses of infused phenylephrine than the unmodified supine position [55], but is seldom achieved in practice [56]. If the table is tilted to 15°, lateral support is required for security. Adequately-applied tilt may make operating awkward for the obstetrician; however, it can be used during the period of preparation before surgery, and reduced at the last moment before surgery if haemodynamic stability has been achieved at that point. Manual displacement of the uterus may be better than left lateral tilt at reducing hypotension at caesarean section [51], but it is difficult to sustain during surgery.

Leg compression has been shown to be more effective than no leg compression in preventing hypotension, although a high level of heterogeneity suggests that its effectiveness may depend on the type and intensity of compression used (bandages, inflatable boots or antithromboembolic stockings) [50]. Venous compression seems to be of limited effectiveness, possibly reflecting the lesser effect of venodilation compared with arteriolar dilation after spinal anaesthesia. A comparison between thromboembolic deterrent (TED) stockings and sequential compression boots/leggings did not show a difference in blood pressure changes [57].

One study found that leg elevation to 30° after spinal anaesthesia reported no significant decrease in incidence of hypotension [58], whereas a larger study found a similar numerical reduction in hypotension that reached statistical significance [59]; an important difference between the studies was that i.v. crystalloid pre-load 20 $ml.kg^{-1}$ was used in the former, but none in the latter.

Intravenous crystalloid pre-loading, first described in the 1960s, was performed using ever-increasing volumes until a landmark study in 1993 challenged this practice [60]. Further studies confirmed that it has very limited effectiveness at reducing the incidence or severity of hypotension [50], and is no longer recommended [61, 62]. Crystalloid coloading may be more effective at decreasing hypotension and vasopressor requirements than pre-loading [63] or no fluid [64]. Although a meta-analysis suggested no benefit vs. pre-loading [65], a recent analysis suggests a moderate additional benefit on top of vasopressor prophylaxis, provided that a sufficient volume is infused under pressure during the first 5–10 min after the spinal [66].

Colloid pre-load is more effective than crystalloid pre-load for prevention of hypotension [50, 67]. A 500-ml pre-load of 6% hydroxyl-ethyl starch (HES; 130/0.4) followed by 500 ml Ringer's lactate, in combination with prophylactic boluses of phenylephrine, was associated with a significantly lower incidence of hypotension compared with a 1000-ml pre-load of Ringer's lactate (37% vs. 55%, respectively) as well as less symptomatic hypotension (4% vs. 14%, respectively) [68]. In general a 500-ml pre-load of colloid

 

appears as effective as a 1000-ml coload of crystalloid [69]. Thus, both fluid-loading techniques can be recommended to improve the haemodynamic stability provided by vasopressor prophylaxis.

## Pre-operative prediction of hypotension

Individual patient characteristics have been suggested as predictors of hypotension, based on multivariate analyses of population data [70, 71]. However, these findings have not been replicated by more specific prospective investigations. Body mass index does not affect the frequency and severity of hypotension [72–74]. Emergency caesarean is associated with less hypotension than elective surgery [70]. This is likely to be more particularly related to the presence of labour [12, 75, 76]. A wide variety of methods have been described to predict the development of hypotension after spinal anaesthesia (Table 2) [73, 77–93]. These include basic cardiovascular variables, cardiovascular measurements that are not part of routine monitoring, complex processed cardiovascular indices, postural manipulations and other methods. Pre-operative baseline heart rate was found to be a useful predictor of hypotension in several studies [80, 81, 89], but a number of others have not supported this [73, 79, 88].

Orbach-Zinger et al. found that high pre-operative anxiety was associated with a greater decrease in SAP than low anxiety, although the incidence of hypotension was not reported [94].

Some studies have investigated changes occurring after the spinal block, as an indicator of impending hypotension. Berlac and Rasmussen suggested that NIRS could provide an early warning of hypotension, with a $\geq$ 5% decrease in saturation preceding hypotension by a median (IQR) 81 (3–281) s [95]. Hanss et al. noted that greater changes in heart rate variability after the spinal were found in women who then developed more severe hypotension [96].

Until a definitive and widely available method of predicting hypotension is identified, we suggest that there is a raised likelihood of developing hypotension if the baseline heart rate is high or there is a clear and recent history of supine intolerance/supine hypotensive syndrome. Furthermore, when intermittent non-invasive blood pressure measurement is being used, an increase in heart rate after the spinal local anaesthetic injection may precede the recognition of hypotension.

## Vasopressor management at elective caesarean section with spinal anaesthesia

### *Drug selection*

A vasopressor with predominantly α-agonist activity is the correct choice to reverse the circulatory effects of spinal anaesthesia; phenylephrine has the most evidence supporting its use [97]. However, concerns about reflex bradycardia and decreased cardiac output associated with phenylephrine have prompted research on noradrenaline and metaraminol, which might have some advantages due to their mild β-adrenergic effects in addition to α-effects [38, 39]. Preliminary studies comparing noradrenaline to phenylephrine in the setting of obstetric spinal anaesthesia have found that noradrenaline may be a reasonable alternative to phenylephrine [39, 40, 98]; however, there are concerns about the use of such a potent agent in a non-intensive care setting such as the labour ward [99, 100]. Further studies of noradrenaline and metaraminol are, therefore, awaited.

A national survey found that there are multiple formulations of phenylephrine available in the UK [8]. The most common presentation is a 1-ml ampoule containing 10 mg, which is diluted into a 100-ml bag of saline to produce a final concentration of 100 $\mu g.ml^{-1}$ (Appendix 1). Solutions containing 50 $\mu g.ml^{-1}$ are the only other commonly used concentration, usually for bolus administration rather than infusion [8].

Clear systems should be in place for dilution of ampoules that contain high-concentration potent vasopressors, in order to reduce the risk of drug error. Anaesthetic departments should consider the benefits vs. risks of sourcing dilute ampoules, or prefilled syringes.

### *Target blood pressure*

As noted earlier, a number of definitions of hypotension are currently used. Ngan Kee et al. showed that there were marked improvements in the incidence of nausea and vomiting when SAP was maintained at the baseline level, compared with < 90% or < 80% baseline [49]; there were also measurable, albeit small, improvements in neonatal umbilical cord blood gas status. We suggest that the aim should be to maintain SAP $\geq$ 90%

 

Table 2 Methods used to predict the development of hypotension after spinal anaesthesia at caesarean section.

| Publication | Population; number of patients | Method | Definition of hypotension | Conclusion | Comments |
|---|---|---|---|---|---|
| Baysinger et al. [77] | 42 | Tilt test – HR increase > 10 beats.min$^{-1}$ and > 10 mmHg fall in SAP after moving from supine with left uterine displacement to sitting position | – | Lower minimum SAP and increased dose of ephedrine in women with positive test | |
| Ouzounian et al. [78] | 42 | Systemic vascular resistance index > 500 | SAP ≤ 80% baseline | Sensitivity 83%, specificity 78%, PPV 83%, NPV 78% | |
| Kinsella and Norris [79] | 27 | Supine stress test; HR increase > 10% during a 5-min period in supine position; combined with leg flexion while supine<br>Tilt test – HR increase > 10 beats.min$^{-1}$ or > 10 mmHg fall in SAP after moving from left lateral to sitting position | Severe hypotension – SAP < 70% baseline | Sensitivity 75%, specificity 82%, PPV 86%, NPV 69% for severe hypotension<br>Not predictive (no positive results) | |
| Frolich and Caton [80] | 40 | Orthostatic challenge – 5 min standing<br>Baseline HR | Mild – MAP < 80% baseline<br>Marked – MAP < 70% baseline | Not predictive<br>Baseline HR > 90 beats.min$^{-1}$ – PPV 83% for marked hypotension<br>Baseline HR < 90 beats.min$^{-1}$ – NPV 75% for marked hypotension | |
| Chamchad et al. [81] | 22 | HRV – point correlation dimension<br>HR > 100 beats.min$^{-1}$ | SAP < 75% baseline | Sensitivity 100%, specificity 100%, PPV 100%, NPV 100%<br>Sensitivity 36%, specificity 100%, PPV 36%, NPV 61% | |
| Hanns et al. [82] | 60 | LF/HF ratio > 2.5 | Severe – SAP < 80 mmHg | Predictive of severe hypotension | |
| Hanns et al. [83] | 40 | LF/HF ratio > 2.5 | Severe – SAP < 80 mmHg | Sensitivity 87%, specificity 82%, PPV 87%, NPV 82% | LF/HF measurements used to guide vasopressor prophylaxis in 40 other women |

(continued)

**Table 2** (*continued*)

| Publication | Population; number of patients | Method | Definition of hypotension | Conclusion | Comments |
|---|---|---|---|---|---|
| Dahlgren et al. [84] | 25 | Supine stress test; one or more of: HR increase > 10% during two consecutive measurements; decrease in SAP < 15 mmHg during 2 consecutive measurements; hip flexion or crossing legs; symptoms requiring change in position; these during a 10-min period in supine position | Hypotension – SAP < 100 mmHg<br>Clinically significant hypotension – hypotension as above with symptoms<br>Severe hypotension – SAP < 80 mmHg | Crystalloid pre-load: Sensitivity 69%, specificity 92%, PPV 90%, NPV 73% for clinically significant hypotension | Hypotension reduced in 28 other women with colloid pre-load |
| Jeon et al. [85] | 66 | Positional blood pressure change; $MAP_{lateral} - MAP_{supine}$ | MAP < 80% baseline | aOR 1.88 for every 1 mmHg increase in MAP after position change | |
| Ledowski et al. [86] | 40 | Skin conductance variables | Multiple thresholds | Not predictive | |
| Meirowitz et al. [87] | 40 | Passive 30° leg raise test; positive response = increase in cardiac output > 12% | MAP < 70% baseline | Not predictive | |
| Toyama et al. [88] | 35 | Perfusion index 3.5<br>Baseline HR | SAP < 75% baseline | Sensitivity 81%, specificity 86%, PPV 89%, NPV 76%<br>Not predictive | |
| Yokose et al. [89] | 81 | Pre-operative heart rate<br>Perfusion index<br>Pleth variability index<br>LF/HF ratio<br>HRV entropy | SAP < 80 mmHg | Grey zone analysis for HR: sensitivity 90% at HR 71 beats.min$^{-1}$; specificity 90% at HR 89 beats.min$^{-1}$<br>Other methods not predictive | |
| Prashanth et al. [90] | 108 | ANS index of HRV ≥ 24 | MAP < 80% baseline | Sensitivity 78%, specificity 66% for hypotension | |
| Kuwata et al. [91] | 50 | Pleth variability index from pulse oximeter | SAP < 90 mmHg or < 80% baseline | Sensitivity 78%, specificity 83%, | |
| Bishop et al. [73] | 102 | LF/HF ratio > 2.0<br>Baseline HR<br>Body mass index | SAP < 90 mmHg | Sensitivity 52%, specificity 76%, PPV 66%, NPV 64%<br>Other methods not predictive | |
| Sakata et al. [92] | 45 | LF/HF ratio change ≥ 2 going from supine to left lateral position | SAP ≤ 80% baseline | Sensitivity 60%, specificity 90%, PPV 96%, NPV 39% | |
| Zieleskiewicz et al. [93] | 40 | Passive 45° leg raise test; optimum threshold = increase in cardiac output > 8% | MAP < 80% baseline | Sensitivity 94%, specificity 73%, PPV 70%, NPV 85% | |

HR, heart rate; SAP, systolic arterial pressure; PPV, positive predictive value; NPV, negative predictive value; MAP, mean arterial pressure; HRV, heart rate variability; LF/HF, low frequency/high frequency; aOR, adjusted odds ratio.

of an accurately measured baseline until delivery of the neonate, with the intention of reducing the frequency and duration of episodes of significant hypotension < 80% baseline. Systolic arterial pressure values < 80% should be treated expeditiously, usually with a vasopressor bolus injection.

### *Measurement of blood pressure*

Guidelines for blood pressure measurement in general medical practice suggest, for accuracy, a 5-min period without movement or speaking [101], although this is unlikely to be achieved in the situation of impending surgery. On the other hand, a potentially conflicting requirement is that the baseline blood pressure should be taken under similar conditions to those after spinal, for example, with regard to position.

Research studies demand a high degree of accuracy in measurement, especially with regard to an accurate baseline blood pressure. For the oscillometric blood pressure method, Ngan Kee et al. set the device to repeat measurements every 1–2 min until three consecutive values of SAP were achieved with a difference of < 10% between them. The baseline pressure was considered to be the mean of those three readings, and heart rate was calculated as the mean of the three concurrent readings [39].

During routine clinical practice, most anaesthetists will only take one baseline measurement of blood pressure. However, repeated measurements should be performed if the value is higher than expected in a woman not known to be hypertensive, or in a woman who is in labour. If it does not settle, check the latest reading from the medical notes, and consider using this as baseline.

After the spinal, measure non-invasive blood pressure every minute. If blood pressure is being measured while the woman is in one or other lateral position, the non-invasive blood pressure cuff should be placed on the dependent arm to reduce error from hydrostatic effects [102].

### *Prophylactic vs. reactive treatment*

Heesen et al. performed a meta-analysis that included comparisons of prophylactic phenylephrine infusion vs. placebo infusion with vasopressor treatment if hypotension developed (reactive management). Prophylactic treatment demonstrated a benefit with regard to the incidence of hypotension both before and after delivery, as well as nausea and vomiting. Prophylactic phenylephrine infusions resulted in the administration of higher doses of phenylephrine overall, when compared with reactive treatment, while the risk of maternal hypertension and bradycardia were similar [103].

A randomised, controlled trial, published subsequent to this meta-analysis, compared prophylactic variable rate infusion and rescue phenylephrine boluses, with rescue boluses alone. This demonstrated that the infusion was more effective at preventing spinal hypotension, nausea and vomiting, with fewer clinical interventions [104].

### *Infusion vs. bolus administration*

Most studies have compared a prophylactic infusion of vasopressor with reactive administration. There are limited data comparing prophylactic phenylephrine infusions with prophylactic phenylephrine boluses. A study by das Neves et al. found that continuous infusion of phenylephrine appeared superior at preventing hypotension, nausea and vomiting when compared with a prophylactic dose of 50 μg phenylephrine [105]. Sen et al. reported similar results when comparing patients having a phenylephrine infusion with those having an initial prophylactic dose of 50 μg phenylephrine, followed by intermittent 50 μg doses [106]. Of note, the phenylephrine boluses used in these studies would be considered to be small; a dose of 100 μg is more widely used both to prevent and treat spinal hypotension [34, 49]. On the other hand, a high-dose (120 $\mu g.min^{-1}$), fixed-rate phenylephrine infusion was comparable with 120 μg boluses, apart from better early blood pressure control in the latter group [107].

From this evidence, it appears that a prophylactic phenylephrine infusion is superior to bolus administration only, and that delaying the start of the infusion could limit its efficacy in reducing the incidence of hypotension. In clinical practice, vasopressor administration at the point of recording a low blood pressure will not be as meticulous as in research studies, and will not be done 'on the clock'. Therefore, the tendency will be for delay in bolus treatment, with subsequent hypotension, in comparison with infusion. The

 

corollary is that the infusion should be started prophylactically immediately after the insertion of the spinal.

### *Optimum dose*

Allen et al. studied four prophylactic fixed-rate phenylephrine infusions. The groups having 25 $\mu g.min^{-1}$ and 50 $\mu g.min^{-1}$ had fewer physician interventions to maintain SAP > 80% baseline, compared with the group having 100 $\mu g.min^{-1}$. In addition, the 75 $\mu g.min^{-1}$ and 100 $\mu g.min^{-1}$ groups had higher incidences of reactive hypertension [108]. It seems preferable to start an infusion at a rate of 25–50 $\mu g.min^{-1}$, and titrate to response. Physician-controlled variable rate infusions are preferable to fixed rate, in order to limit the total dose of phenylephrine infused.

If a vasopressor infusion is commenced at a fixed rate after spinal insertion, there will be a delay in achieving effective blood levels, whereas adding a bolus dose of vasopressor immediately after the spinal will allow more rapid effect. Kuhn et al. demonstrated that an initial phenylephrine bolus of 0.25 $\mu g.kg^{-1}$, followed by an infusion at 0.25 $\mu g.kg.min^{-1}$, maintained SAP without any adverse effects [45]. Further work is required to identify an optimum dose for a prophylactic bolus, and ensure that there is not a risk of reactive hypertension and bradycardia.

### *Second-line drugs*

There are no comparative studies of drugs used as a second-line agent after the initial administration of an α-agonist. When using an α-agonist as the first-line vasopressor, low doses of ephedrine are suitable to manage SAP < 90% baseline when combined with a low heart rate, in order to restore blood pressure and cardiac output [31, 109]. There is no evidence to indicate the heart rate threshold requiring treatment, in the absence of severe hypotension; individual clinicians should use their clinical judgement.

For significant bradycardia with hypotension, an anticholinergic (glycopyrronium (glycopyrrolate) or atropine) may be required. There is insufficient evidence to recommend routine use of glycopyrronium for the prevention of hypotension [110].

Although not used to treat hypotension, ondansetron has beneficial side-effects producing a modest reduction in hypotension and bradycardia after spinal anaesthesia. More research is needed to establish its role conclusively [111, 112].

### *Computer-controlled vasopressor administration*

Close-loop automated vasopressor delivery systems use a microprocessor-based control unit to vary the dose of vasopressor according to maternal blood pressure. There are several aspects of administration that may be altered when using computer-controlled feedback systems. The algorithm may utilise an on-off or a proportional principle. For the on-off algorithm, the controller automatically triggers a fixed infusion of vasopressor when it detects blood pressure below a pre-set threshold [113], whereas for the proportional algorithm, the vasopressor dose delivered by infusion is varied in accordance with the degree of hypotension, for instance between 0 $\mu g.min^{-1}$ and 100 $\mu g.min^{-1}$ [114]. The system may deliver the vasopressor as a bolus or as an infusion in response to low blood pressure. Blood pressure control is more precise, with smaller doses of vasopressor, using boluses [115].

Suggested advantages of noradrenaline compared with phenylephrine, when administered in this way, include better precision in blood pressure control and higher cardiac output for the mother, and better cord pH and lower catecholamine levels for the neonate [39, 98, 116].

Continuous blood pressure monitoring ensures no lag time between the development and recognition of hypotension and, hence, the use of a continuous blood pressure measurement device may allow control with minimal delay and deviation. Several continuous, non-invasive blood pressure devices based on the vascular-unloading or volume-clamp method have been developed, including the Nexfin® (BMEYE B.V., Amsterdam, the Netherlands), CNAP® (CNSystems, Graz, Austria) and T-line (Tensys Medical, Inc., San Diego, CA, USA). These devices have the potential to detect rapid blood pressure changes, including hypotensive episodes [117–119]. Sia et al. used CNAP monitoring for their automated system, but also incorporated a double-vasopressor system that administered phenylephrine or ephedrine according to heart rate, to reduce reactive bradycardia found with phenylephrine [109, 120]. This group's most recent development included a simple proportional algorithm that allowed administration of

 

larger doses if blood pressure change is greater, along with a Nexfin monitor (Fig. 1). This system was able to achieve 80% of all SAP readings > 80% baseline, with good maternal and fetal outcomes [121].

These data suggest a potential role for automation of vasopressor administration, together with non-invasive continuous blood pressure monitoring, to allow more precise maintenance of haemodynamic stability. Safe performance of these systems in the presence of measurement artefacts needs to be demonstrated.

## Non-elective caesarean section and other anaesthetic techniques

Fetal acidaemia increases during the course of labour. Although it has not been demonstrated that ephedrine is worse than phenylephrine for neonatal outcomes in this situation [12, 29], ephedrine causes dose-related acidosis and, therefore, phenylephrine would seem to be the best vasopressor choice in the presence of significant fetal acidaemia. When caesarean section is required for a woman in labour, hypotension after spinal anaesthesia is reduced compared with elective cases [12, 75, 76]. It is advisable to start a vasopressor infusion at a lower rate than for elective cases. Furthermore, in the category-1 case, preparation of an infusion should not delay other measures taken to achieve rapid delivery of the fetus.

## Other anaesthetic techniques

The rate and severity of hypotension is greatest after full-dose spinal and combined spinal epidural anaesthesia compared with low-dose spinal, combined spinal-epidural and epidural techniques. Low-dose combined spinal-epidural and spinal catheter techniques provide excellent haemodynamic stability, with little requirement for vasopressor medication [122–124].

## Special circumstances

### *Pre-eclampsia*

Patients with severe pre-eclampsia experience less hypotension and have lower vasopressor requirements during spinal anaesthesia, compared with healthy women undergoing caesarean section [125–127]. These findings suggest that women with pre-eclampsia either have greater endogenous vasoactive mediators, or are more sensitive to exogenous vasopressors, compared with healthy pregnant women.

There are few studies comparing vasopressors in women with pre-eclampsia. A study evaluating the haemodynamic status of 15 women with severe pre-eclampsia having spinal anaesthesia for caesarean

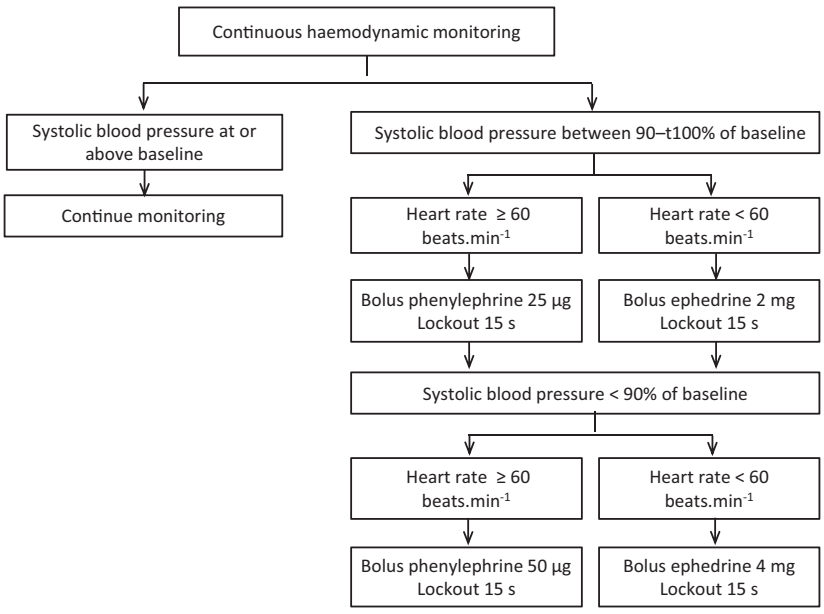


**Figure 1** Schematic diagram of the algorithm used in a double-intravenous vasopressor automated system (from [121]).

section for a maternal indication, found that 50–100 μg phenylephrine boluses to treat spinal hypotension increased MAP and systemic vascular resistance, but did not significantly change the stroke volume or cardiac output [128]. In a subsequent randomised trial investigating spinal anaesthesia for caesarean section in early onset severe pre-eclampsia, the maternal haemodynamic effects of ephedrine and phenylephrine were formally compared. After a 300-ml colloid pre-load, a median bolus dose of 50 μg phenylephrine returned the spinal anaesthesia-induced changes in systemic vascular resistance, heart rate and cardiac output towards baseline more effectively than 15 mg ephedrine boluses [129].

A retrospective comparison of ephedrine and phenylephrine for the treatment of hypotension after spinal anaesthesia in women with pre-eclampsia found no difference in neonatal umbilical artery pH [130], nor did a further study in high-risk women that included an unspecified proportion of women with pre-eclampsia [131]. A recent randomised trial has shown that in patients with severe pre-eclampsia and fetal compromise, fetal acid–base status is independent of the use of bolus ephedrine vs. phenylephrine to treat spinal hypotension [132].

These studies suggest that phenylephrine is the optimal first-line vasopressor to reverse the maternal haemodynamic changes induced by spinal anaesthesia in women with severe pre-eclampsia. The dose of phenylephrine required may be lower than in healthy women; hence a prophylactic vasopressor infusion may not be required and, if used, should be started at a low dose with the effect on blood pressure monitored carefully. The choice of vasopressor, whether administered by bolus or infusion, does not appear to influence neonatal outcome.

The ideal target blood pressure for women with gestational hypertension is unknown; figures of < 140–150 mmHg are suggested for SAP [14, 133]. The aim should be to allow SAP to come down slowly, as rapid reduction risks a decrease in uteroplacental blood flow.

### *Cardiac disease*

Neuraxial techniques are frequently used in women with cardiac disease undergoing caesarean section in contemporary clinical practice. In women with pulmonary hypertension, there is a trend towards lower mortality during caesarean section with neuraxial compared with general anaesthesia [134]. Single-shot spinal anaesthesia is best avoided in women with significant cardiac disease; the rapid-onset sympathectomy and haemodynamic changes associated with spinal anaesthesia are often poorly tolerated, especially with pre-load-dependent physiology (e.g. Fontan circulation) or fixed cardiac output states (e.g. aortic or mitral stenosis). Titratable, catheter-based neuraxial techniques, such as epidural, low-dose combined spinal-epidural or continuous spinal anaesthesia, are well described [124, 135, 136].

There are no studies evaluating the optimal vasopressor to prevent or treat hypotension after neuraxial anaesthesia in women with cardiac disease undergoing caesarean section. Recommendations are based on evidence from case series, case reports and expert opinion. Women with cardiac disease undergoing caesarean section with neuraxial anaesthesia have been managed with phenylephrine infusions guided by invasive or non-invasive monitoring [135, 136]. However, given the marked heterogeneity among cardiac lesions, phenylephrine should not be routinely administered to all women with cardiac disease. The haemodynamic goals of the patient's specific cardiac lesions, and the likely haemodynamic changes induced by neuraxial anaesthesia, should guide the selection of the most suitable vasopressor [137]. Phenylephrine is the agent of choice in women with hypertrophic cardiomyopathy as it has no inotropic effects, in contrast to ephedrine, whose intrinsic β-agonist activity may worsen dynamic ventricular outflow obstruction [138]. A sudden decrease in systemic vascular resistance after neuraxial anaesthesia in the presence of fixed cardiac output lesions, such as severe aortic or mitral stenosis, are best prevented or treated with phenylephrine; tachycardia induced by ephedrine may worsen haemodynamic status in patients with stenotic valvular disease [138]. Similarly, phenylephrine may be preferable in women with ischaemic cardiac disease, where tachycardia should be avoided to minimise increases in myocardial oxygen demand and optimise blood supply [139]. On the other hand, ephedrine may be preferable to phenylephrine in woman with regurgitant valvular lesions, where bradycardia should be avoided.

 

### *Limited resource environments*

Hospital environments may be classified as either resource rich, resource constrained, where facilities are present although potentially overloaded, or resource poor. In the latter, there are differences in anaesthetic staffing, availability of drugs, monitoring and syringe pumps, and operating theatre and recovery facilities; patients may also present late, as a result of inadequate antenatal care, with hypovolaemia, electrolyte disturbances and undiagnosed underlying pathology [140].

Facilities must be able to allow conversion of spinal to general anaesthesia [141–143]. Continuous ECG and pulse oximetry monitoring should be available. If automated non-invasive oscillometric blood pressure monitoring is available, this should be set to cycle every minute. If not available, the anaesthetist or delegate should check the blood pressure as frequently as possible using the available apparatus, preferably every 2-min at least until delivery.

Women having emergency caesarean section need a careful assessment of volume status, taking into account potential losses including haemorrhage, vomiting and prolonged labour. The importance of the shock index (ratio of heart rate: SAP) as an indicator of poor outcomes in women with peripartum haemorrhage is now well recognised [144]. Significant hypovolaemia is an absolute contraindication to spinal anaesthesia for caesarean section; hypovolaemia, particularly due to haemorrhage, results in compensatory splanchnic vasoconstriction and mobilisation of blood into the circulation [145]. In this situation, sympathectomy following spinal anaesthesia can cause potentially fatal reduction in venous return and cardiac pre-load.

A dose of 10 mg hyperbaric bupivacaine plus 10 μg fentanyl is usually appropriate for caesarean section. This may be increased or decreased for extremes of height, but does not need to be adjusted for body mass index. If no fentanyl is available, administer hyperbaric bupivacaine 10 mg alone. If no hyperbaric bupivacaine is available, an isobaric solution is acceptable [146], although there are concerns related to less reliable anaesthesia. It is also acceptable to mix dextrose with isobaric bupivacaine, to produce a hyperbaric solution; for example, mix 4 ml of 0.5% isobaric bupivacaine with 0.5 ml 50% dextrose to produce a solution of 0.44% bupivacaine with 5.55% dextrose. Other local anaesthetics have been used, but there are limited data available. Strict aseptic technique must be used, including sterile gloves and a surgical mask, and particular care must be taken to avoid drug errors and contamination with antiseptic skin preparation solution.

There is limited evidence for the optimal management of hypotension after spinal anaesthesia in resource-poor environments. A recent paper has described the use of a fixed low-rate phenylephrine infusion to provide background pharmacological action, with supplementary boluses as needed. This is an easier option for the unskilled anaesthetist than a titrated infusion, with a low risk of side-effects [147]. In general, our suggestions are based on principles studied in resource-rich environments and modified for local practice, based on expert opinion.

It is unacceptable to proceed with spinal anaesthesia without the availability of a vasopressor and an anticholinergic agent. The vasopressor of choice, if available, is phenylephrine; however, resource limitations may mean that other agents may have to be considered. These would be, in order of preference: other synthetic α-agonists, ephedrine and then adrenaline (Appendix 2).

Crystalloid coload with a resuscitation fluid such as modified Ringer's lactate is suggested; 0.9% saline is an acceptable alternative. Ensure adequate hydration pre-spinal anaesthesia, and then coload with 15 $ml.kg^{-1}$ (approximately one litre) once the spinal injection is performed.

Spinal anaesthesia has been promoted in limited resource environments because it is, in principle, safer than general anaesthesia. However, spinal anaesthesia has become the leading anaesthetic cause of maternal death in South Africa, because of high block, uncontrolled hypotension or a combination of the two [143]. Recent guidelines have been introduced to aid inexperienced anaesthetists or medical officers in identifying the progression of local anaesthetic block to dangerously high levels, and making the appropriate response [143]. Furthermore, four basic patterns of haemodynamic response to spinal anaesthesia for caesarean section are highlighted.

 

*1. Hypotension and increase in heart rate*
This is the usual response to spinal anaesthesia. Arteriolar, and to a lesser extent venous dilation, reduces systemic vascular resistance; a baroreceptor response results in an increase in cardiac output. The changes are corrected by an α-agonist. In the event of failure of, or unreliable, blood pressure recordings, the vasopressor should be titrated to reduce the heart rate to the baseline value.

Do not administer anticholinergic agents in response to α-agonist-induced bradycardia unless the blood pressure is proven to be low (see 2 below); this can cause tachycardia and hypertension, particularly in patients with pre-eclampsia.

*2. Hypotension and bradycardia*
An uncommon pattern caused by a vasovagal response; rather than 'appropriate' tachycardia and vasoconstriction in the upper body in response to hypotension, the opposite changes occur. This should be treated by anticholinergic agents and/or ephedrine, in addition to the α-agonist.

*3. Persistent refractory hypotension*
If there is a poor response to vasopressors or anticholinergic agents, the cardiovascular status of the mother should be reviewed immediately. Undiagnosed hypovolaemia, cardiac disease (cardiomyopathy, valvular heart disease) and pre-eclampsia-induced heart failure should be checked for. Treatment may include i.v. fluids, inotropic support or diuretics, depending on the findings.

*4. High spinal block with cardiorespiratory failure*
Hypotension and bradycardia are likely (see 2 above) together with other indicators of high sensory and motor block, respiratory compromise and decreased consciousness. Aggressive treatment to correct the cardiovascular changes is required together with respiratory support including tracheal intubation if indicated.

## Future directions

Further research is required on the ideal pharmacological profile for a single α-agonist or, alternatively, the role for combined agents. The more widespread availability of smart pumps that can deliver computer-controlled vasopressor regimens may further improve blood pressure control after spinal anaesthesia.

The importance of enhanced monitoring, such as cardiac output, needs clarification in relation to important maternal and fetal outcomes, especially for compromised fetuses. Currently, these devices are best used for research purposes in order to identify underlying physiological and pathophysiological mechanisms. In individual high-risk cases, specific, extra non-invasive or invasive monitoring, including echocardiography, might be indicated if available.

Methods to predict hypotension would be welcome if they were inexpensive, built into current monitors and well proven across a variety of practice situations. In the long term, genetic typing may predict individual response to vasopressors [148].

## Acknowledgements

We thank Reena Nian-Lin Han, Adrienne Stewart, David G. Bishop and Sarah Ciechanowicz for their invaluable input into the drafting of these recommendations.

SK and AV are Editors of *Anaesthesia*, and this manuscript has undergone additional external review. BC has received support from Smiths Medical (consulting), Covidien (funded research). RF has received support from Smiths Medical (consulting). FM has received support from Aguettant (honoraria for lectures and consulting), Fresenius Kabi (honoraria for lectures, consulting and funded research). AS has investments in Innovfusion Pte. Ltd. MdV has received support from Smiths Medical (consulting), Grunenthal (consulting), Sintetica (funded research) and Nordic Pharma (consulting). The remaining authors declare no competing interests. No external funding declared.

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## Appendix 1

Recommendations for manually titrated vasopressor infusion at elective caesarean section under spinal/combined spinal-epidural anaesthesia.

### *Vasopressor preparation*

Add 10 mg phenylephrine to a 100-ml bag of normal saline, to give a concentration of phenylephrine of 100 $\mu g.ml^{-1}$. In a 50-ml syringe, draw up 25 ml of the phenylephrine solution. Attach an extension line to the 50-ml syringe and prime with the vasopressor solution in the syringe.

### *Before the spinal*

Insert a suitable size cannula (14- or 16-G) to allow rapid intravenous (i.v.) infusion. Connect 1 l warmed crystalloid to a wide-bore giving set that has a Y-

 

connector with an antireflux valve; attach the vasopressor infusion to the Y-connector. Connect to the patient's i.v. cannula and run the crystalloid slowly.

[Alternative: start colloid pre-load, aim to complete before spinal injection.]

Apply non-invasive blood pressure (NIBP) monitoring.

Write down the following values (repeat the baseline measurements if they are outside the normal range):

1 Baseline systolic arterial pressure (SAP).
2 90% baseline SAP.
3 80% baseline SAP.

### *At the end of the spinal injection*

Start the vasopressor infusion at a rate of between 15 $ml.h^{-1}$ and 30 $ml.h^{-1}$ (25–50 $\mu g.min^{-1}$).

Switch the NIBP measurements to 1-min cycles.

Start i.v. crystalloid coloading by turning the i.v. infusion to maximum (use a pressure bag if needed).

### *Adjusting the vasopressor infusion*

Aim to maintain the maternal SAP at ≥ 90% baseline.

- Hypotension, heart rate maintained
  - SAP < 90% baseline: increase phenylephrine infusion by 10 $ml.h^{-1}$ and re-assess.
  - SAP < 80% baseline: administer 100 μg phenylephrine bolus and increase phenylephrine infusion by 10 $ml.h^{-1}$.
- Hypotension, heart rate reduced
  - SAP < 90% baseline, heart rate low: administer 3–6 mg ephedrine.
  - SAP < 80% baseline, heart rate < 60 $beats.min^{-1}$: administer 200 μg glycopyrronium/atropine.

When the woman is positioned supine for surgery, ensure left lateral displacement of the uterus from the inferior vena cava, aiming for at least 15° pelvic tilt (with lateral tilt of the operating table or a wedge).

### *After delivery*

After delivery, the vasopressor infusion can be weaned down rapidly, although beware of hypotensive effects of oxytocic drugs given at delivery.

If the woman is stable and asymptomatic, then relative hypotension can be tolerated; the requirement for tight control of blood pressure applies to the pregnant state.

If there are symptoms such as nausea and vomiting with hypotension as the infusion is reduced, check for hidden blood loss.

At the end of the case, the vasopressor infusion should be disconnected and the cannula should be flushed slowly to ensure that there is no residual vasopressor in the cannula.

If there is still a requirement for vasopressor at the end of elective surgery, a full assessment of the patient should be made, with particular attention to the cardiovascular system and fluid balance.

## Appendix 2

Recommendations for management of hypotension after spinal anaesthesia for caesarean section in limited resource environments.

### *Preparation of the patient*

Careful assessment of volume status; exclude hypovolaemia.

### *Vasopressor treatment*

The vasopressor of choice, if available, is phenylephrine:

1 Preparation: Mix 10 mg phenylephrine in 200 ml 0.9% saline. This gives a concentration of 50 $\mu g.ml^{-1}$.
2 Infusion options, if a syringe driver is available:
   2.1 Administer a 50 $\mu g.ml^{-1}$ infusion at 60 $ml.h^{-1}$ (50 $\mu g.min^{-1}$), and titrate to effect (this requires a skilled anaesthetist).
   2.1 Run a fixed rate infusion at 30 $ml.h^{-1}$ (25 $\mu g.min^{-1}$). Treat any hypotension with boluses of 50–100 μg phenylephrine in addition to the infusion.
3 If no syringe driver is available, options are:
   3.1 No infusion, bolus as required with 50–100 μg (2 ml). Start treatment when heart rate increases and/or blood pressure decreases to 90% baseline.

3.2 Add 500 μg phenylephrine to the first litre of Ringer's lactate and administer rapidly once the spinal anaesthetic has been administered. If this runs over 10–20 min it will approximate a 25–50 $\mu g.min^{-1}$ infusion, and can be titrated to the heart rate.

A number of alternative options are acceptable, such as:

1 Ephedrine (50 mg ephedrine added to 9 ml 0.9% saline in a 10-ml syringe to give 5 $mg.ml^{-1}$) – bolus dose of 10 mg.
2 Metaraminol (10 mg metaraminol added to 19 ml 0.9% saline in a 20-ml syringe gives 0.5 $mg.ml^{-1}$) – bolus dose of 0.5 mg.
3 Adrenaline may be used in the absence of alternatives (1 mg added to 200 ml 0.9% saline gives 5 $\mu g.ml^{-1}$) – bolus dose of 10 μg.

### *Monitoring*

Ensure free-flowing intravenous (i.v.) infusion, using cannula of at least 18-G.

Apply non-invasive blood pressure (NIBP) monitoring.

Record the following values:

1 Baseline systolic arterial pressure (SAP).
2 90% baseline SAP.
3 80% baseline SAP.
4 Baseline heart rate.
5 120% baseline heart rate.

### *At the end of the spinal local anaesthetic injection*

Commence vasopressor infusion (if used) at the predetermined starting rate.

Switch the NIBP measurements to 1-min cycles/manual blood pressure measurements every 1–2 min until BP stable, or the baby is delivered.

Start i.v. crystalloid coloading 15 $ml.kg^{-1}$ by turning the i.v. infusion to maximum (use a pressure bag if needed).

Treat hypotension early and aggressively. Aim to keep the SAP ≥ 90% of baseline SAP and the heart rate ≤ 120% of baseline heart rate.

Look for these patterns:

- Hypotension and tachycardia: give vasopressor
  - Tachycardia with no/unreliable blood pressure measurement: titrate vasopressor to bring heart rate to baseline level
- Hypotension and bradycardia: give anticholinergic and vasopressor
- Persistent hypotension: check for other cause (hypovolaemia, heart disease or heart failure). Check that measurements are accurate.
- Hypotension with high block: treat hypotension as above, with a low threshold for adrenaline by infusion if there is no early response to first-line vasopressor therapy; support ventilation, intubate trachea if required.

Treat as for hypotension if the patient complains of nausea, if she is feeling faint/sweaty or if she is unable to talk. Do not wait for NIBP readings before administering vasopressor in these situations.

When the woman is positioned supine for surgery, ensure left lateral displacement of the uterus from the inferior vena cava by applying at least 15° pelvic tilt (with lateral tilt of the operating table, a wedge or rolled towels).

### *After delivery*

If an infusion is being used, wean this rapidly over 5 min or so. If hypotension occurs, check for a cause, as above.