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Obstetric Spinal Hypotension

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Contents

Introduction

Context is king!

Anaesthesia is a critical component of any obstetric service, bridging multiple disciples involved in maternal and fetal care[1]. In low and middle-income countries (LMICs) this service is not readily available due to: poor infrastructure, shortage of health care providers, lack of basic equipment, and drug shortages[2,3]. In LMICs anaesthesia is often provided by junior physicians with no formal training in the discipline, which is an independent risk factor for maternal mortality[2]. The ratio of anaesthetic provider's to maternity patients is one per million in LMICs. Anaesthesia related mortality is high and accounts for 2.8% of maternal deaths of which 13.8% follows cesarean section[2]. Mortality rate is higher with non-anaesthetic physician anaesthetists (9.8 per 1000) compared to physician anaesthetists (5.2 per 1000)[2]. The 2013 national committee for confidential enquiry into maternal deaths (NCCEMD) reported a 3.35% anaesthetic related maternal mortality, with more than half of these deaths attributed to spinal hypotension. The estimated cesarean section rate is 25.7% in South Africa, and 30.5% in KwaZulu-Natal, a figure higher than the national average[4].

In developed countries (USA) which are better resourced, there is a favorable physician to patient ratio. Non-physician anaesthetic providers undergo additional training compared to their counterparts in LMICs. The anaesthetic related maternal mortality rate is 6.5% for general anaesthesia, and 3.8% for regional anaesthesia per million anaesthetics. There is no significantly measured difference in anaesthetic complications between physicians and non-physician anaesthetists in this setting[2].

A comparison between these vastly different clinical contexts demonstrates alarming figures and importance of the difference in clinical context. Context appropriate interventions are required to improve maternal services. A classification describing the different clinical contexts encountered in obstetric practice is outlined by Bishop et al[3]. In South Africa we have a varied clinical context. Tertiary centers and private facilities operate as resource rich context, while regional and district hospitals falling into the resource constrained and poor context[3]. This is also apparent in the varied mortality rates in the different settings.

General anaesthesia vs. Spinal anaesthesia for cesarean section

Spinal anaesthesia is preferred over general anaesthesia for obstetric patient undergoing a cesarean section [2]. It is safe, cost effective, simple to perform, providing rapid, reliable, and good quality surgical conditions with a failure rate of <1%[5]. It avoids instrumentation of the airway, drug transfer to the fetus, while allowing early bonding of the mother and her new born child. The NICE guidelines recommend a general anaesthetic in less than 1% of all elective cesarean section and less than 5% of emergency cesarean section deliveries[5]. Significant maternal hypotension is commonly following spinal anaesthesia, and leads to maternal (nausea, vomiting, dizziness, loss of consciousness, and cardiac arrest) and fetal (fetal acidosis and neurological injury) morbidity[6,7].

The aim of this document is to provide

A. A review of recent advances related to the definition of obstetric spinal hypotension.
B. An understanding of the hemodynamic changes following spinal anaesthesia.
C. Evaluate risk factors known to predict the occurrence of obstetric spinal hypotension.
D. And to review management strategies for obstetric spinal hypotension relevant to the specific clinical context.

Definitions

A consensus definition for obstetric spinal hypotension is not available[8-10]. Frequently cited definitions use either an absolute systolic artery pressure thresholds, and/or a threshold relative reduction from a baseline value[9]. The heterogeneity of definitions is demonstrated in a systematic literature search by Klohr et al[9]. Fifteen definitions are cited in obstetric literature. Only 3 out of 15 definitions are based on absolute systolic arterial pressure. Twelve of the definitions are related to a baseline systolic arterial pressure, which was defined in only 53 of 65 studies. The frequently used baseline definition was a systolic arterial pressure measured after arrival of the patient in the operation theater, either as a single value or as a mean of repeated measurements. This creates a problem as values obtained at this point differ from the patient's actual baseline systolic artery pressure due to anxiety. The two commonly cited definitions are:

1) A decrease in systolic arterial pressure below 80% of the baseline value (used in 25.4% of the studies), and
2) Systolic arterial pressure below 100mmHg or a decrease of systolic arterial pressure below 80% of the baseline (used in 20.6% of the studies)[9].

Klohr et al applied these definitions to 107 patients. They observed an increase in the incidence of hypotension by a factor of 10 when comparing a systolic arterial pressure < 80mmHg (incidence of 7.4%) and a systolic arterial pressure < 90% of the baseline (74.1 %).

Zwane et al also demonstrated a variation in incidence with change in definition of spinal hypotension[8]. The incidence of hypotension followed a sigmoid distribution, with a higher incidence of hypotension when relative definitions are used as opposed to absolute threshold definitions[8].

Challenges that result from a lack of a standardized definition include [8-10]

1. Limits the generalization of clinical research findings.
2. Inaccurate incidence estimations of spinal hypotension.
3. Limits comparability of research findings evaluating the effect of an intervention on hypotension.
4. Inability to benchmark the quality of care we provide as anaesthetists.
5. Impact in sample size calculation.

The physiological rational of an appropriate definition of obstetric hypotension remains uncertain. No human study evaluates a clinically relevant threshold for obstetrics spinal hypotension. Prolonged durations of hypotension is a prognostic factor for low umbilical artery blood pH[7]. Mean arterial pressure are used in ICU'S to direct intervention as they better determine organ perfusion, however limited evidence support their use in obstetrics[8,10].

Current consensus recommendation is to

1) Targeting a systolic arterial pressure > 90 % of an accurately measured baseline.
2) To administer a vasopressor when systolic blood pressure is less than 80% of the baseline[10].

This may not be practical in the resource poor setting, due to limitations addressed above. Use of absolute trigger thresholds is more practical and has been proposed for the resource poor context.

1) Targeting a MAP of ≥ 70mmHg or an SBP ≥ 100mmHg
2) Initiate vasopressor when MAP ≤ 65mmg, SBP ≤ 90mmhg[8].

Basic science consideration

At term the inferior vena cava is almost completely occluded by the gravid uterus in the supine position. This obstruction impedes blood flow returning from the lower limbs resulting in paravertebral collateral flow via the epidural, azygos, and vertebral veins to the heart. A reduction in venous return, stroke volume and cardiac output develops. Aorto-iliac compression occurs in 15% to 20 % of pregnant woman leading to reduce in the arterial blood pressure and flow to the uteroplacental unit. This can occur without any maternal symptoms, and may not be appreciated by upper limb blood pressure measurements. A compensatory increase in the peripheral vascular resistance secondary to activation of the sympathetic nervous systems occurs in order to maintain arterial blood pressure despite the reduction in venous return, stroke volume and cardiac output. In 15% of pregnant patient these compensatory mechanism are inadequate and supine hypotension syndrome occurs. Anaesthesia further inhibits these compensatory mechanism and hypotension insures[11].

The uteroplacental circulation is a low resistance circulation with no auto regulation. At term blood vessels are maximally dilated to allow flow. Perfusion depends on maternal cardiac output rather than on arterial blood pressure. Thus, a reduction in cardiac output results in reduced uteroplacental unit perfusion leading to fetal distress [12].

Aorto-caval compression with reduced venous return and cardiac output has been the predominant mechanism of spinal hypotension. However interventions directed at addressing aorto-caval compression fail to consistently prevent hypotension. Pregnant patients are more sensitive to local anaesthesia. They have an altered endothelial vascular tone, with reduced response to endogenous vasopressors coupled with an increase synthesis of vasodilator compounds (prostaglandins and nitric oxide)[13]. Thus, they depend on the sympathetic nervous system to maintain vascular tone. Dyer et al showed a reduction in systemic vascular resistance accompanied with an increase in

stroke volume and heart rate following spinal anaesthesia[14]. This resulted in a compensatory increase in cardiac output following spinal anaesthesia. Pre-eclamptic patients are more resilient to spinal hypotension due to the pathophysiology of pre-eclampsia which leads to an increased vascular tone opposing the pharmacological sympathectomy from a spinal anasehtsia[13]. This lesson from pre-eclampsia emphases that a reduction in sympathetic vascular tone as a mechanism of spinal hypotension.

Hypotension leads to significant maternal morbidity due to unpleasant signs and symptoms following reduced organ perfusion. Cerebral hypo-perfusion leads to nausea, vomiting, dyspnea, a sense of impending doom, and loss of consciousness. Prolonged hypotension result in multi organ ischemia, cardiovascular collapse, and reduced uteroplacental perfusion [12].

Four hemodynamic response patterns follow spinal anaesthesia and should be recognised as they guide treatment[10].

1. Hypotension and tachycardia: This is the typical response resulting from a decreased vascular resistance and compensatory baroreceptor reflex to improve cardiac output.
2. Hypotension and bradycardia: This is an uncommon and vasovagal response leading to a hypotension and bradycardia.
3. Refractory hypotension: This is often due to undiagnosed hypovolaemia, cardiac disease, pre-eclampsia induced heart failure and require detailed maternal evaluation.
4. High spinal block with cardiorespiratory failure

Risk factors for post SA hypotension

Predicting patients at risk of spinal hypotension allows for better stratification, early referral to the appropriate level of care, early vasopressor use, and increase vigilance of the anaesthetist[15].Factors described that predict the occurrence of hypotension include:

Patient characteristics

1. **Anxiety:** Perioperative anxiety as assessed using a verbal analog anxiety scoring system is a predictor for spinal hypotension. This emphasizes the importance of alleviating patient anxiety in the preoperatively[16].
2. **Age:** Maternal age is a non-modifiable risk factor for the development of hypotension. The age range varies from 25 – 35 years[17,18].
3. **Maternal weight gain**: Weight gain less then 11kg has been associated with the development of spinal hypotension[19].
4. **Body mass index (BMI):** Conflicting results are observed when BMI is used to predictor spinal hypotension. Nain et al reported increased hypotension and vasopressor use with an increased BMI[20]. While López Hernández et al and Ngaka et al, failed to support this association[21,22]. The 2018 consensus does not recommend the use of high BMI as a predictor for spinal hypotension[10].
5. **Fetal birth weight:** A neonatal birth weight > 3900g is associated with a high incidence of spinal hypotension[21].
6. **Heart rate:** Preoperative heart rate has been described to predict spinal hypotension. Values cited range from 73 - 90 beats.min[18,23].

Postural changes

Postural changes in heart rate, systolic arterial pressure (> 12mmHg) have been shown to predict spinal hypotension. This is due to sympathetic reactivity with postural change[24].

Heart rate variability

Heart rate variability assessment of the autonomic nervous system has been shown to predict spinal hypotension[25-27]. This can be done by evaluating the Low Frequency /High Frequency ratio, which is a frequency domain parameter reflecting the balance between the sympathetic and parasympathetic nervous system. Low frequency indicates sympathetic and parasympathetic cardiac activity, while high frequency indicates parasympathetic. An elevated ratio indicates an increased in sympathetic activity and is associated with spinal hypotension. A threshold of 2 is associated with an increased incidence of spinal hypotension[27]. Heart rate variability is not a standard bedside assessment limiting its use in clinical setting[27].

Point of care ultrasound

Point of care ultrasound can be used to predict obstetric spinal hypotension. A Velocity Time Integral (VTI) > 21% predicted the occurrence of hypotension, with a sensitivity of 87%, specificity of 65%, positive predictive value of 58% and negative predictive value of 87%. A VTI of > 21% was also associated with increased vasopressor use[28]. By using this method, care can be individualized to patients, limiting the routine use of preload or co-load[28].

Perfusion index

Perfusion index (PI) derived from pulse oximeter, is the ratio of pulsatile blood (infrared signal) and non pulsatile (infrared signal) blood expressed as a percentage. It assesses peripheral perfusion dynamics due to changes in peripheral vascular tone. A high baseline perfusion index is associated with a decrease in systolic arterial pressure, mean arterial pressure, and an increase in phenylephrine requirements. The cutoff that predicts hypotension is 3.5, with a specificity of 86% (95% CI 57-98%) and sensitivity of 81% (95% CI 58 – 95%) [29].

Local anaesthesia

Maximal sensory block level (≥ T5 or T4) is associated with an increased incidence of hypotension[30-32]. This is due to a more extensive block of preganglonic sympathetic nerve fibers responsible for the vasomotor tone. Maximal sensory block level is influenced by the local anesthetic agent used (high baricity and high volume), rate of injection, and lumbosacral CSF volume. Independently, the sensory level does not predicting and explaining the occurrence of hypotension as studies have shown different incidences of hypotension with similar block levels. This is associated with the rate of rise to maximal sensory block level. A sensory block level ≥ T8 at 3 minutes following spinal anaesthesia predicts hypotension, with a sensitivity of (0.82) and specificity of (0.88). Prolonged timing in achieving maximal sensory block allows for physiological compensation thus less hypotension[30,33].

Emergency vs. elective:
Elective cesareans have a higher incidence of hypotension then emergency cesarean section. The physiological bases remain to be described[10].

Available scoring system: The PRAM score
Despite a large number of studies looking at predictive factors for obstetric spinal hypotension no validated scoring system exist. The PRAM score is a novel score to predict obstetric spinal hypotension using three perioperative maternal parameters: Pulse Rate (> 90 beats.min), Age (> 25 years), and Mean arterial pressure (<90mmHg). The incidence of hypotension is 21.6% with one, 35.8% with two, and 53.1% with three parameters. This scoring system is a simple bedside tool that can be used preoperatively. However it is limited by lack of validation by large multicenter trails[18].

Management options
1. Preventing aorto-caval compression,
2. Fluid loading,
3. Vasopressors, and
4. Other.

Preventing aorto-caval compression
A. Uterine displacement
Uterine displacement relieves compression of the aorta and inferior vena. This is achieved by the wedge placement, table tilt, and manual uterine displacement. Uterine displacement reduces hypotension, improves cardiac output, and decreases vasopressor requirement. An angle of 15 degrees is required for clinical benefit. This is rarely achieved with wedge placement in clinical practice. Table tilt can compromise operating conditions, require parturients to be secures on to the surgical table to avoid falling. Table tilt can be used during the preparation period, then reduced moments before the surgery when hemodynamic stability has been achieved[10].

B. Leg compression
Leg compression reduces the incidence of hypotension. The efficacy of this method depends on the type and intensity of compression modality used (bandage, inflatable boots, antithrombotic stockings)[34]. However the incidence on hypotension remains when this method is used alone[34,35].

C. Leg elevation
Leg elevation to 30 degrees has demonstrated conflicting results in the efficacy on reducing the incidence of hypotension. This method improves preload and cardiac output [36].

Fluid loading
Fluid loading strategies are well summarised in the analysis by Frederic J. Mercier et al, and the review article by Singh Bajwa [37,38]. Four possible strategies are described:

A. Crystalloid preload

Is administration of crystalloid before (with the majority of literature stating 15 to 20ml/kg over 10 to 20minutes) induction of spinal anaesthesia. This aims to maintain intravascular volume thus preventing hypotension. Literature shows unequivocal results with this technique. Failure of preload strategy is attributed to the pharmacokinetics of crystalloid. They have a short half life, and rapidly redistribution out of the intravascular compartment before induction of spinal anaesthesia[37]. There is an increased in Arial Naturetic Peptide, possibly leading to vasodilatation and fluid excretion following acute fluid loads. This strategy is not recommended by the 2018 international consensus[10].

B. Colloid preload

Colloid preloading offers more beneficial then crystalloid preload. Colloids remain in the intravascular compartment longer and resist a decrease in intravascular volume following spinal anaesthesia. Several concerns limit colloid use: cost, derangement in coagulation, allergic reaction risk, and renal impairment[12].

C. Crystalloid co-loading

Fluid administered rapidly at induction of spinal anaesthesia improved mean arterial pressure better then a preload strategy. This is due to the pharmacokinetics of crystalloid[12].

D. Colloid co-loading

Similar benefits occur with colloid co-load and preload. Colloids remain in the intravascular space longer and increase the intravascular volume as noted by Macdonald et al[12].

These techniques described above although beneficial, lack reliability in preventing hypotension. The current accepted mechanism of obstetric spinal hypotension is the reduction in systemic vascular resistance secondary to pharmacological sympathectomy, with a minor contribution from venous pooling. Pharmacological methods opposing the decrease in systemic vascular resistance are most reliable in preventing and treating hypotension [39].

Vasopressor therapy

The most common used vasopressors in obstetrics anaesthesia are summarised in the table below[10].

	Ephedrine	Phenylephrine	Metaraminol	Noradrenaline	Adrenaline	Mephentermine
Receptor	B1, β2, α	α1	α1, weak β	β, α	β, α	β, α
Mechanism of action	Indirect, weak direct	Direct	Direct, indirect	Direct	Direct	Indirect
Onset	Slow	Immediate	1-2min	Immediate	Immediate	Immediate
Duration	Prolonged	Intermediate	Prolonged	Short	Short	Prolonged
Comment	Tachyphylaxis	Easy to Titrate, Gold standard		Effects similar to Phenylephrine.	For circulatory shock.	Literature is limited. Fewer dilutions.

The physiological response obtained will depend on the type and location of the receptors. Agents that stimulate the α-1 receptor lead to vasoconstriction, while β-1 and β-2 agonist will lead to positive inotropy and positive chronotropy. Reflex cardiovascular responses may occur with the use of vasopressors (i.e. bradycardia with phenylephrine). Vasopressor choice influence fetal outcome. The ideal vasopressor maintains maternal blood pressure, prevents maternal symptoms, with minimal detrimental effects on the uteroplacental blood flow, and neonatal outcomes[10,40].

Historically ephedrine was the vasopressor of choice for the treatment of obstetric spinal hypotension. This was based on multiple animal studies, which demonstrated ephedrine as better at restoring maternal blood pressure and preserving uterine blood flow when compared to alpha agonists [41]. Ngan kee et al showed greater placental transfer of ephedrine, associated with reduction in umbilical vein and artery pH and base excess, and an increase in lactate, glucose, epinephrine, Norepinephrine, PaCO2 and PaO2 when compared to phenylephrine [42]. The authors suggested avoiding the use of ephedrine before delivery as it contributed to fetal acidosis. In current practice low dose ephedrine is recommended for hypotension when associated with bradycardia[10].

Phenylephrine is currently the first line vasopressor for obstetric spinal hypotension. It reduces the incidence of hypotension, and has favorable fetal acid base profile over ephedrine. The ED 95 for prevention of obstetric spinal hypotension is 159µg (95% CI, 122 – 371 µg), and the ED 90 for the treatment of SIH is 147µg (95% CI, 98 – 222µg) [43,44]. At high doses phenylephrine causes bradycardia decreasing the cardiac output, despite the increase in systemic vascular resistance and mean arterial pressure. Since cardiac output is an important component of oxygen delivery to the peripheral tissue, this reduction may not be well tolerated by parturients with compromised fetuses (preeclampsia, fetal compromise and fetal distress). Practice guidelines from the American task force recommend the use of either ephedrine or phenylephrine for the treatment of spinal hypotension. They also suggest that in the absence of maternal bradycardia the use of phenylephrine should be considered because of improved fetal acid base status in uncomplicated pregnancy[10].

Other
Anticholinergic agents can be used for treatment of significant bradycardia associated with spinal hypotension however routine use is not recommended[10]. Prophylactic use of 5-HT3 receptor antagonist lowers spinal hypotension, vasopressor dose and maternal symptoms. Ondansetron is the commonly investigated agent at a dose of 2-12mg[45].

Management strategies
Reactive vs. prophylactic
The approaches for managing hypotension can be **reactive** and **prophylactic**, based on the timing of intervention in relation to the occurrence of hypotension[3]. The reactive approach involves early and aggressive use of fluid and vasopressor following the development of hypotension [3,46]. Current practice has moved away from reactive approach to a proactive strategy to improving maternal comfort [40].

Bolus vs. infusion

Prophylactic infusions are more beneficial than a bolus strategy in preventing spinal hypotension[10]. Current recommendations by the American task force is to use a bolus strategy in emergency cases, and to consider infusion in elective cases if one has been trained in the use of the equipment and techniques[47]. The current international consensus recommends titration of phenylephrine infusion starting at 25 – 50µg.min to maintain maternal systolic artery pressure > 90% of baseline[10].

Infusion combined with coload

Combining crystalloid co-load with phenylephrine almost eliminates hypotension[48]. Current practices recommend use of a vasopressor and fluid coloading[10].

***What is trending in the obstetric literature*?**

Noradrenaline is increasingly being evaluated as an alternative to phenylephrine. Phenylephrine has pure α1 effects resulting in bradycardia and reduced cardiac output at high doses. Noradrenaline is a potent α with some β activity thus increasing cardiac output and heart rate in addition to vasoconstriction[10,49]. This might be more beneficial in maintaining uteroplacental oxygen delivery. A met-analysis comparing noradrenaline and phenylephrine showed comparable benefit between the two agents with no difference in fetal acid base profile [49]. However, noradrenaline may not be available in out setting due to limitations described above.

CONCLUSION

One must always keep in mind the clinical context in which they practice obstetric anaesthesia and use this to select the appropriate strategies to combat obstetric spinal hypotension thus ensuring maternal comfort and safety.

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