Managing hypotension induced by spinal anesthesia for caesarean section

INTRODUCTION

Maternal mortality associated with anaesthesia becomes substantially reduced (around 80%) when general anaesthesia is not used for caesarean sections according to studies published in the USA and the UK at the end of the 1970s and 1980s. The possible risks and complications associated with the general technique for a caesarean section include definitive management of the airway route, respiratory assistance or failed intubation, bronchoaspiration of gastric content, oral, pharyngeal or laryngeal trauma, postoperative nausea and vomiting, retarded lactation and sedation of the neonate.

The mother and her child can share the birth with all the accompanying emotional implications.
deriving from this if regional anaesthesia is used. The need for using systemic opiates during the postoperative period becomes reduced and the risks described for the general technique are avoided.

The advantages of using spinal anaesthesia include the technique’s simplicity, its action’s rapid initiation, the low failure rate, the use of minimum drug volume and concentration, an important move away from applying a systemic toxic dose and there is suitable muscular relaxation during surgery. The foregoing reasons make this the method of choice for most elective caesarean sections and a large percentage of emergency caesareans when an expectant mother does not have an epidural catheter functioning or does not present a contraindication for neuroaxial techniques.

Hypotension is a frequently occurring adverse effect in the obstetric population to which neuraxis anaesthesia or analgesia is to be administered. It occurs more frequently in patients requiring anaesthesia for surgical procedures than in patients receiving neuraxis analgesia during labour due to the need for denser and more extensive blocks in the former group. Haemodynamic changes occur abruptly with spinal anaesthesia compared to the epidural technique, thereby leading to clinical manifestations and maternal-foetal complications associated with hypotension frequently happen with subarachnoideal anaesthesia.

DEFINITION

Even though there is variability in defining hypotension for expectant mothers involving neuroaxial anaesthesia, most authors define it as being a 20% to 30% reduction in systolic blood pressure, comparing it to initial values (prior to drugs being placed in the neuraxis) or absolute systolic blood pressure values between 100 mmHg and 90 mmHg.

It must be born in mind that blood pressure (the same as other haemodynamic and physiological variables) is constantly changing and adapts to different phenomena affecting homeostasis; it must be interpreted within a suitable clinical context, meaning that placing cut-offs points for operationalising the definition of hypotension may only provide a guide and is not suitable for intensifying a definition which (as explained above) has many versions and variability.

As one is dealing with measurement, there may be variability explained by random or systematic errors inherent in the measurement method (direct or indirect) and individual variability (i.e. of a patient at different moments) which must be born in mind when interpreting isolated blood pressure figures.

MECHANISMS EXPLAINING MATERNAL HYPOTENSION

It is expected that T4 sensory level will be reached when the subarachnoid anaesthesia technique is used for a caesarean section, thereby providing a comfortable intra-operative period for the patient and gynaecologist, reducing the risk of conversion to general anaesthesia, the use of parenteral medication and patient dissatisfaction with the anaesthetic technique. This explains why it is practically inevitable that a patient presents total pharmacological sympathectomy.

Spinal anaesthesia-induced hypotension for caesarean section is triggered by many factors, including:

- The sympathectomy explains reduced peripheral vascular resistance, venous return and cardiac output, which could be reduced by low venous return and bradycardia (extensive blocks);
- Aortocaval compression caused by mechanical phenomena of the pregnant uterus during the last trimester of pregnancy when a patient adopts a supine position;
- Normal expectant mothers also present an autonomic imbalance explaining relative sympathetic hyperactivity making them more susceptible to hypotension due to neuroaxial block.

It should not be forgotten that these patients are, occasionally, submitted to very prolonged periods of fasting.

Frequency

The frequency of giving birth by caesarean section depends on each country’s cultural, social and economic factors, personal beliefs and available resources. This may be as high as 55% in South America, or as low as 15.5% in England. According to an ecological study carried out in Colombia, the national frequency for giving birth by caesarean section is 16.8%; there is a substantial difference when comparing this frequency for public hospitals and social security system ones with private hospitals, 32.5% and 58.6% prevalence being reported, respectively.

More than 90% of caesarean sections are carried out under regional anaesthesia in developed countries, spinal anaesthesia being used in elective...
caesarean sections and emergencies in more than 80% and more than 40% of cases, respectively.1

There is a 33% incidence of hypotension caused by spinal block in the general population (non-expectant mothers). This is greater than 90% in pregnant females (depending on the definition used) making this the most frequently occurring adverse effect caused by the intervention described to date. Multiple pregnancies are not considered to be a risk factor for hypotension caused by spinal anaesthesia for caesarean section compared to single pregnancies.6

Maternal effects

Even though maternal hypotension is presented in most females where spinal anaesthesia is used for caesarean section, the probable clinical implications arising from this phenomenon are not clear; however, patients may present uncomfortable symptoms such as nausea, vomiting and dizziness. If hypotension is sustained and is not suitably treated, it can lead to serious adverse effects for the mother, such as loss of consciousness, apnoea, bronchoaspiration of gastric content, aspiration pneumonia and cardiorespiratory arrest.4,6

Foetal effects

Uteroplacentary blood flow depends directly on maternal blood pressure.10,11 The clinical compromise associated with sustained different levels of hypotension is also not clear for the foetus.10,6 Several animal models have suggested greater foetal compromise related to profound, sustained hypotension.11

Slight hypotension is associated with hypoxemia and foetal acidosis; if such conditions are maintained, then this could trigger off profound neurological compromise and foetal death.10,11

TREATMENT

Prophylaxis

It seems reasonable to think that by preventing maternal hypotension then the frequency and severity of the probable maternal-foetal consequences described will become reduced. Many ploys and treatments are currently being used for preventing spinal block-associated hypotension such as a patient’s suitable position with displacement of the pregnant uterus for avoiding aortocaval compression12,13, using endovenous crystalloid and colloid liquids for increasing available vascu-
lar volume14,15 using ephedrine for raising heart-rate, cardiac output and peripheral vascular resistance16,17,18 using alpha 1 agonists for increasing peripheral vascular resistance and mechanical compression of the lower limbs for increasing venous return.6

Administering intravenous liquids is a frequent practice during caesarean section, before or after placing the spinal block.14,19,20 Administering crystalloids or colloids depends on local availability, cost (crystalloids are generally cheaper) and the balance between possible risks and benefits.14,21

Colloids generally have infrequently occurring but potentially serious adverse effects, such as anaphylactic reactions, renal failure, coagulopathy, the transmission of diseases such as hepatitis C with the use of human albumin and bovine spongiform encephalopathy with the use of bovine-derived pharmaceutical preparations such as gelatine haemaccel.19

Vasoconstrictor agents are not innocuous and the controversy regarding which of them to use prophylactically also extends to managing established hypotension.16

The conclusions drawn in the metanalysis by Cyna et al.12,22 concerning techniques for preventing hypotension during spinal anaesthesia for caesarean section are given below.

75 assays were included (4,624 females). Crystalloids were more effective than any type of therapy involving endovenous liquids (relative risk [RR] 0.78; 95%: confidence interval [95%CI] 0.60 to 1.00) and colloids were more effective than crystalloids (RR 0.68; 95%CI: 0.52 to 0.89; 11 assays; 698 females) for preventing hypotension following spinal anaesthesia for caesarean section. Differences were not detected for the different doses, infusion speeds or methods for administering colloids or crystalloids.

Ephedrine was significantly more effective for preventing hypotension than passive control (RR 0.51; 95%CI: 0.33 to 0.78; seven assays; 470 females) or crystalloids (RR 0.70; 95%CI: 0.50 to 0.96; four assays; 293 females). No significant differences were observed between ephedrine and phenylephrine regarding hypotension (RR 0.95; 95%CI: 0.37 to 2.44; three assays; 97 females) and phenylephrine was more effective than the controls (RR 0.27; 95%CI: 0.16 to 0.45; two assays; 110 females). Infusion speed or high ephedrine doses could increase the incidence of high blood pressure and tachycardia.

Compressing the lower limbs was more effective for preventing hypotension than no compression
beta 1 adrenergic action, thereby explaining positive

tions can be explained by an increase in nitric oxide

directly (norepinephrine release).

Ephedrine was the vasoconstrictor
agent of choice in obstetric anaesthesia for many
years due to its favourable pharmacodynamic
profile; many animal models have demonstrated a
marked increase in uteroplacentary blood flow.6,24

This medicament has a dual effect (direct and
indirect). It is a direct agonist for adrenergic alpha
and beta receptors and stimulates norepinephrine
release from adrenergic binding. It mainly acts in-
directly (norepinephrine release).6,16

Favourable effects on uteroplacentary circula-
tion can be explained by an increase in nitric oxide
synthase and reduced sympathetic innervation of
the vascular uterine layer. Ephedrine also presents
beta 1 adrenergic action, thereby explaining positive

(esp. 0.69; 95%CI: 0.53 to 0.90; seven assays; 399
females), even though the effectiveness of different
compression methods seems to be variable. Com-
paring action regarding different physical methods,
such as position, were also not seen to be effective;
however, such assays were frequently small and
had little power for detecting true effects (if indeed
they did exist).

Reducing the local anaesthetic dose used in
spinal anaesthesia could reduce the incidence and
severity of maternal hypotension caused by subara-
chnoideal anaesthesia. Clinical experiments which
have been published comparing fixed and weight-
adjusted spinal dose have thus found clinically
significant (20% difference between groups) and
statistically significant lower hypotension frequency
on adjusting a dose for weight.2,3

**Treatin hypotension**

In spite of using all the prophylactic meas-
ures described, some being effective for preventing
hypotension such as using crystalloids, colloids,
ephedrine, phenylephrine and compressing the
lower limbs, none of these prophylactic interventions
can totally avoid treating maternal hypotension be-
coming established during caesarean section with
spinal anaesthesia. Thus, 40% to 60% of patients
will continue being treated with vasoconstrictor agents
in the context described above.6

Phenylephrine and ephedrine are the vasocon-
strictor agents which are currently being recom-
manded and used for controlling hypotension,4 the
phenylephrine: ephedrine potency ratio is taken as
being 80:1.16,17 An ideal vasoconstrictor agent must
have a short latency period and duration, favourably
affect foetal heart rate, preserve uteroplacentary
perfusion and be economic and easily obtained.18

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chronotropism, inotropism and chronotropism, the-
reby substantially increasing heart rate and cardiac
load and exercising a modest effect on adrenergic
beta 2 receptors. This may partly explain utero-
placentary vasculature dilatation. Its vasoconstric-
tor action (arterial and venous) is mediated by alpha
1 action.18

Ephedrine is excreted in urine without being
metabolised and its action is ended due to pre-
synaptic recapture in adrenergic binding, thereby
making its pharmacokinetic profile (beginning of
action and prolonged duration) not very favourable
and thus might partly explain its therapeutic
failures because it presents its vasopressor and
sympathicomimetic action at different moments
during episodes of hypotension.24,6

Studies have been carried out for determining
the ideal dose presenting suitable effectiveness for
treating hypotension and presenting fewer adverse
effects. Studies have been carried out for determining
the ideal dose for treating hypotension with fewer
adverse effects. It has been determined that the ideal
dose should be greater than 12 mg by contrast with
that recommended by most texts (10 mg)2,5,6

Ephedrine increases myocardial demand and
consumption of oxygen. It also increases the amount
of circulating catecholamines thereby making the
myocardial and ventricular conduction system more
susceptible to cardiac arrhythmia.25

Many studies have related ephedrine use to foetal
acidosis; the action mechanism so implicated is an
increase in foetal catecholamines thereby increasing
metabolism, mainly in foetal brown fat, and increa-
sing foetal carbon dioxide production. In spite of
this, foetal clinical adverse effects caused by reduced
foetal pH have not been demonstrated.25

**Phenylephrine.** Phenylephrine is a synthetic
sympathicomimetic agent acting as a short latency and
duration vasoconstrictor due to it being metabolised
by catechol-O-methyltransferase and monoami-
nooxidase. It acts on adrenergic alpha 1 receptors
mediating vasoconstriction.24,6 Sympathectomy-
mediated hypotension is mainly due to vasodilata-
tion with reduced peripheral vascular resistance, an
effect clearly antagonised by phenylephrine.6

It increases venous return and preload, in turn
mediating negative chronotropism; there is also an
increase in systolic, diastolic and medium blood
depressor reflex and, in turn,
explaining its protection-inducing profile against
arrhythmias compared to ephedrine.

Other alpha 1 agonists were initially investigated
for managing pharmacological sympathectomy-me-
diated hypotension (like metoxamine); however, vasoconstriction of the uteroplacental vascular layer was presented in animal models, thereby hampering their early development within the pertinent therapeutic arsenal.\textsuperscript{16,17} However, phenylephrine was introduced as vasoconstrictor agent to be applied whilst giving birth due to ephedrine’s therapeutic failures (many being explained by inadequate qualification and administration time).\textsuperscript{18}

It has been shown that phenylephrine has an uteroplacental layer vasoconstrictor effect; however, this effect does not result in foetal clinical complications or paraclinical changes (acid-base imbalance) in umbilical arterial blood. On the contrary, it has better safety as foetal physiological pH is maintained.\textsuperscript{6}

Several clinical studies have concentrated on phenylephrine, supporting its use in obstetric anaesthesia; however, it should be stressed that no clinical evidence is available regarding emergency situations such as unsatisfactory foetal state, premature foetus or mothers suffering from high blood pressure.\textsuperscript{6}

\textit{Ethylephrine}. Few clinical studies have evaluated this drug’s effectiveness and safety for the clinical indication in question. This medicament is easily obtained in our setting and its clinical effects may be extrapolated to other alpha 1 agonists, such as phenylephrine.

\textit{Other vasoconstrictor agents and forms of administration.} Metaraminol, metoxamine and angiotensin II are other vasoconstrictor agents which are used in clinical practice; fewer clinical trials have been carried out on them and they have few advantages regarding their effectiveness and safety compared to ephedrine or phenylephrine.\textsuperscript{6}

Methodologically supported benefits for the indication in question have not been shown when administering vasopressor infusions or combined therapy.\textsuperscript{2,6}

**PATIENTS SUFFERING FROM HYPERTENSIVE DISORDERS DURING PREGNANCY**

Patients presenting hypertensive disorders during pregnancy (especially preeclampsia) have increased vascular tone due to endothelial changes, partly because of increased sympathetic influx, thereby making them more prone to hypotension from pharmacological sympathectomy than healthy pregnant females. However, some studies have shown that spinal anaesthesia-induced hypotension in patients with preeclampsia is less frequent and less severe, possibly due to planetary alterations and growth restriction being presented.\textsuperscript{26,6}

Little research has been aimed at identifying the vasoconstrictor agent and dose of choice in this group of patients; however, publications concerning severe preeclampsics have used a 3 to 6 mg dose of ephedrine with suitable outcomes. Many authors recommend reducing vasopressor dose for preventing the risk of high blood pressure associated with its use.\textsuperscript{6}

**INVESTIGATION**

Studies are currently being carried out for determining genetic polymorphism in adrenergic receptors, explaining individual susceptibility to hypotension during pharmacological sympathectomy and response to vasoconstrictor agents. Furthermore, one hypothesis proposes that analysing heart rate variability is directly related to individual sympathetic activity and indirectly so to the risk of hypotension or responding to vasoconstrictor agents.\textsuperscript{6}

**REFERENCIAS**


