# 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.[1,2] 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.[1,3]

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.[1,4] 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.[5]

Hypotension is a frequently occurring adverse effect in the obstetric population to which neuraxis anaesthesia or analgesia is to be administered.[1,5,6] 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.[5,6] 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.[5]

## 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.[2,3,4]

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.[6] 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 sympatectomy 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;[4,6] and
- 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[7] or as low as 15.5% in England.[8,14] 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.[9]

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 compression[12,13], using endovenous crystalloid and colloid liquids for increasing available vascular volume[14,15], using ephedrine for raising heartbeat rate, cardiac output and peripheral vascular resistance[16,17,18], 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.*,[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

(RR 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. Comparing 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 subarachnoideal 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.[23]

## Treating hypotension

In spite of using all the prophylactic measures 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 becoming 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 vasoconstrictor agents which are currently being recommended and used for controlling hypotension[6]; 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]

*Ephedrine.* 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 indirectly (norepinephrine release).[6,16]

Favourable effects on uteroplacentary circulation 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 chronotropism, inotropism and chromotropism, thereby substantially increasing heart rate and cardiac load and exercising a modest effect on adrenergic beta 2 receptors. This may partly explain uteroplacentary vasculature dilatation. Its vasopressor 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 presynaptic 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).[25,6]

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 arrythmia.[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 increasing 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 monoaminooxidase. It acts on adrenergic alpha 1 receptors mediating vasoconstriction.[24,6] Sympathectomy-mediated hypotension is mainly due to vasodilatation 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 pressure, explaining bradycardia reflex and, in turn, explaining its protection-inducing profile against arrythmias compared to ephedrine[6]

Other alpha 1 agonists were initially investigated for managing pharmacological sympathectomy-me-

diated hypotension (like metoxamine); however, vasoconstriction of the uteroplacentary vascular layer was presented in animal models, thereby hampering their early development within the pertinent therapeutic arsenal.[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).[18]

It has been shown that phenylephrine has an uteroplacentary 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.[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.[6]

*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.

*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.[6]

Methodologically supported benefits for the indication in question have not been shown when administering vasopressor infusions or combined therapy.[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.[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 preeclamptics 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.[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.[6]

## REFERENCIAS


1. Ng K, Parsons J, Cyna AM, Middleton P. Anestesia raquídea versus epidural para la cesárea. Biblioteca Cochrane Plus 2008.
2. Mercier FJ, Bonnet MP, De la Dorie A, Moufouki M, Banu F, Hanaf A et al. Spinal anaesthesia for caesarean section: fluid loading, vasopressors and hypotension. Ann Fr Anesth Rean. 2007; (26): 688-93.
3. Macarthur A. Solving the problem of spinal-induced hypotension in obstetric anesthesia. Can J Anesth. 2002; (49): 536-9.
4. Burns SM, Cowan CM, Wilkes RG. Prevention and management of hypotension during spinal anaesthesia for elective Caesarean section: a survey of practice. Anaesthesia. 2001; (56):777-98.
5. Simmons SW, Cyna AM, Dennis AT, Hughes D. Analgesia espinal y epidural combinadas versus analgesia epidural en el trabajo de parto. Biblioteca Cochrane Plus 2008.
6. Reidy J, Douglas J. Vasopressors in obstetrics. Anesthesiol Clin. 2008; (26): 75-88.

7. Behague DP, Victora CG, Barros FC. Consumer demand for caesarean sections in Brazil: informed decision making, patient choice, or social inequality? A population based cohort study linking ethnographic and epidemiological methods. BMJ. 2002;324:942.
8. Chamberlain G, Steer P. ABC of labour care: operative delivery. BMJ 1999;318(7193):1260-4.
9. Belizán JM, Althabe F, Barros FC, Alexander S. Rates and implications of Caesarean section in Latin America: Ecological study. BMJ. 1999; (319): 1.397-1400.
10. Valli J, Pirhonen J, Aantaa R, Erkkola R, Kanto J. The effects of regional anaesthesia for caesarean section on maternal and fetal blood flow velocities measured by Doppler Ultrasound. Acta Anaesthesiol Scand. 1994; (38): 165-9.
11. Ngan WD, Lee A. Multivariate analysis of factors associated with umbilical arterial pH and standard base excess after Caesarean section under spinal anaesthesia. Anaesthesia. 2003; (58):125-30.
12. Kundra P, Khanna S, Habeebullah S, Ravishankar M. Manual displacement of the uterus during Caesarean section. Anaesthesia. 2007;(62):460-5.
13. Kundra P, Kahana S, Habeebullah S, Ravishankar M. Manual displacement of the uterus during Caesarean section. Anaesthesia. 2007; (62): 460-5.
14. Hofmeyr GJ, Cyna AM, Middleton P. Precarga profiláctica por vía intravenosa para la analgesia regional durante el trabajo de parto. Biblioteca Cochrane Plus 2008.
15. Chanimov M, Gershfeld S, Cohen ML, Sherman D, Bahar M. Fluid preload before spinal anaesthesia in Caesarean section: the effect on neonatal acid-base status. Eur J Anesthesiol. 2006; (23): 676-9.
16. Saravanan S, Kocarev M, Wilson RC, Watkins E, Columb MO, Lyons G. Equivalent dose of ephedrine and phenylephrine in the prevention of post-spinal hypotension in Caesarean section. Br J Anaesth. 2006; (96): 95-9.
17. Riley ET. Spinal anaesthesia for Caesarean delivery: keep the pressure up and don't spare the vasoconstrictors. Br J Anaesth. 2004 May;92(5):782.
18. Cooper DW, Mowbray P. Ephedrine or phenylephrine to prevent or treat hypotension during spinal anaesthesia for caesarean section. Int J Obst Anesth. 2004; (8):197-8.
19. Perel P, Roberts I. Coloides versus cristaloides para la reanimación con líquidos en pacientes en estado crítico. Biblioteca Cochrane Plus 2008
20. Ngan WD, Khaw KS, Lee BB, Ng FF, Wong MS. Randomized controlled study of colloid preload before spinal anaesthesia for Caesarean section. Br J Anaesth. 2001; (87):772-4.
21. Siddik SM, Aouad MT, Kay GE, Sfeir MM, Baraka AS. Hidroxyethylstarch 10% is superior to Ringer's solution for preloading before spinal anesthesia for Cesarean section. Can J Anesth. 2000; (47):616-21.
22. Cyna AM, Andrew M, Emmett RS, Middleton P, Simmons SW. Técnicas para la prevención de la hipotensión durante la anestesia espinal para la cesárea. Biblioteca Cochrane Plus. 2008.
23. Harten JM, Boyne I, Hannah P, Varveris D, Brown A. Effects of a height and weight adjusted dose of local anaesthetic for spinal anaesthesia for elective Caesarean section. Anaesthesia. 2005; (60): 348-53.
24. Lee A, Warwick D, Ngan WD, Gin T. A quantitative, systematic review of randomized controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean delivery. Anesth Analg. 2002; (94):220-6.
25. Kluger MT. Ephedrine may predispose to arrhythmias in obstetric anaesthesia. Anaesth Intensive Care. 2000; (28):336.
26. Aya A, Vialles N, Tanoubi I, Mangin R, Ferrer JM, Robert C, et al. Spinal anesthesia-induced hypotension: a risk comparison between patients with severe preeclampsia and healthy women undergoing preterm Cesarean delivery. Anesth Analg. 2005; 101: (869-75).