

End report of survey to the European Society of Anaesthesiologists

**Management of spinal anaesthesia-induced hypotension for cesarean delivery: a European
survey**

Running title: Hypotension after spinal anaesthesia.

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Summary

Hypotension following administration of spinal anaesthesia for caesarean delivery is common. Substantial research has been published on how best to prevent or treat hypotension. However, the degree to which these new findings have been implemented in clinical practice in Europe is unknown. We conducted an online survey in 2010; members of the European Society of Anaesthesiology and the European Society of Regional Anaesthesia and Pain Therapy were invited by email to participate. The response rate was 351/5409 (6.5%). The main findings of the study were that despite growing evidence concerning potential adverse effects, ephedrine was still routinely used by more than 70% of the responders. In comparison to previous surveys in the United States and United Kingdom, we observed a trend towards increased use of phenylephrine to treat hypotension, in keeping with a growing evidence-base suggesting its side-effect profile is superior to ephedrine in most cases.

Keywords

Spinal anaesthesia, cesarean section, hypotension, phenylephrine, ephedrine, survey.

Hypotension following administration of spinal anaesthesia for caesarean delivery is common; the reported incidence varies between 50 and 100%. [1] Several strategies have been suggested to reduce the incidence, or mitigate the severity, of hypotension, such as patient positioning, fluid administration, and use of vasopressors to prevent or correct hypotension. [2] The last decade has seen extensive research efforts to devise the optimal regimen for prevention or treatment of spinal anaesthesia-induced hypotension, including type of intravenous fluid (crystalloid or colloid), timing of fluid administration (before or after initiation of spinal anaesthesia), and choice of vasopressor (ephedrine or phenylephrine). [3] However, the degree to which these new findings have been incorporated into clinical practice is unknown. A survey conducted among American obstetric anaesthesiologists in 2007 [4] found considerable change in clinical practice compared to a UK survey conducted in 1999. [5] Specifically, the use of ephedrine had dropped from 95% [5] to 32%, [4] likely reflecting increased awareness of the potential adverse effects of ephedrine, i.e. tachyarrhythmia and foetal acidosis. [6,7] There exist no recent data on clinical practice among anaesthesiologists providing care for parturients in Europe.

The aim of the present survey was to determine the clinical practice of spinal anaesthesia for caesarean delivery, focusing on prevention and treatment of post-spinal anaesthesia hypotension among European anaesthesiologists in 2010.

Methods

We developed a web-based survey questionnaire using an online survey engine (www.2ask.at). The initial pilot version was tested by several anaesthesiologists not involved in the study. The survey questions were created by two authors (P.L., I.H.) after reviewing literature about vasopressor and fluid therapy use in obstetric anaesthesia. Following approval by the Scientific Committees of the European Society of Anaesthesiologists (ESA) and the European Society of Regional Anaesthesia and Pain Therapy (ESRA), an e-mail containing an invitation to participate in the survey was distributed to members of the two societies. A total number of 5540 emails were sent, of which 131 were returned undelivered, resulting in 5409 contacted members. The invitation email was sent out in May 2010, and the survey remained open for two months. To ensure confidentiality, survey responses did not contain personal or institutional identifying information. Moreover, the invitation emails were distributed by ESA and ESRA headquarters anonymously. No follow-up of non-responders was done. All responses were stored on a secure database and were exported to Microsoft Excel 2003 and SPSS 16.0 for analysis. Plausibility testing was performed and three responses were discarded.

The survey collected demographic data and assessed practitioners' routine methods for preventing and treating hypotension during spinal anaesthesia, focussing on intravenous fluid administration and vasopressor use. The questionnaire employed multiple branching, allowing responders to loop through a set of multiple-choice questions based on their initial responses to several key questions. The complete survey questionnaire is found in the Appendix.

Results

A total of 5409 email invitations were delivered. We received 351 responses with fully completed questionnaires, which represented an overall response rate of 6.5%. Sixty-seven incomplete questionnaires were excluded from further analysis.

Demographics

Demographic characteristics of the responders are found in Table 1. The responders were distributed among 36 European or Mediterranean countries, with 12 participants (3.4%) from the United States and Australasia. A third of the responders were members of a professional obstetric anaesthesia society (Society for Obstetric Anesthesia and Perinatology or Obstetric Anaesthetists Association). The most common type of anaesthesia for caesarean delivery was spinal anaesthesia.

Performance of spinal anaesthesia

Details of monitoring and spinal anaesthesia technique are found in Table 2. Blood pressure, heart rate, electrocardiography and pulse oximetry were used by almost all practitioners; other techniques such as bispectral index, fetal heart rate, and urinary output were used by less than 1% of participants. The majority of responders routinely administer oxygen. Spinal anaesthesia was initiated in the sitting position by the majority of anaesthesiologists. The most common spinal anaesthetic was bupivacaine. The use of adjuvants, particularly opioids, was common.

Management of post-spinal anaesthesia hypotension

Details of preventative and treatment measures for spinal anaesthesia-induced hypotension are found in Table 3. Responders estimated that the mean incidence of post-spinal anaesthesia hypotension was 42% (range 1% to 100%).

Over 80% of responders routinely administer fluid, most commonly crystalloid, between 500 and 1000 mL. Preload is administered more commonly than coload. Eighty-three percent of responders agreed that patients generally fall into two possible categories: hypotension associated with tachycardia, or hypotension associated with bradycardia (Figure 1). Responders estimated tachycardia occurs more often (63%) than bradycardia (36%). Slightly more than 60% of anaesthesiologists routinely used a vasopressor to *prevent* hypotension. The most common vasopressor was ephedrine; fewer used phenylephrine and a small minority used another vasopressor. Almost half of the responders always used ephedrine as the first choice vasopressor to *treat* hypotension, whereas only 14% always used phenylephrine for this indication. Others chose the drug depending on the patient's heart rate.

Discussion

The main findings of this 2010 survey are that ephedrine was still routinely used by more than 70% of survey responders practicing primarily in Europe, for the treatment of hypotension associated with spinal anaesthesia in women undergoing caesarean delivery; however, more than 40% also use phenylephrine. One quarter of responders used either ephedrine or phenylephrine, depending on heart rate and / or blood pressure.

Response rate and demographics

A limitation of our results is our low response rate. The low rate most likely represents the anonymity with which participants were contacted, and the lack of follow-up. Hazard Munro postulated that the minimal number of survey responses required for survey validity is equal to the number of questions times ten;[8] therefore the current 28- question survey required at least 300 response, a number which was exceeded in the present study. The preferred method to increase response rate would be to decrease sample size while increasing efforts to contact non-responders.[9] Unfortunately, due to the distribution of the invitation email by the two anaesthesiology societies, this technique was not possible in the present study. As in all surveys, nonresponder bias may constitute a source of error. However, the characteristics of the test persons in our study compare well with those of previous surveys, with a slight majority working in community hospitals, and slightly less than half practicing academic anaesthesiology.[4] Also, our responders were distributed over different European and Mediterranean countries, therefore meeting our aim of surveying predominantly European anaesthesiologists. The share of caesarean deliveries among overall deliveries was reported by responders to be approximately 25%, corresponding well with previous investigations.[10] Most responders performed elective caesarean delivery under spinal anaesthesia or other neuraxial anaesthesia modalities (epidural, combined spinal-epidural), although 16.2% of caesarean deliveries were estimated to occur under general anaesthesia. These numbers correspond with recent European surveys on use of general anaesthesia for caesarean deliveries. In Germany the rate of general anaesthesia decreased from 71% in 1998[11] to 27% in 2005, in Italy the rate was 34% in 2007,[12] and in Israel the rate was 15% in 2010.[13] Finally, the response rate may have been negatively affected by the specific nature of the survey. Because almost 80% of responders perform obstetric anaesthesia routinely, we surmise that the survey was completed by a group of anaesthesiologists with a dedicated and collective interest in obstetric anaesthesiology.

Performance of spinal anaesthesia

The practice of administering oxygen to parturients in women with normal oxygen saturation is controversial, although a majority of the survey's responders do so routinely. High inspired oxygen concentrations during elective caesarean delivery under spinal anaesthesia have been controversially discussed to cause oxygen free radical activity in both mother and foetus.[14,15] Potential adverse effects of high neonatal oxygen concentrations have been demonstrated in several neonatal diseases such as bronchopulmonary dysplasia, and retinopathy of prematurity.[summarized in 14] Historically, it has been thought that supplementary oxygen delivered to the mother might protect the foetus against desaturation in the event of prolonged incision-to-delivery interval during elective caesarean section, but this was disproved by Khaw and colleagues.[16] Administration of 60% oxygen to parturients undergoing emergency caesarean section under spinal anaesthesia resulted in improved oxygenation indices in the fetus, without increase in lipid peroxidation, and similar outcome.[17] The clinical relevance of these findings remains unclear, but the routine administration of oxygen to every parturient irrespective of peripheral oxygen saturation is not supported by literature. Some anaesthesiologists may be administering oxygen solely because doing so allows simultaneous measurement of end-tidal carbon dioxide.

The majority of responders used bupivacaine as the local anaesthetic, combined with fentanyl, sufentanil, or morphine. Very few used clonidine or epinephrine, while 13% did not use any adjuvants. Interestingly, the majority of responders base the anaesthetic dose on clinical experience or body-mass or height nomograms, while approximately 20% use the same dose of local anaesthetics in all patients. The latter practice is supported by recent investigations which found no relationship between body mass index (BMI) and dose-response for spinal anaesthesia for elective caesarean delivery.[18,19] Hence, current literature does not support altering the local anaesthetic dose based on body habitus.

Management of post-spinal anaesthesia hypotension

Many responders were not aware of guidelines for the prevention and treatment of hypotension. The reported incidence of post-spinal hypotension varies widely, with a range of 7% to 74% in prospective studies, depending on the definition of hypotension and method of measurement.[20] Wide heterogeneity exists in the definition of hypotension, and consequently, the treatment goal. The most common definitions of hypotension after spinal anaesthesia for caesarean delivery are "below 80% of baseline" or a combined "below 80% of baseline or 100 mmHg systolic".[20]

In our survey, the target blood pressure goal among clinicians varied widely. In a recent North American survey by Allen *et al.*, the most common threshold for treatment of hypotension was less than 20% of baseline pressure, whereas 13% tried to maintain BP at baseline level.[4] In survey of British obstetric anaesthesiologists a systolic blood pressure of 100 mmHg was defined as threshold for vasopressor administration by 44% of responders; 41% chose a threshold of 90 mmHg.[5] Recent data suggest that maintaining blood pressure close to baseline compared to 80% baseline is associated with higher umbilical artery pH values[21] In our survey, the overwhelming majority of responders tried to maintain blood pressure at more than 80% of baseline level, which is in keeping with previous investigations; less than 5% aimed to keep pressure at baseline.

Research has attempted to determine risk factors for post-spinal hypotension. Retrospective analysis suggests chronic alcohol consumption, history of hypertension, increased body mass index, sensory block height and urgency of surgery as independent risk factors for post-spinal hypotension.[22] Recently, body mass index, sensory block level and older maternal age were identified as independent risk factors for maternal hypotension, but inclusion of these factors into a prospective risk assessment showed moderate sensitivity[23] and despite preventive measures, clinicians should continue to anticipate hypotension in every parturient in which spinal anaesthesia is performed for caesarean delivery.

Adverse effects of hypotension are both maternal (syncope, nausea and vomiting) and foetal/neonatal (placental hypoperfusion, hypoxia, acidosis).[2] In a retrospective study of 919 mother-infant pairs, maternal hypotension was not found to predict perinatal complications if promptly treated,[24] but prolonged hypotension is associated with foetal acidosis [25] and may cause maternal and foetal morbidity.[26] The wide range of responses of our responders estimating the incidence of post-spinal hypotension (1% to 100%), may reflect individual anaesthesiologists' experiences with various preventive strategies, as well as prophylactic versus treatment use of vasopressors. Maintenance of blood pressure was most often achieved by a combination of fluid and vasopressor therapy. The crystalloid volume range reported by responders was consistent with the volumes reported in most clinical trials.[27]

Fluid loading appears insufficient on its own to prevent or treat hypotension following spinal anesthesia in parturients. Most responders administered crystalloid as a preload despite evidence suggesting that this practice is ineffective. [2,28] [29,30] Measurements of cardiac output during caesarean delivery show that the beneficial effects of a pre-load fluid bolus are not sufficient to maintain hemodynamic stability after the initiation of spinal anaesthesia.[31] It is likely that the increases in cardiac output that result from fluid loading are insufficient to compensate for the decrease in systemic vascular resistance caused by high-thoracic neuroblockade.[31] Moreover,

rapid pre- or coload may lead to activation of atrial natriuretic peptide in response to increased intravascular volume, thereby counteracting desired volume-expanding effects in both healthy and pre-eclamptic parturients.[32,33]

Colloid is more reliable than crystalloid in preventing hypotension in a systematic review,[34] but a 2010 meta-analysis concluded that the incidence of maternal hypotension remains high, no matter whether crystalloid or colloid is administered as a preload or coload.[27] Since colloids are associated with a small but measurable risk of allergic reactions,[34] choice of fluid must weigh the small risk of allergic reactions (estimated at 0.03% [35]) associated with colloid administration against its value in preventing hypotension following spinal anaesthesia.[34]

In a recent trial, colloid pre-load was found to increase cardiac output transiently for the first five minutes after spinal anaesthesia, but there was no difference in vasopressor requirements or blood pressure changes between colloid preload and coload.[36] The rationale behind fluid pre- and co-load is to counteract decreased cardiac output due to decreased venous return following spinal anaesthesia. However, recent evidence emphasizes the importance of changes in systemic vascular resistance in post-spinal anaesthesia hypotension,[28] with the possible exception of patients who are hypotensive and bradycardic after spinal anaesthesia. This latter group of patients should preferentially be treated using fluid, ephedrine or epinephrine, and possibly anticholinergic agents.[28,37] The proportion of bradycardic patients after spinal anaesthesia was estimated by our responders, on average, to comprise around a third of patients, whereas a much lower incidence was reported in recent trials[37] and a recent review of hemodynamic changes following spinal anaesthesia for caesarean section described the incidence as low.[28]

Despite preventive measures and fluid co-load, hypotension after spinal anaesthesia is common.[38] In a recent study, the combination of prophylactic phenylephrine and rapid crystalloid cohydration was found to be effective in preventing spinal-induced hypotension for caesarean delivery.[26] Ngan Kee et al. postulated that cohydration better coincides with peak sympathetomy effect of spinal anaesthesia, and promotes faster circulation of vasopressor.[26] This latest study achieved a very low incidence of maternal hypotension, albeit at the cost of overcorrecting blood pressure in a substantial share of patients.[26]

Perioperative measurements of cardiac output have shown that have shown that the major changes induced by spinal anaesthesia are a decrease in systemic vascular resistance accompanied by a compensatory increase in cardiac output.[28] This pathogenic mechanism is directly counteracted by phenylephrine, which increases systemic vascular resistance, and decreases cardiac output.[37] Ephedrine, in contrast, increases heart rate and (to a lesser extent) stroke volume and

therefore cardiac output,[37] but is often not potent enough to correct changes in vascular resistance.

Whether ephedrine or phenylephrine is the vasopressor of choice for post-spinal hypotension in elective caesarean delivery remains controversial. However, recent editorialists suggest that based on current evidence, phenylephrine is the drug of choice.[39] Ephedrine has been associated with foetal acidemia, and both the spinal anaesthesia - delivery interval and total ephedrine dose are positively correlated with neonatal acidemia.[40] In a secondary analysis of the EPIPAGE trial data, neonatal mortality of preterm infants was higher after spinal than general or epidural anaesthesia; it has been hypothesized that the widespread use of ephedrine may be responsible for this finding.[41] The mechanism of action of ephedrine's potential adverse effects has not been clearly elucidated. Ephedrine crosses the placenta to a greater extent than phenylephrine, and it may exert beta-adrenergic mediated stimulatory effects on foetal metabolism.[42]

Accumulating evidence that phenylephrine is superior to ephedrine appears to have resulted in an increased use of phenylephrine for the prevention and treatment of hypotension in the past 11 years. Results of surveys in North America and the United Kingdom in 1999 and 2007 suggest that the use of phenylephrine in the obstetric population is increasing. In the 1999 survey, ephedrine was used by 95% of responders.[5] In contrast, a 2007 survey found 23% and 26% of responders used phenylephrine for the prevention and treatment of hypotension, respectively. In the same survey, 40% of anaesthesiologists used either agent based upon heart rate.[4] In our survey, 26% of responders used either agent based upon heart rate. This is also in concordance with recent literature, which recommends that phenylephrine may be the better choice in situations when hypotension coincides with tachycardia, whereas ephedrine may be better suited in situations when hypotension coincides with bradycardia.[37] However, in light of the strong evidence to support routine use of phenylephrine, we note the relatively large number of responders who still always use ephedrine as the first choice, while a much smaller number of responders reported the exclusive use of phenylephrine.

In conclusion, we describe results from a 2010 European survey investigating contemporary clinical practice in the management of hypotension following spinal anaesthesia for caesarean delivery. In contrast to previous surveys, we found increased use of phenylephrine to treat hypotension, in keeping with a growing evidence-base suggesting its side-effect profile is superior to that of ephedrine in most cases. Recent literature supports the use of phenylephrine as the first-line drug to treat most patients with hypotension. Nevertheless, many clinicians appear to continue to use ephedrine routinely.

Competing interests

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Appendix – Survey questionnaire

Demographics

- 1) Geographical area of hospital (choice between Countries of the World)
- 2) Type of hospital (choice between University, Community)
- 3) Size of hospital (number of beds, categorical between <100 beds, 101-250 beds, 251-500 beds, 501-750 beds, 751-1000 beds, >1000 beds)
- 4) Number of births per year (numerical)
- 5) Number of cesarean deliveries per year (numerical)
- 6) How many % of caesarean deliveries are performed under general anaesthesia versus spinal versus epidural versus CSE in your hospital? (numerical)
- 7) What position do you occupy (training, consultant/attending, program director/division director)? (multiple answers possible, tick boxes to check)
- 8) Are you member of a professional obstetric anesthesia society? (multiple answers possible, tick boxes to check SOAP, OAA, other)
- 9) Do you perform obstetric anesthesia ... (multiple answers possible, tick boxes to check between rarely, routinely, full-time)

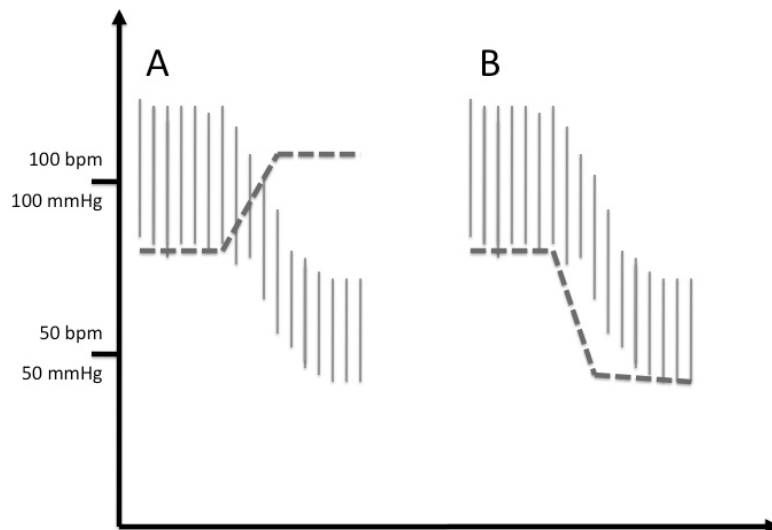
Anesthetic management of spinal anesthesia

- 1) Which monitoring modalities are routinely used for anesthesia for cesarean delivery? (tick boxes to check BP, HR, EKG, SpO2, ETCO2)
- 2) Do you ROUTINELY administer oxygen to the mother before delivery of baby? (yes/no)
- 3) Which local anesthetic do you ROUTINELY use for spinal anesthesia? (multiple answers possible, tick boxes to choose bupivacaine, ropivacaine, levobupivacaine, lidocaine, other)
- 4) Which adjuncts do you ROUTINELY add to local anesthetic?(multiple answers possible, tick boxes to choose morphine, sufentanil, fentanyl, clonidine, epinephrine, other)

- 5) What puncture site to you ROUTINELY target during spinal anesthesia?(tick boxes to choose L2/3, L3/4, L4/5)
- 6) How do you choose the dose of local anesthetic?(tick boxes to choose between „according to table (taking into account e.g. body weight and height), „according to clinical experience”, “ same dose for all patients”)
- 7) In what patient position do you ROUTINELY initiate spinal anesthesia? (sitting, left lateral, right lateral)?
- 8) How often do you estimate hypotension to occur after spinal anesthesia for cesarean delivery in your patient population? (numerical)
- 9) Do you ROUTINELY administer intravenous fluid to PREVENT hypotension? (yes, no)
- 10) If YES, which fluid do you ROUTINELY use? (crystalloid, colloid)
- 11) If YES, when do you administer the fluid? (fluid bolus administered before spinal anesthesia, fluid bolus administered together with spinal anesthesia)
- 12) If YES, how much fluid do you ROUTINELY administered? (categorical: < 500 mL, 500 – 1000 mL, 1000 – 1500 mL, > 1500 mL).
- 13) Do you ROUTINELY use a vasopressor prophylactically to PREVENT hypotension? (yes, no)
- 14) Which agents do you ROUTINELY use to TREAT hypotension (tick boxes to choose between ephedrine, phenylephrine, theodrenaline, norepinephrine, epinephrine, other)
- 15) Are you aware of any guidelines in your hospital delineating which agent should be preferred to correct hypotension (yes/no).
- 16) Which drug do you ROUTINELY use as a first choice to TREAT hypotension (tick boxes to choose between always ephedrine, always phenylephrine, always theodrenaline, always norepinephrine, always epinephrine, depends on patient hemodynamics, algorithm with ephedrine first followed by phenylephrine, algorithm with phenylephrine first followed by ephedrine)
- 17) If you chose ”always one drug“ above, how do you choose your preferred agent to TREAT hypotension (a practice guideline, evidence from literature, institutional guideline, personal experience, other) (multiple answers possible).
- 18) If you chose ”depends on patient hemodynamics“ above, which factors do you take into account? (tick boxes to choose between heart rate, blood pressure, oxygen saturation, clinical observation of mother, other)

- 19) What is your blood pressure goal when preventing/treating hypotension associated with spinal anesthesia for cesarean delivery? (> 99% baseline, 90-99% baseline, 80-89% baseline, >70% baseline)
- 20) Which blood pressure parameter do you monitor? (systolic BP, mean BP, diastolic BP)
- 21) How do you ROUTINELY administer vasopressor for the prevention/treatment of hypotension associated with spinal anesthesia for cesarean delivery? (IV bolus, IV infusion, combination of bolus and infusion).
- 22) What is your usual starting dose of the vasopressor mentioned in question (30)? Bolus dose (mg), infusion rate (mg).
- 23) Would you agree that hypotensive patients after spinal anesthesia can be divided into two groups (A hypotensive and tachycardic, and B hypotensive and bradycardic) as shown in the Figure below? (yes/no)

Hypotension defined as drop in BP by 20% or greater. Figure depicts timecourse of blood pressure (vertical lines delineate blood pressure amplitude (given as mmHg), dotted line representing heart rate (given as beats per minute – bpm).



- 24) If yes, what percentage would you attribute to each group of patients in your practice? (A: numerical, B: numerical)
- 25) Do you treat groups A and B similarly when choosing a drug to restore hemodynamics?
- 26) If you answered „yes“ above, which agent would you ROUTINELY use to correct these derangements (tick boxes to choose between always ephedrine, always phenylephrine, always theodrenaline, always norepinephrine, always epinephrine, algorithm with

ephedrine first followed by phenylephrine, algorithm with phenylephrine first followed by ephedrine)

27) If you answered „no“ above, which agent would you ROUTINELY use to correct hemodynamics for a patient whose hemodynamics are shown in Figure A (tick boxes to choose between always ephedrine, always phenylephrine, always theodrenaline, always norepinephrine, always epinephrine, algorithm with ephedrine first followed by phenylephrine, algorithm with phenylephrine first followed by ephedrine)

28) If you answered „no“ above, which agent would you ROUTINELY use to correct hemodynamics for a patient whose hemodynamics are shown in Figure B (tick boxes to choose between always ephedrine, always phenylephrine, always theodrenaline, always norepinephrine, always epinephrine, algorithm with ephedrine first followed by phenylephrine, algorithm with phenylephrine first followed by ephedrine)

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Table 1. Responder demographic characteristics.

<i>Hospital setting</i>	
Community hospital	57%
University hospital	43%
Provider type	
Trainee	14%
Consultant	66%
Director	18%
Obstetric anaesthesia practice	
Full time	10%
Routinely	78%
Rarely	12%

Table 2. Characteristics of spinal anaesthesia.

Administration of oxygen yes/no	60%/40%
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<u>Local anesthetic (multiple answers possible)</u>	
Bupivacaine	89%
Levobupivacaine	7%
Ropivacaine	6%
Lidocaine/Mepivacaine	2%

<u>Additives (multiple answers possible)</u>	
Fentanyl	48%
Sufentanil	29%
Morphine	21%
Clonidine	1%
Epinephrine	< 1%
Dehydrobenzperidol	< 1%
Pethidine, Diamorphine	< 1%

Table 3. Hemodynamic variables and treatment

Blood pressure goal

at/above baseline	4%
above 90% of baseline	40%
above 80% of baseline	54%

Fluid pre-load or co-load (multiple answers possible)

Fluid preload	85%
Crystalloid fluid preload	65%
Colloid fluid preload	27%
Fluid co-load	39%
Fluid volume 500-1000 ml	71%
Fluid volume 1000-1500 ml	16%

Preventive vasopressor (multiple answers possible)

Routinely used	63%
Ephedrine	72%
Phenylephrine	46%
Other	9%

Therapeutic vasopressor

Always ephedrine	48%
Always phenylephrine	14%
Phenylephrine 1 st line, ephedrine 2 nd line	4%
Ephedrine 1 st line, phenylephrine 2 nd line	9%
Choice based upon heart rate	26%
Others: metaraminol, theodrenaline, noradrenaline	