

Prevention of Hypotension by a Single 5-mg Dose of Ephedrine During Small-Dose Spinal Anesthesia in Prehydrated Cesarean Delivery Patients

Marcel P. Vercauteren, MD, PhD, Hilde C. Coppejans, MD, Vincent H. Hoffmann, MD, Els Mertens, MD, and Hugo A. Adriaensen, MD, PhD

Department of Anesthesiology, University Hospital Antwerp, Edegem, Belgium

To evaluate the effectiveness of prophylactic ephedrine for the prevention of hypotension associated with spinal anesthesia, 50 parturients undergoing cesarean delivery received either ephedrine 5 mg or saline IV in a double-blinded fashion immediately after the induction of spinal anesthesia. Spinal anesthesia was performed with hyperbaric bupivacaine 6.6 mg combined with sufentanil 3.3 μ g as part of a combined spinal-epidural technique. All patients received 1000 mL of lactated Ringer's solution and 500 mL of hydroxyethylstarch 6% before the spinal injection. Additional ephedrine boluses (5 mg) were administered IV when the systolic blood pressure or heart rate decreased by more than 30% from baseline values, when systolic blood pressure became <100 mm Hg, or when patients complained of nausea or feeling faint. The height of the block was equal in the groups; however, more patients in the placebo group were found to develop hypotension (58% vs 25%, $P < 0.05$). Only 2 (8%) patients in the

ephedrine group developed hypotension with systolic blood pressure values <90 mm Hg, whereas 10 patients (42%) in the saline group experienced hypotension of this severity ($P < 0.05$). In addition, there was a higher incidence of nausea in the placebo-treated patients. The total amount of ephedrine administered did not differ between groups. These findings suggest that the incidence and severity of hypotension are significantly reduced by the IV administration of a prophylactic dose of 5 mg ephedrine in patients receiving small-dose spinal anesthesia for cesarean delivery. **Implications:** Ephedrine is the drug most often used to correct hypotension during spinal anesthesia for cesarean delivery in healthy patients. A single IV dose of 5 mg decreases the occurrence and limits the severity of hypotension in prehydrated subjects receiving a small-dose spinal local anesthetic-opioid combination.

(Anesth Analg 2000;90:324-7)

Spinal anesthesia is very popular for cesarean delivery because it offers a fast, profound, and symmetrical sensory and motor block of high quality. However, despite crystalloid or colloid preloading, hypotension remains a common complication (1-3).

In a recent study, we found a very low incidence of hypotension in well hydrated patients receiving a small-dose spinal with hyperbaric bupivacaine and the administration of 5 mg ephedrine before turning the parturient to the supine position (4). However, the benefit of the prophylactic ephedrine dose in that study was unclear. The prophylactic administration of

ephedrine by the IM route is very controversial because its systemic absorption and peak effect are difficult to predict, thus, possibly resulting in rebound hypertension (5,6). The IV route may be more effective and controllable, but despite large doses, the incidence of hypotension was still high in some studies (7,8).

Small-dose spinal anesthesia, with the potential for epidural supplementation, has gained popularity since the advent of the combined spinal-epidural (CSE) technique. We evaluated whether a 5-mg prophylactic ephedrine dose lowers the incidence of hypotension after a small-dose spinal anesthetic for cesarean delivery.

Methods

After obtaining approval by the hospital ethics committee and written, informed consent, 50 patients scheduled for elective cesarean delivery were enrolled

Accepted for publication September 27, 1999.

Address correspondence and reprint requests to M. Vercauteren, MD, PhD, Department of Anesthesiology, University Hospital Antwerp, Wilrijkstraat 10, B-2650 Edegem, Belgium. Address e-mail to marcel.vercauteren@uza.uia.ac.be.

in the study. Patients presenting for semiurgent cesarean delivery, parturients in active labor, and those presenting with a gestational age of <37 wk were excluded. Patients with an initial systolic blood pressure exceeding 150 mm Hg were also excluded.

All patients received oral cimetidine 900 mg with sodium citrate 1 h before the induction of anesthesia. An IV infusion of 1000 mL lactated Ringer's solution was started 10 min before transfer to the operating room, where all patients received 500 mL hydroxyethylstarch (6%) on arrival.

A CSE procedure, with a BD-Durasafe Adjustable device (Becton Dickinson, Franklin Lakes, NJ), was initiated at the time both fluid volumes were nearly completely infused, but no later than 40 min after the start of the crystalloid infusion. With the patient in the right lateral decubitus position, bupivacaine 6.6 mg plus sufentanil 3.3 μ g was injected intrathecally. After the epidural catheter was inserted and the puncture site was dressed, patients received, in a double-blinded fashion, either 5 mg IV ephedrine (E-group) or saline placebo (P-group). Subsequently, patients were turned to a 15° left lateral supine position. All parturients received 3 L of oxygen via a face mask. Heart rate and oxygen saturation were continuously measured. Blood pressure was measured automatically (Datex AS3, Helsinki, Finland) at 1-min intervals. If systolic blood pressure decreased below 100 mm Hg or by more than 30% from the baseline (measured on admission to the labor and delivery suite), a further 5 mg bolus of IV ephedrine was given. IV ephedrine supplements of 5 mg were also given when heart rate decreased by 30% from baseline or as soon as patients complained of nausea, vomiting, or feeling faint, regardless of the hemodynamic recordings at that time.

Surgical incision was allowed after 15 min, provided that the block had reached the T5 dermatome. The height of the block was determined by loss of sensation to alcohol swabs. If the upper sensory level did not reach the T6 dermatome after 10 min, plain lidocaine 2% was given via the epidural catheter in incremental doses of up to 2 mL per unblocked segment.

Motor block was scored using the Bromage scale (0 = none, 1 = ability to flex knees but not the hip, 2 = unable to flex knees, but no problems with ankle movement, 3 = no movement possible in any lower extremity joint). Intervals of time between the spinal injection, delivery, and completion of surgery were recorded. Apgar scores, at 1 and 5 min, and umbilical blood gases were measured after delivery.

Statistical evaluation was performed with the unpaired, two-tailed Student's *t*-tests and the Fisher's exact test, as appropriate. A *P* value < 0.05 was considered significant.

Table 1. Patient Demographics

	E-group (<i>n</i> = 24)	P-group (<i>n</i> = 24)
Age (yr)	29 \pm 4	30 \pm 5
Weight (kg)	74 \pm 10	77 \pm 19
Height (cm)	166 \pm 4	168 \pm 6
Duration of pregnancy (wk)	38.5 \pm 1	38.3 \pm 1.2
Interval CSE-birth (min)	26 \pm 5	29 \pm 7
Interval CSE-end of surgery	68 \pm 9	67 \pm 7

Results are mean \pm sd. There were no statistically significant differences. E-group = ephedrine group, P-group = placebo group, CSE = combined spinal-epidural.

Results

There were no differences between the groups with respect to patient demographics and the time intervals between spinal injection to birth and completion of surgery (Table 1).

One patient in the E-group was excluded because of technical difficulties with the CSE procedure, necessitating a single-dose spinal injection. Another patient, in the P-group, required 200 mg lidocaine to increase the anesthesia level from T11 to T5 and was also excluded.

All other CSE procedures were uneventful, and the average upper level of sensory block (T2-3) was the same in both patient groups (Table 2). Epidural supplementation with \leq 3 mL of lidocaine 2% was required for one patient in each group, and a patient in the placebo group received 120 mg lidocaine at wound closure. Because the initial sensory levels were equal to or higher than T7, these patients were included in the analysis.

Movement of the ankle joint was still possible for eight patients in the E-group and nine patients in the P-group. The mean lowest systolic blood pressure was higher (*P* < 0.01) in the E-group (Table 2). In the P-group low systolic blood pressure values were common, <100 mm Hg and \leq 90 mm Hg in 58% and 42% of patients, respectively. Ephedrine pretreatment significantly decreased this incidence to 25% and 8%, respectively (*P* < 0.05). Twelve patients in the P-group required more than one ephedrine dose, compared with only three patients in the E-group (*P* < 0.05). In approximately half of the patients in the P-group, hypotension occurred within the first 5 min after the spinal injection as compared with only one of six patients of the E-group.

The lowest maternal heart rate recorded before delivery was significantly lower in the placebo group (67 \pm 15 vs 77 \pm 12 bpm, *P* < 0.05). More patients in the P-group required additional ephedrine (18 vs 8 patients in the E-group, *P* < 0.05). In six patients (three in each group) ephedrine was administered without any evidence of hypotension because of nausea (*n* = 5) or bradycardia (*n* = 1). Nausea occurred more often in

Table 2. Spinal Block Data and Hemodynamic Stability

	E-group (n = 24)	P-group (n = 24)	P value
Height of block	T3 (T1-T5)	T3 (C8-T4)	NS
Lowest SBP (mm Hg)	108 ± 17	92 ± 16	<0.01
Lowest heart rate (bpm)	77 ± 12	67 ± 15	<0.05
Patients requiring additional ephedrine	8 (33%)	18 (75%)	<0.05
Supplemental doses ephedrine administered	0.5 ± 0.8	1.7 ± 1.7	<0.01
Patients with SBP			
<100 mm Hg	6 (25%)	14 (58%)	<0.05
<90 mm Hg	2 (8%)	10 (42%)	<0.05

Data are expressed as mean ± SD or number of patients (%).

E-group = ephedrine group, P-group = placebo group, SBP = systolic blood pressure, NS = not significant.

the placebo group ($P = 0.04$). One patient in each group vomited (Table 3).

No differences were found between groups with regard to Apgar scores and neonatal umbilical blood gases. None of the patients complained of symptoms consistent with postdural puncture headache.

Discussion

This study demonstrates that a small dose of ephedrine may significantly lower the incidence and limit the severity of hypotension during elective cesarean delivery under small-dose spinal anesthesia. Gutsche (5) similarly demonstrated that 25–50 mg ephedrine given IM within 30 minutes of instituting a subarachnoid block significantly decreased the incidence of hypotension. However, two other studies reported an unacceptably high risk of fetal acidosis and rebound hypertension when using these large ephedrine doses (6,9). Not every study has found benefit to the prophylactic administration of ephedrine. Several studies, in fact, have reported little or no benefit from prophylactic ephedrine (10–12).

The IV route for administering ephedrine, either as an incremental dose or by infusion, may be more effective and predictable than the IM route (13,14). Other studies have shown that ephedrine infusion compared favorably with prehydration, phenylephrine, or angiotensin II infusions in minimizing hypotension (15–20).

In addition to ephedrine pretreatment, the contribution of small-dose intrathecal anesthesia and prehydration play key roles. Using CSE anesthesia for cesarean delivery, Fan et al. (21) reported that 5 mg intrathecal bupivacaine was the optimal dose, requiring only moderate epidural supplementation and causing lower incidences of hypotension than larger spinal bupivacaine doses. With the doses we used, epidural supplementation was necessary in approximately 10% of the patients (4).

Crystalloid prehydration is also important to prevent hypotension. Rout et al. (1) demonstrated that the

Table 3. Side-Effects and Neonatal Outcome

	E-group (n = 24)	P-group (n = 24)	P value
Nausea	9 (37.5%)	16 (67%)	<0.05
Vomiting	1 (4.1%)	1 (4.1%)	
Apgar score			
<7 (1 min)	2 (8.3%)	2 (8.3%)	
<8 (5 min)	1 (4.1%)	1 (4.1%)	
pH of umbilical blood			
Venous <7.3	1 (4.1%)	2 (8.3%)	
Arterial <7.25	1 (4.1%)	1 (4.1%)	

Values are number of patients (%) with given outcome.

E-group = ephedrine group, P-group = placebo group.

incidence of hypotension decreased significantly from 71% to 55% for unpreloaded versus preloaded subjects, respectively. Increasing the crystalloid preload from 10 to 30 mL/kg may further reduce the incidence of hypotension (2). However, two studies demonstrated that 1000 mL of crystalloid alone did not appear to be more effective than preloading with 200 mL or no prehydration at all (7,8). In both studies, ephedrine was administered by infusion and was started after completion of the spinal injection, resulting in total ephedrine requirements of approximately 50 mg. Although placental transfer of such large ephedrine doses may result in elevated neonatal catecholamine levels, this does not seem to affect neonatal outcome (22,23).

Colloids may maintain the oncotic pressure of plasma. Two studies have suggested that hydroxyethylstarch 6% is beneficial as a preloading substance before cesarean delivery. Riley et al. (3) compared a preloading regimen as used in this study with 2000 mL of crystalloids and found the incidence of hypotension (<100 mm Hg) to decrease from 85% to 45%, despite prophylactic administration of ephedrine 10 mg IV. The higher incidence of hypotension in that study, as compared with ours, may be explained by the larger bupivacaine dose of 12 mg used by Riley et al. (3).

For ethical reasons we did not include a group without prehydration. The 5-mg dose of ephedrine

for both prophylaxis and treatment was chosen because that is the usual clinical practice among many anesthesiologists.

The prophylactic ephedrine dose appeared to decrease the speed of onset of hemodynamic instability and, thus, make it more controllable than in the placebo group. It remains unclear why such a small dose of ephedrine was able to minimize the risk of hypotension, as opposed to the higher incidences reported in other studies, in which much larger doses of ephedrine were administered (5–8,22). Most probably, inadequate prehydration, combined with large-dose spinal anesthetics, produced a more profound hypotension.

In conclusion, our results confirm that small-dose spinal anesthesia can be successfully used for cesarean delivery via CSE and that, when these low doses of spinal medication are used, potential hypotension can be alleviated with prehydration and small-dose ephedrine prophylaxis.

References

1. Rout CC, Rocke DA, Levin J, et al. A re-evaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective cesarean section. *Anesthesiology* 1993;79:262–9.
2. Park GE, Hauch MA, Curlin F, et al. The effects of varying volumes of crystalloid administration before cesarean delivery on maternal hemodynamics and colloid oncotic pressure. *Anesth Analg* 1996;83:299–303.
3. Riley ET, Cohen SE, Rubenstein AJ, Flanagan B. Prevention of hypotension after spinal anesthesia for cesarean section: six percent hetastarch versus lactated Ringer's solution. *Anesth Analg* 1995;81:838–42.
4. Vercauteren M, Coppejans H, Hoffmann V, et al. Small-dose hyperbaric versus plain bupivacaine during spinal anesthesia for Cesarean section. *Anesth Analg* 1998;86:989–93.
5. Gutsche BB. Prophylactic ephedrine preceding spinal analgesia for cesarean section. *Anesthesiology* 1976;45:462–5.
6. Rout CC, Rocke DA, Brijball R, Koovarjee RV. Prophylactic intramuscular ephedrine prior to cesarean section. *Anaesth Intensive Care* 1992;20:448–52.
7. Jackson R, Reid JA, Thorburn J. Volume preloading is not essential to prevent spinal-induced hypotension at cesarean section. *Br J Anaesth* 1995;75:262–5.
8. Husaini SW, Russell IF. Volume preload: lack of effect in the prevention of spinal-induced hypotension at cesarean section. *Int J Obstet Anesth* 1998;7:76–81.
9. Rolbin SH, Cole AF, Hew EM, et al. Prophylactic intramuscular ephedrine before epidural anaesthesia for caesarean section: efficacy and actions on the fetus and newborn. *Can J Anaesth* 1982;29:148–53.
10. King SW, Rosen MA. Prophylactic ephedrine and hypotension with spinal anesthesia for cesarean delivery. *Int J Obstet Anesth* 1998;7:18–22.
11. Webb AA, Shipton EA. Re-evaluation of i.m. ephedrine as prophylaxis against hypotension associated with spinal anaesthesia for caesarean section. *Can J Anaesth* 1998;45:367–9.
12. Brizgis RV, Dailey PA, Shnider SM, et al. The incidence and neonatal effects of maternal hypotension during epidural anesthesia for cesarean section. *Anesthesiology* 1987;67:782–6.
13. Datta S, Alper MH, Ostheimer GW, Weiss JB. Method of ephedrine administration and nausea and hypotension during spinal anesthesia for cesarean section. *Anesthesiology* 1982;56:68–70.
14. Kang YG, Abouleish E, Caritis S. Prophylactic intravenous ephedrine infusion during spinal anesthesia for cesarean section. *Anesth Analg* 1982;61:839–42.
15. Chan WS, Irwin MG, Tong WN, Lam YH. Prevention of hypotension during spinal anaesthesia for caesarean section: ephedrine infusion versus fluid preload. *Anaesthesia* 1997;52:908–13.
16. Gajraj NM, Victory RA, Pace NA, et al. Comparison of an ephedrine infusion with crystalloid administration for prevention of hypotension during spinal anesthesia. *Anesth Analg* 1993;76:1023–6.
17. Alahuhta S, Räsänen J, Jouppila P, et al. Ephedrine and phenylephrine for avoiding maternal hypotension due to spinal anaesthesia for caesarean section. *Int J Obstet Anesth* 1992;1:129–33.
18. Hall PA, Bennett A, Wilkes MP, Lewis M. Spinal anaesthesia for caesarean section: comparison of infusions of phenylephrine and ephedrine. *Br J Anaesth* 1994;73:471–4.
19. Ramin SM, Ramin KD, Cox K, et al. Comparison of prophylactic angiotensin II versus ephedrine infusion for prevention of maternal hypotension during spinal anesthesia. *Am J Obstet Gynecol* 1994;171:734–9.
20. Vincent RD, Werhan CF, Norman PF, et al. Prophylactic angiotensin II infusion during spinal anesthesia for elective cesarean delivery. *Anesthesiology* 1998;88:1475–9.
21. Fan SZ, Susetio L, Wanh YP, et al. Low dose of intrathecal hyperbaric bupivacaine combined with epidural lidocaine for cesarean section: a balanced block technique—looking for the adequate spinal dose. *Anesth Analg* 1994;78:474–7.
22. Kangas-Saarela T, Hollmen A, Tolonen U, et al. Does ephedrine influence newborn neurobehavioural responses and spectral EEG when used to prevent maternal hypotension during caesarean section? *Acta Anaesthesiol Scand* 1990;34:8–16.
23. Hughes SC, Ward MMG, Levinson G, et al. Placental transfer of ephedrine does not affect neonatal outcome. *Anesthesiology* 1985;63:217–9.