

# Prospective, Randomized Trial Comparing General with Spinal Anesthesia for Cesarean Delivery in Preeclamptic Patients with a Nonreassuring Fetal Heart Trace

Robert A. Dyer, F.C.A.(S.A.),\* Ilse Els, F.C.Ped.(S.A.),† Josef Farbas, F.C.A.(S.A.),‡ Gregory J. Torr, F.C.A.(S.A.),§ Leann K. Schoeman, F.C.O.G.(S.A.),|| Michael F. James, Ph.D.#

**Background:** There are no randomized studies on neonatal outcome after spinal versus general anesthesia for cesarean delivery in preeclamptic patients with a nonreassuring fetal heart trace. This study examined both markers of neonatal hypoxia and maternal hemodynamics.

**Methods:** Seventy patients were randomized to general (n = 35) or spinal anesthesia (n = 35). The general anesthesia group received thiopentone, magnesium sulfate, and suxamethonium intravenously before intubation, followed by 50% nitrous oxide in oxygen, 0.75–1.5% isoflurane, and morphine after delivery. The target end-tidal partial pressure of carbon dioxide (Pco<sub>2</sub>) was 30–34 mmHg. The spinal anesthesia group received 1.8 ml hyperbaric bupivacaine plus 10 µg fentanyl at the L3–L4 interspace. Heart rate and blood pressure were measured at specific time points. Hypotension was treated with ephedrine. Maternal arterial and neonatal umbilical arterial blood gas samples were taken at delivery. Resuscitation requirements were recorded.

**Results:** In both groups, hemodynamic measures remained within acceptable limits. Spinal anesthesia patients required more ephedrine (13.7 vs. 2.7 mg). Maternal Paco<sub>2</sub> was lower in the spinal group (28.9 vs. 32.4 mmHg). One-minute Apgar scores were lower after general anesthesia. Base deficit was greater (7.13 vs. 4.68 mEq/l) and neonatal umbilical arterial pH was lower (7.20 vs. 7.23) after spinal anesthesia. *Post hoc* analysis showed that if maternal diastolic blood pressure on admission was greater than 110 mmHg, neonatal umbilical arterial base deficit was greater after spinal anesthesia. There was no difference in the number of patients with Apgar scores less than 7 at 1 or 5 min or umbilical arterial pH less than 7.2 or in the requirements for resuscitation.

**Conclusions:** In preeclamptic patients with a nonreassuring fetal heart trace, spinal anesthesia for cesarean delivery was associated with a greater mean neonatal umbilical arterial base deficit and a lower median umbilical arterial pH. The clinical significance remains to be established. Maternal hemodynam-

ics were similar and acceptable with either anesthetic technique.

IN the past decade, regional anesthesia, in particular spinal anesthesia, has become the first choice for operative delivery in elective cesarean delivery, largely because of the recognition of the dangers of failed intubation, which occurs approximately eight times more frequently in the obstetric population than in the general surgical population.<sup>1</sup> When one considers the cardiovascular pathophysiology of severe preeclampsia, there has been an understandable caution as regards regional anesthesia in these patients because of the theoretical possibility of precipitous hypotension, decreased cardiac output, and associated placental hypoperfusion.

Spinal anesthesia has only recently been recognized to have a place in operative management in preeclampsia. In 1995, three groups of patients with severe preeclampsia were randomized to receive epidural, combined spinal-epidural, or general anesthesia for cesarean delivery, with similar hemodynamic stability (as assessed by heart rate and blood pressure) and fetal outcome in each group. However, patients with nonreassuring fetal heart traces were excluded from this study.<sup>2</sup>

A recent editorial highlighted a study demonstrating, albeit retrospectively, that hemodynamic stability was equivalent in patients receiving spinal or epidural anesthesia for nonemergency cesarean delivery. However, fluid requirements were higher in the spinal group.<sup>3,4</sup> Despite the gradually emerging evidence that spinal anesthesia is safe in preeclampsia,<sup>2,3,5</sup> at least one editorial has called for caution and stresses the value of epidural anesthesia.<sup>6</sup>

Some nonrandomized retrospective studies suggest that early markers of neonatal compromise, such as fetal acidemia, may be less favorable in spinal than in general anesthesia for elective cesarean delivery.<sup>7</sup> No studies have prospectively addressed the problem as to whether fetal outcome is influenced by the method of anesthesia in preeclamptic patients requiring emergency cesarean delivery for a nonreassuring fetal heart trace. It was therefore decided to test the hypothesis that the mode of anesthesia influenced markers of neonatal hypoxia. Patients with preeclampsia and a nonreassuring fetal heart trace were randomized into two groups, receiving either spinal or general anesthesia for cesarean delivery. A study to examine neonatal outcome would require a prohibitively large number of patients. Therefore, surro-

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\* Senior Specialist Anesthesiologist, ‡ Senior Resident, § Specialist Anesthesiologist, # Professor and Head, Department of Anesthesia, † Specialist Neonatologist, Department of Pediatrics, || Specialist Obstetrician and Gynecologist, Department of Obstetrics and Gynecology, University of Cape Town and New Groote Schuur Hospital, Cape Town, South Africa.

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Address reprint requests to Dr. Dyer: D23 Department of Anesthesia, University of Cape Town and New Groote Schuur Hospital, Anzio Road, Observatory 7925, Cape Town, South Africa. Address electronic mail to: dyer@cormack.uct.ac.za. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

**Table 1. Fetal Heart Rate Abnormalities Indicating Cesarean Delivery**

Fetal Heart Rate Abnormalities	Intrapartum FHR Abnormality		Antepartum FHR Abnormality	
	GA	SP	GA	SP
Loss of STV	1	2	2	2
Loss of STV, and bradycardia	1	1	1	1
Loss of STV, early decelerations	2	2	NA	NA
Late decelerations	4	4	NA	NA
Variable decelerations	2	1	NA	NA
Recurrent decelerations, not in labor	NA	NA	20	21
Loss of STV and decelerations	NA	NA	1	1
Total, No.	10	10	24	25

FHR = fetal heart rate; GA = general anesthesia; NA = not applicable (because defined FHR abnormalities are specific to the presence or absence of active labor); SP = spinal anesthesia; STV = short-term variability.

gate markers of neonatal outcome, primarily umbilical arterial base deficit, as well as umbilical arterial pH, Apgar scores, requirements for resuscitation, and complications, were assessed. As further secondary outcome measures, maternal hemodynamics, namely pulse rate and noninvasive blood pressure data, were also collected.

## Materials and Methods

Preeclampsia was diagnosed if the diastolic blood pressure after 20 weeks' gestational age was greater than or equal to 90 mmHg on two separate occasions at least 4 h apart and proteinuria was found of greater than or equal to 1 g or 2+ on urine dipstix in two clean midstream samples taken at least 4 h apart, or greater than or equal to 300 mg protein per 24 h. Preeclampsia was regarded as severe if the systolic blood pressure exceeded 160 mmHg and/or the diastolic blood pressure exceeded 110 mmHg, obtained on at least two separate occasions, or if the patient had symptoms of imminent eclampsia (namely severe headache, visual disturbance, epigastric pain, hyperreflexia, dizziness and fainting, or vomiting) and proteinuria on urine dipstix was 3+ or worse.

Patients with preeclampsia and a nonreassuring fetal heart trace were randomized by sealed envelopes into two groups of 35 for either spinal or general anesthesia for cesarean delivery. Informed written consent was taken at the time of decision to proceed to cesarean delivery. The study commenced after the approval of the Ethics Committee of the University of Cape Town (Cape Town, South Africa).

Exclusion criteria were patient refusal or any other relative contraindication to either general or spinal anesthesia, in particular oral intake other than clear fluids within 4 h of the intended surgery; body mass index greater than 35 kg/m<sup>2</sup>; Mallampati score greater than 2; clinical signs of hypovolemia; abruptio placentae; placenta praevia; coagulation abnormality; thrombocytopenia (platelet count < 75 × 10<sup>9</sup>/l); local or generalized sepsis; spinal deformity; cord prolapse; less than 30 weeks' gestation; or twin pregnancy.

Should any spinal anesthetic take longer than 15 min to perform, the patient would receive general anesthesia, and the data would be recorded as a failure of the technique. The data from these subjects would be assessed as a separate subgroup.

The antepartum management was according to the established protocol of our institution: If the patient was in established labor, an intravenous line was inserted, and a balanced crystalloid solution administered at 120 ml/h. Patients not in labor were allowed free oral fluids. Seizure prophylaxis was administered to patients with severe preeclampsia and consisted of magnesium sulfate (MgSO<sub>4</sub>), administered as a loading dose of 4 g intravenously, followed by 1 g hourly intravenously. Dihydralazine was administered intravenously as a vasodilator for additional blood pressure control against a standardized protocol that was identical in both groups. Previous use of other agents (alpha-methyl dopa, morphine, and dexamethasone) was recorded.

In the absence of labor, a baseline fetal heart rate of less than 100 or greater than 150 beats/min, decreased or absent fetal heart rate variability (< 5 beats/min) of 60 min in duration, and the presence of repetitive decelerations were considered to be indications for cesarean delivery. Intrapartum abnormalities of the fetal heart rate that indicated cesarean delivery were, in addition to the above, the presence of late decelerations and variable decelerations greater than 60 beats/min (table 1). The decision to proceed with operative delivery was made by the obstetric team independent of the investigators.

After a nonreassuring fetal heart trace had been identified, all patients were placed in the lateral position before transfer to the operating room and received 40% oxygen by facemask.

Both groups of patients received 30 ml sodium citrate orally in the operating room. Noninvasive monitoring consisted of electrocardiography, blood pressure monitoring, and pulse oximetry in both groups, as well as capnography in the general anesthesia group.

In the general anesthesia group, a preload of modified Ringer's lactate (< 750 ml) was given before induction. Induction was not delayed in either group for the spe-

cific purpose of fluid administration, in keeping with recent published guidelines for normal parturients.<sup>8</sup> After adequate preoxygenation, induction of general anesthesia was with 5 mg/kg thiopentone, followed by an appropriate dose of intravenous magnesium sulfate for control of the pressor response to tracheal intubation. The dose of MgSO<sub>4</sub> was 45 mg/kg if there had been no previous administration of MgSO<sub>4</sub> and 30 mg/kg if the patient was currently receiving the drug. Muscle relaxation was achieved with 1.5 mg/kg suxamethonium, and 1 min after administration, a rapid-sequence intubation was performed. Maintenance of anesthesia was with 50% nitrous oxide in oxygen and 0.75–1.5% end-tidal isoflurane, and patients were ventilated to a target end-tidal carbon dioxide concentration of 30–34 mmHg, using a circle system with fresh gas flows of 5 l/min until delivery. Maternal arterial blood gas measurement was taken immediately postdelivery. Neuromuscular blockade was maintained using an infusion of suxamethonium (200 mg/200 ml plasmalyte B at 4 mg/min), monitored by a peripheral nerve stimulator. Oxytocin, 5 IU intravenously, and morphine, 0.05 mg/kg intravenously, were administered at delivery. Thereafter, a continuous infusion of oxytocin was administered (20 IU/l, at 60–100 ml/h). A further 0.05 mg/kg morphine was administered intravenously before extubation if the hemodynamic and respiratory status allowed it. Patients were extubated awake. Recordings of heart rate and noninvasive measurements of systolic, diastolic, and mean blood pressure (Dinamap; Critikon, Tampa, FL) were made at the following time points: Blood pressure was recorded before induction (starting systolic, diastolic, and mean blood pressures were taken as the mean of two consecutive readings taken in the 3 min before induction of anesthesia), immediately before intubation, at 1-min intervals after intubation for 10 min, and thereafter every 5 min until arrival in the recovery room.

The treatment of patients in the spinal anesthesia group was as follows: A preload of modified Ringer's lactate (< 750 ml) was given. All patients received 1.8 ml hyperbaric bupivacaine, 0.5%, with 10 µg fentanyl, administered at the L3–L4 interspace in the absence of uterine contractions. After 20 s in the sitting position, patients were positioned supine, with 20° of left lateral tilt, to minimize aortocaval compression. Block height was assessed using cold sensitivity to ethyl chloride spray. All mothers received 40% oxygen by facemask. Oxytocin therapy after delivery was as for the general anesthesia group. Heart rate and blood pressure were measured before induction of spinal anesthesia in the same manner as in the general anesthesia group, at 1-min intervals after induction for the next 10 min, and thereafter every 5 min until arrival in the recovery room. Hypotension in either group, defined as a decrease in systolic blood pressure of more than 25% below the preinduction value, was treated with ephedrine (5-mg

boluses) given every minute until blood pressure recovered to within 25% of the starting value. However, no ephedrine was given to patients with a mean arterial pressure greater than 100 mmHg. The total dose of ephedrine was recorded. Maternal arterial blood gas measurement was taken immediately postdelivery.

Further important time intervals were recorded:

1. time from arrival in the operating room until induction of anesthesia
2. induction to skin incision time
3. induction to uterine incision time
4. uterine incision to delivery time

All maternal medication received in the 24 h before anesthesia was carefully noted. Severity of disease (as assessed by the degree of hypertension and the requirement for vasodilator and/or seizure prophylaxis therapy, and degree of proteinuria) and presence or absence of labor were also recorded. In some patients, antenatal fetal assessment was performed (umbilical artery Doppler and amniotic fluid index) at the discretion of the attending obstetrician. Resistance index was calculated from Doppler measures of umbilical arteries using peak systolic velocity (S) and end-diastolic velocity (D) (resistance index =  $S - D/S$ ). Amniotic fluid index is the sum total of the deepest vertical pool of amniotic fluid in four quadrants (normal range, 5–25 cm). Where available, these data were recorded. Intraoperative maternal blood loss was estimated from suction bottle measurement and weighing of swabs.

Neonatal outcome was assessed by a pediatrician dedicated to the study and blinded to the method of anesthesia. Assessment criteria were as follows:

1. At birth: Neonatal weight, sex, gestational age (Ballard score), 1- and 5-min Apgar scores, arterial cord blood gas, and degree of resuscitation (facemask ventilation, intubation and ventilation, cardiopulmonary resuscitation) were recorded.
2. In the nursery: Signs of respiratory distress using clinical and radiologic diagnosis and the need for respiratory support in the form of head box oxygen, nasal continuous positive airway pressure, intermittent positive-pressure ventilation, high-frequency oscillatory ventilation, or surfactant replacement therapy were recorded.

A hypoxic-ischemic encephalopathy score<sup>9</sup> was performed in all neonates with a 5-min Apgar score of less than 6 or with a cord pH of less than 7.1 and a base deficit of more than 10 mEq/l, daily for 5 days. An ultrasound scan of the head was performed on day 5 in all preterm neonates with a birth weight of below 1,500 g. Mortality at discharge was recorded. All the neonatal recordings were normal practice in the neonatal nursery and intensive care unit, and no additional blood sampling was performed solely for the purpose of the study.

Table 2. Demographic Data

	General (n = 35)	Spinal (n = 35)
<b>Maternal</b>		
Age, yr (mean $\pm$ SD)	26 $\pm$ 6	25 $\pm$ 7
Weight, kg (mean $\pm$ SD)	74 $\pm$ 11	75 $\pm$ 13
Height, cm (mean $\pm$ SD)	157 $\pm$ 13	157 $\pm$ 12
Preinduction systolic blood pressure, mmHg (mean $\pm$ SD)	159 $\pm$ 30	155 $\pm$ 30
Preinduction diastolic blood pressure, mmHg (mean $\pm$ SD)	98 $\pm$ 20	97 $\pm$ 21
Preinduction mean blood pressure, mmHg (mean $\pm$ SD)	120 $\pm$ 22	121 $\pm$ 24
Gravidity, median (range)	1.5 (1–4)	1 (1–6)
Parity, median (range)	0.5 (0–3)	0 (0–5)
Active labor, No.	11	10
Induced, not in labor, No.	6	11
Not induced, no labor, No.	18	14
Diastolic blood pressure > 110 mmHg, No.	20	20
MgSO <sub>4</sub> therapy, No.	19	20
Dihydralazine therapy, No.	9	13
Proteinuria 1–2+, No.	10	12
Proteinuria 3–4+, No.	22	23
Gestational age, weeks	35.1 (3.2)	34.9 (2.6)
Gestational age < 35 weeks, No.	18	15
Gestational age < 34 weeks, No.	11	11
Gestational age 30 weeks, No.	3	1
<b>Fetal/neonatal</b>		
Umbilical artery Doppler (resistance index)		
Normal, No.	12	10
Absent end-diastolic flow, No.	2	3
Amniotic fluid index (normal, 5–25 cm)	9 (1–16), n = 22	6.5 (1–18), n = 20
Neonatal weight, g	2,236 (728)	2,138 (614)
Placental weight, g	474 (151)	452 (164)

There were no significant differences between the groups.

### Statistical Analysis

Sample size was calculated as follows: Previous studies have reported a normal value for umbilical arterial base deficit after elective cesarean delivery of the order of  $5 \pm 3$  mEq/l.<sup>10,11</sup> It was hypothesized that a mean base deficit of 8 mEq/l or more would, therefore, represent a clinically relevant level of acidosis. Assuming an SD of 7.5, the study would have a minimum power of 90% to detect this magnitude of difference with 66 subjects (33 in each group). We therefore studied 70 patients. The null hypothesis was that the method of anesthesia (spinal or general) made no difference to neonatal umbilical arterial base deficit in patients with preeclampsia and a nonreassuring fetal heart trace undergoing cesarean delivery.

Hemodynamic data were analyzed within groups by analysis of variance for repeated measures and between groups by multiple dependent (group and time) analysis of variance using the 95% confidence interval method for *post hoc* detection of significant differences. Qualitative data were assessed using appropriate nonparametric tests including the Fisher exact test, chi-square, and Kruskal-Wallis analysis of variance for multiple comparisons. Correlation between the use of ephedrine and neonatal base deficit was performed using regression analysis. Nonnormally distributed data were compared between groups using the Mann-Whitney U test. Regression analysis was also performed on maternal and neo-

natal umbilical arterial base deficit. All statistical analysis was performed using the Statistica Version 6 statistical package (StatSoft Inc, Tulsa, OK).

### Results

Demographic data are presented in table 2. The two groups of 35 patients were equivalent. There were no differences between groups in the use of nonstudy medications (alpha-methyl dopa, dihydralazine, morphine, or dexamethasone). Similar numbers of patients in each group were in active labor, and the severity of preeclampsia (as judged by the requirement for magnesium sulfate therapy, diastolic blood pressure > 110 mmHg, dihydralazine therapy, both in terms of numbers receiving the drug and total dose, and proteinuria) was similar in the two groups, as were the gestational ages. In those patients in whom antenatal fetal assessment (umbilical artery Doppler and amniotic fluid index) was performed, there were no statistically significant between-group differences. Table 1 shows the similar fetal heart rate abnormalities that indicated cesarean delivery in the two groups.

No patient was excluded because the allowed time for spinal anesthesia was exceeded, and no patients required conversion from spinal to general anesthesia. The range of block height obtained was between T<sub>2</sub> and T<sub>6</sub>,

**Table 3. Anesthesia Data, Including Maternal and Neonatal Measures**

	General	Spinal	P Value
<b>Fluid Management</b>			
Preload, ml	393 ± 114	454 ± 110	0.025
Total fluid, ml	1,053 ± 421	1,131 ± 357	0.4
Blood loss, ml	446 ± 126	394 ± 64	0.036
<b>Time postsurgery</b>			
TTIA, min	9.7 ± 3.9	11.1 ± 5.7	0.24
TISI, min	4.2 ± 2.6	6.3 ± 2.6	0.001
TIUI, min	7.1 ± 3.3	9.6 ± 2.9	0.002
TUID, min	1.1 ± 0.6	1.2 ± 0.8	0.82
Duration of surgery, min	36.5 ± 13.1	37.3 ± 13.4	0.80
Ephedrine total dose, mg	2.7 ± 8.9	13.7 ± 17.5	0.002

Data are presented as mean ± SD.

TISI = time from induction to skin incision; TIUI = time from induction to uterine incision; TTIA = time from arrival in operating room until induction of anesthesia; TUID = time from uterine incision to delivery.

with 19 patients having a sensory level of T<sub>4</sub>. No patient reported pain or required supplemental analgesia. One severely preeclamptic patient in the general anesthesia group was inappropriately recruited to the study because she had a normal fetal heart trace. She was included in the data analysis. There were no differences in the outcome variables when the data analysis was performed with and without this patient. A further patient in the general anesthesia group had an undiagnosed abruptio placentae, which resulted in a stillbirth; maternal data for this patient were analyzed, but there were no neonatal data. Consequently, 70 mothers were included in the data analysis, but only 69 neonates. There was a single case of sudden infant death syndrome in the spinal anesthesia group on day 5 after delivery.

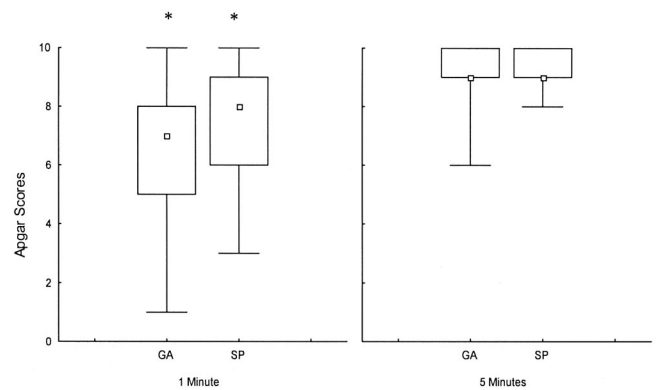
Anesthesia parameters and blood gas values are presented in tables 3 and 4. The spinal anesthesia group received significantly more fluid before induction of anesthesia. Induction to skin incision times were longer by

**Table 4. Blood Gas Data in Mothers and Neonates**

	General	Spinal	P Value
<b>Maternal</b>			
pH	7.35 ± 0.07	7.37 ± 0.04	0.064
Pco <sub>2</sub> , mmHg	32.4 ± 5.1	28.9 ± 3.7	0.002
Po <sub>2</sub> , mmHg	165.7 ± 52.5	172.5 ± 47.2	0.48
Base deficit, mEq/l	6.6 ± 2.8	6.5 ± 2.7	0.69
Standard bicarbonate, mEq/l	19.5 ± 2.3	20.0 ± 1.9	0.35
<b>Neonatal umbilical arterial</b>			
pH, median (range)	7.23 (7.05–7.4)	7.20 (6.93–7.34)	0.046
Pco <sub>2</sub> , mmHg	50.2 ± 10.5	48.7 ± 12.0	0.44
Po <sub>2</sub> , mmHg	22.5 ± 18.7	21.0 ± 19.5	0.67
Base deficit, mEq/l	4.68 ± 3.3	7.13 ± 4.0	0.02
Standard bicarbonate, mEq/l	20.4 ± 3.0	18.4 ± 3.3	0.04

Data are presented as mean ± SD, unless otherwise stated.

Pco<sub>2</sub> = partial pressure of carbon dioxide; Po<sub>2</sub> = partial pressure of oxygen.



**Fig. 1. Apgar scores at 1 and 5 min in the spinal (SP) and general anesthesia (GA) groups. \*Significant differences between groups;  $P < 0.05$ . Small boxes = median; large boxes = 25–75%; bars = minimum–maximum.**

a mean of 2.1 min in the spinal group, and induction to uterine incision times were longer by 2.5 min. There was significantly more blood loss in the general anesthesia group (446 vs. 393 ml); however, no patient was regarded as having more than normal hemorrhage associated with cesarean delivery, and no patient required transfusion.

Maternal arterial carbon dioxide tension (Paco<sub>2</sub>) values were significantly lower in the spontaneously breathing spinal anesthesia group patients than in the general anesthesia group patients whose Paco<sub>2</sub> was controlled by the anesthesiologist (28.9 vs. 32.4 mmHg).

Considering the primary outcome variable, the mean base deficit in the spinal anesthesia group was significantly higher than in the general anesthesia group (7.13 vs. 4.68 mEq/l).

The neonatal pH data were found to be nonnormally distributed. Median umbilical arterial pH and mean standard bicarbonate values were significantly lower in the spinal anesthesia group (7.20 vs. 7.23 and 18.4 vs. 20.4 mEq/l, respectively; table 4). Median 1-min Apgar scores were significantly lower in the general anesthesia group (fig. 1). There were no significant differences in the 5-min scores (fig. 1) and no correlation between Apgar scores and neonatal umbilical arterial base deficit.

Considering categorical data (table 5), there were 22 neonates with a cord pH less than 7.2, of whom 14 were in the spinal anesthesia group and 8 were in the general anesthesia group. Of the five neonates with a cord pH less than 7.1, four were in the spinal anesthesia group and one was in the general anesthesia group. Of the seven infants with a base deficit of 8–10 mEq/l, three were in the spinal anesthesia group and three were in the general anesthesia group, while of the nine with base deficits greater than 10 mEq/l, three were in the general anesthesia group and six were in the spinal anesthesia group. Neonatal blood gases could not be obtained in two patients from the general anesthesia group and one patient from the spinal anesthesia group. There were no

**Table 5. Markers for Fetal Hypoxia**

	General	Spinal	P Value
Apgar score, No.			
1-min Apgar < 7 (n = 27)	14	13	1
5-min Apgar < 7 (n = 1)	1	0	1
Neonatal acidosis, No.			
Umbilical arterial pH			
pH < 7.2 (n = 22)	8	14	0.20
pH < 7.1 (n = 5)	1	4	0.20
Umbilical arterial base deficit, No.			
Base deficit 5–7.9 mEq/l (n = 23)	6	17	0.02
Base deficit 8–10 mEq/l (n = 6)	3	3	1
Base deficit > 10 mEq/l (n = 9)	3	6	0.49
Neonates requiring resuscitation, No.			
Facemask oxygen (n = 30)	18	12	0.20
Intubation (n = 5)	3	2	1
CPR + drugs (n = 2)	1	1	1
Total requiring resuscitation	22	15	0.07
Complications: respiratory distress, No.			
Total = 8	5	3	0.6
Requiring IPPV	2	2	1
Hypoxic ischemic encephalopathy	0	0	

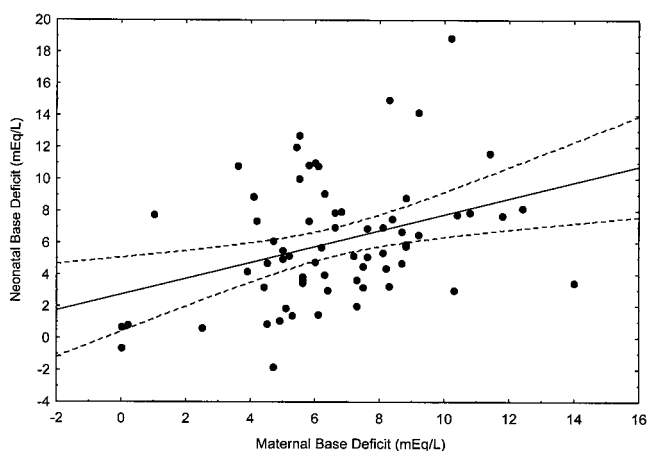
Ultrasound of head: normal in 10 neonates where indicated.

CPR = cardiopulmonary resuscitation; IPPV = intermittent positive-pressure ventilation.

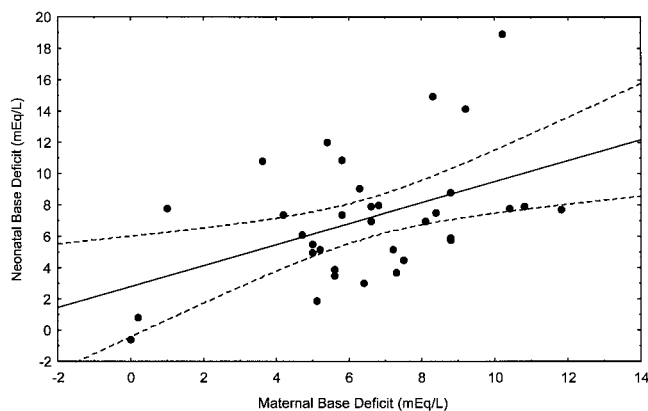
significant between-group differences, apart from a higher incidence of mild base deficit in the spinal anesthesia group (5–7.9 mEq/l). The requirements for resuscitation in the operating room or nursery were similar.

There was a weak correlation ( $r = 0.36$ ) between maternal base deficit and neonatal base deficit (fig. 2). This correlation was stronger in the spinal anesthesia group ( $r = 0.47$ ; fig. 3) than in the general anesthesia group ( $r = 0.29$ ; fig. 4).

Hemodynamic data for the preanesthetic measurement, the subsequent 10 min, and the immediate post-operative measurement are presented in figure 5. At several time points, the heart rate and the systolic, diastolic, and mean blood pressures were significantly



**Fig. 2.** Correlation between maternal and neonatal base deficit (BD) in the entire study cohort, showing regression line and 95% confidence intervals of the mean. Maternal BD:neonatal BD:  $r = 0.36$ ,  $P = 0.003$ . Neonatal BD =  $2.73 + 0.50 \times X$ .

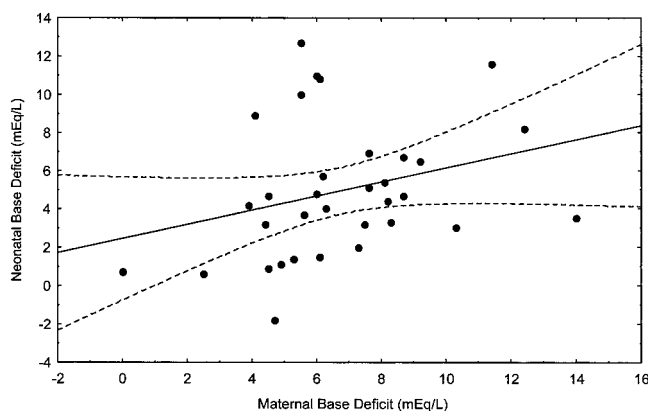


**Fig. 3.** Correlation between maternal and neonatal base deficit (BD) in the spinal anesthesia group, showing regression line and 95% confidence intervals of the mean. Maternal BD:neonatal BD:  $r = 0.47$ ,  $P = 0.005$ . Neonatal BD =  $2.791 + 0.6694 \times X$ .

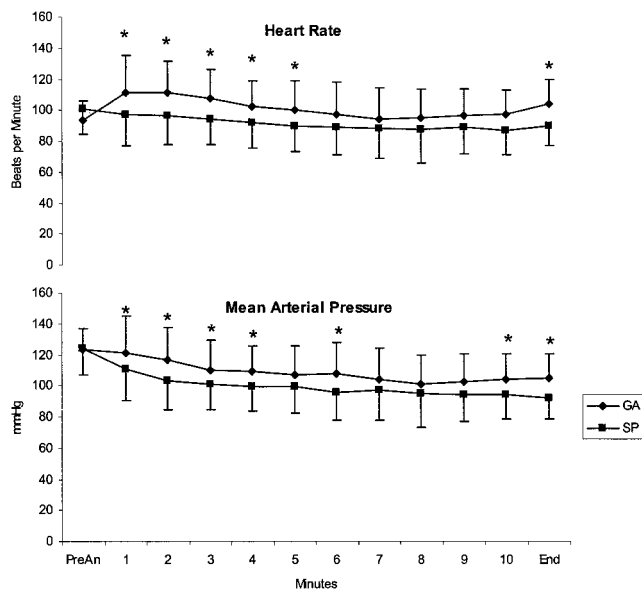
lower in the spinal anesthesia group. There was no significant correlation between the number of minutes spent at more than 25% below the baseline mean arterial blood pressure and the neonatal base deficit in either group ( $r = 0.23$  for the general anesthesia group and  $-0.14$  for the spinal anesthesia group). There was also no significant correlation between absolute changes in mean arterial pressure and neonatal base deficit in either group ( $r = 0.09$  for the general anesthesia group and  $-0.09$  for the spinal anesthesia group). There was no significant between-group difference in the duration of time spent at blood pressures less than 25% of baseline. Significantly more ephedrine was required in the spinal anesthesia group (13.7 vs. 2.7 mg; table 3), but there was no correlation between ephedrine use and neonatal base deficit in either group.

## Discussion

There have been no previous published prospective randomized trials comparing spinal and general anesthe-



**Fig. 4.** Correlation between maternal and neonatal base deficit (BD) in the general anesthesia group, showing regression line and 95% confidence intervals of the mean. Maternal BD:neonatal BD:  $r = 0.29$ ,  $P = 0.09$ . Neonatal BD =  $2.45 + 0.37 \times X$ .



**Fig. 5.** Changes in heart rate and mean arterial pressure in the general anesthesia (GA) and spinal anesthesia (SP) groups (mean  $\pm$  SD). \*Significant differences between groups;  $P < 0.05$ . Time points refer to minutes after induction of anesthesia. End = immediate postsurgical measurement; PreAn = preanesthetic measurement.

sia for cesarean delivery in severe preeclampsia in which the indication for operative intervention is a nonreassuring fetal heart trace. The current study addressed the issue of neonatal outcome while also comparing hemodynamic data in the two groups. The primary outcome measure was mean neonatal umbilical arterial base deficit because variations in maternal ventilation will alter umbilical arterial pH, and therefore, umbilical arterial base deficit is a more specific index of the metabolic component of acid-base balance.<sup>12</sup> Spinal anesthesia was associated with a significantly greater mean umbilical arterial base deficit and a lower median umbilical arterial pH than general anesthesia. One-minute Apgar scores were lower after general anesthesia. Pulse rate and blood pressure measurements were acceptable in these two groups presenting for emergency cesarean delivery.

It is likely that there are many influences on neonatal outcome after cesarean delivery in preeclampsia. These include severity of the maternal and fetal condition, anesthesia, and surgical management. Fetal development is related to gestational age and to chronic uteroplacental insufficiency, which results in intrauterine growth restriction. In addition, any acute maternal deterioration may impact unfavorably on fetal outcome. The equivalence between the two study groups in terms of maternal and neonatal demographic and clinical data, in particular the severity of maternal disease, the presence or absence of active labor, and the gestational age, allowed the influence of anesthesia to be assessed independently.

To identify perinatal morbidity, the positive predictive

value of an antepartum fetal heart rate nonstress test in high-risk pregnancy is approximately 55%,<sup>13</sup> while the positive predictive value of late decelerations during labor for fetal acidemia is 30–40%.<sup>14</sup> In the current study, the neonates clearly represent a high-risk group because in addition to the abnormal fetal heart trace, a large proportion of the mothers had severe preeclampsia, and most had a compensated metabolic acidosis, probably indicating poor tissue perfusion; furthermore, a large proportion of the neonates were preterm. Fetal scalp blood sampling could not be performed because of the possibility of an increased risk of vertical transmission of HIV.

In our study, considering the data pertaining to anesthesia, the time from induction of anesthesia to skin incision was statistically but probably not clinically significantly shorter in the general anesthesia group. Thus, potentially harmful delays attributable to spinal anesthesia<sup>15</sup> did not apply in this study. The significantly lower Apgar scores at 1 min in the general anesthesia group are in keeping with previous studies<sup>7,10,16</sup> and probably represent transient sedation of the neonate from the anesthetic agents.

In elective, uncomplicated term pregnancies, one major recent retrospective study has indicated a significantly increased degree of neonatal acidosis (umbilical arterial pH) in parturients receiving either spinal or epidural anesthesia when compared with general anesthesia.<sup>16</sup> The acidosis was attributed in part to an increased umbilical arterial  $P_{aCO_2}$  due to maternal hypoventilation during regional anesthesia. There was also a higher incidence of maternal hypotension in patients receiving regional anesthesia in this study. The significantly lower maternal  $P_{aCO_2}$  in the spinal anesthesia group in the current study probably reflects respiratory compensation in a patient with a metabolic acidosis. The resultant mild hypocapnia may have adversely influenced uterine perfusion, although a previous study suggests that more severe hypocarbia than that seen in our study may be required to decrease uterine perfusion significantly.<sup>17</sup> We are unaware of any study that has looked at the influence of maternal ventilation on uteroplacental perfusion in patients with preeclampsia.

One recent major retrospective study in 5,806 patients undergoing elective uncomplicated cesarean delivery demonstrated umbilical arterial pH less than 7.10 in 4.7, 2.3, and 1.1% of patients receiving spinal, epidural, and general anesthesia, respectively.<sup>7</sup> Once again, the increased incidence of acidosis was attributed to hypotension and the need for vasopressors. However, such retrospective analyses have the obvious limitation of selection bias.

In the current prospective, randomized study, the significantly greater mean neonatal umbilical arterial base deficit and lower median umbilical arterial pH in the spinal anesthesia group require explanation. Signifi-

**Table 6. Influence of Maternal Disease Severity on Neonatal Base Deficit**

	General	Spinal	P Value
Between-group analysis			
DBP < 110 mmHg, No.	15	15	
NN base deficit	4.4 ± 3.1	5.2 ± 3.1	0.49
DBP > 110 mmHg, No.	20	20	
NN base deficit	5.0 ± 3.7	8.7 ± 4.0	0.007
Within-group analysis			
DBP < 110 mmHg, No.	15	15	
NN base deficit	4.4 ± 3.1	5.2 ± 3.1	
DBP > 110 mmHg, No.	20	20	
NN base deficit	5.0 ± 3.4	8.7 ± 4.0	
P Value	0.6	0.009	

Data are presented as mean ± SD.

DBP = diastolic blood pressure; NN = neonatal.

cantly less ephedrine was used in the general anesthesia group. Some recent investigations of ephedrine as the vasopressor in spinal anesthesia for cesarean delivery in healthy parturients have suggested that ephedrine may be associated with more neonatal acidosis than phenylephrine.<sup>18</sup> An increased umbilical arteriovenous carbon dioxide difference has recently been demonstrated in a comparison between ephedrine and phenylephrine, implying an increased fetal metabolic rate secondary to ephedrine-induced  $\beta$ -adrenergic stimulation.<sup>19</sup> In the current study, there was no correlation between ephedrine use and neonatal base deficit in the spinal anesthesia group overall, in particular in the case of neonates with severe acidosis (base deficit > 10 mEq/l). Thus, the significantly higher base deficit in the spinal anesthesia group did not appear to be attributable to a few patients with severe hypotension.

After the difference in base deficit was discovered, *post hoc* analysis was performed to examine the influence of disease severity (maternal diastolic blood pressure > 110 mmHg; table 6). This showed that, in the absence of a diastolic blood pressure greater than 110 mmHg, there was no difference in mean neonatal base deficit between groups. However, in those mothers with a diastolic blood pressure greater than 110 mmHg, the spinal anesthesia group had a significantly greater neonatal base deficit than the general anesthesia group. Furthermore, when this criterion was applied within groups, there was no difference in neonatal base deficit in the general anesthesia group, but in the spinal anesthesia group, those neonates whose mothers had a diastolic blood pressure greater than 110 mmHg had significantly higher base deficit values than neonates whose mothers did not show this degree of hypertension. These results should be interpreted with caution in view of the fact that the original hypothesis was not designed to test differences between groups based on maternal disease severity.

It should be noted that after uncomplicated vaginal delivery, umbilical arterial base deficit is between 4 and

10 mm.<sup>12,20</sup> Therefore, the range of base deficit found in this study is relatively reassuring. Although the degree of acidosis was worse in the spinal anesthesia group, the median value for 1-min Apgar scores was lower in the general anesthesia group. A recent study suggesting that Apgar scores are a better predictor of neonatal outcome than fetal pH suggests that the small differences in the base deficit are clinically unimportant given the similar 5-min Apgar scores in this study.<sup>21</sup>

Considering the categorical neonatal data, statistical significance was only achieved when comparing the incidence of base deficit in the range of 5–7.9 mEq/l, where the incidence was higher in the spinal anesthesia group. Accepted criteria used to identify newborn infants at risk of fetal hypoxia are Apgar scores less than 7 at 1 and 5 min, neonatal umbilical arterial pH less than 7.20, and umbilical arterial base deficit greater than 10 mm.<sup>22</sup> The increased numbers in the spinal group in the categories of pH less than 7.20 and base deficit greater than 10 mEq/l suggest that in a much larger study powered to detect differences in these distributive data, there might have been a low but significantly increased incidence of clinically important acidosis in the spinal group. There was a trend toward an increased requirement for resuscitative measures in the general anesthesia group (table 5). Retrospective analysis suggests that the data had 90% power to detect differences in this variable.

There were two neonatal deaths in this study. The one neonatal death in the general anesthesia group was due to undiagnosed abruptio placentae, which resulted in a stillbirth, and could not be attributed to the anesthetic technique. The single case of sudden infant death syndrome at 5 days of age in the spinal anesthesia group was also unlikely to be attributable to the method of anesthesia.

One early study performed in the absence of acute fetal compromise demonstrated that the differences between base deficit values between women with preeclampsia and their fetuses was greater than in healthy parturients (simultaneous blood microsamples were taken from the maternal ear and uterine cervix and the fetus).<sup>23</sup> In the current study, the correlation ( $r = 0.36$ ) between maternal base deficit and neonatal base deficit, which was stronger in the spinal anesthesia group ( $r = 0.47$ ) than in the general anesthesia group ( $r = 0.29$ ), suggests some association between preeclampsia and poor placental perfusion, although the relation is weak. Measuring the maternal base deficit may therefore help identify infants at greatest risk.

One early study comparing general and epidural anesthesia for cesarean delivery in preeclampsia showed considerable hemodynamic instability in the general anesthesia group, including marked systemic and pulmonary hypertension on intubation. However, the sample sizes were small (a total of 17 patients were studied), and no



pharmacologic measures were used to obtund the intubation response.<sup>24</sup> In the current study involving emergency cesarean delivery, a previously validated method of controlling intubation response was used,<sup>25</sup> and hemodynamic responses were acceptable. Similar hemodynamic responses were achieved in the spinal anesthesia group, although the blood pressures were significantly lower in this group at several time points. However, it should be recognized that cardiac output may correlate better than upper limb blood pressure with fetal acidosis.<sup>26</sup> The mean ephedrine dose was only 13.7 mg in the spinal anesthesia group, including one patient requiring 100 mg. Blood loss was slightly greater in the general anesthesia group, but the difference was not clinically important, particularly given the relatively crude methods of estimation. In a previous study involving a group of 12 preeclamptic patients undergoing spinal anesthesia for elective cesarean delivery in whom the placental uterine artery circulation was studied using a pulsed color Doppler technique, a marked increase in uterine artery pulsatility index as a sign of increased vascular resistance was seen in only one patient during a period of severe maternal hypotension.<sup>27</sup> In the current study, blood pressure changes of the magnitude measured in the spinal anesthesia group might well have had no clinically detrimental effect on the fetus in normal parturients. However, in the setting of emergency cesarean delivery in severe preeclampsia with fetal compromise and in combination with the use of ephedrine and mild hypocapnia induced by maternal hyperventilation, even a modest lowering of the blood pressure could have contributed to decreased placental perfusion. This could explain the increased umbilical arterial base deficit demonstrated in the spinal group.

This study shows that spinal anesthesia for cesarean delivery in preeclamptic patients with a nonreassuring fetal heart trace may be associated with a higher mean neonatal umbilical arterial base deficit and a lower median umbilical arterial pH than general anesthesia. The clinical significance remains to be established.

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