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Mode of anaesthesia on fetal acid-base status at caesarean section

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Abstract

Objective: To study fetal acid-base status and its implications under different modes of anaesthesia for caesarean sections.

Methods: A prospective cohort study was conducted of 196 consecutive women with singleton non-anomalous fetuses who underwent either elective or emergency caesarean section after 36 completed weeks. Immediately after the baby was delivered, blood was drawn from the umbilical vein and one of the umbilical arteries and sent in ice for acid-base analysis. Maternal demographics, pre-existing medical conditions and antenatal complications were retrieved from antenatal records. Apgar scores and admissions to neonatal intensive care units (NICUs) were noted.

Results: Six women were excluded from analysis because the umbilical venous blood was either not collected or clotted. Another two were excluded because of placental abruption. The number of subjects that received spinal, epidural and general anaesthesia were 134, 36 and 18, respectively. Apgar scores were higher in spinal anaesthesia and epidural anaesthesia group ($P<0.01$). General anaesthesia was associated with a higher incidence of fetal acidaemia, both in the umbilical artery and vein. Spinal anaesthesia was associated with the highest pH in umbilical venous blood. Base excess in umbilical venous samples was highest in the spinal anaesthesia group ($P=0.006$), although pH values were similar for the three groups. There was no difference in admissions to NICU.

Conclusions: This study provided evidence of the advantages of spinal anaesthesia over epidural and general anaesthesia. Our findings are in contrast with recent evidence in the literature.

Keywords: Acid-base assessment; caesarean section; general anaesthesia; regional anaesthesia.

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Introduction

Regional anaesthesia for caesarean sections has gained increasing popularity in recent decades [16]. Regional anaesthesia (RA) allows the expectant mothers to remain conscious during the entire procedure so that they feel more involved in the delivery of their babies. This is believed to enhance the bonding between mother and baby that commences from the time of birth. Hence, it is widely accepted that RA for caesarean section is preferable to general anaesthesia (GA). In particular, spinal anaesthesia (SA) is considered the better form of RA as it is safer and more practical for the mother than epidural anaesthesia (EA). As SA can be easily administered, it is therefore used widely for both elective and emergency caesarean sections [13]. However, the advantages of RA compared with GA for the baby are generally taken for granted as there is a paucity of published studies on this issue. For an otherwise uncomplicated pregnancy that requires a caesarean delivery, the merits of RA vs. GA for the neonate can best be assessed objectively by acid-base balance in the newborn. In this regard, however, SA has been associated with a higher incidence of fetal acidosis [9, 15]. The explanation for this remains obscure. Factors, such as magnitude and duration of maternal hypotension have been proposed [12]. As a result, various measures have been suggested and implemented to minimize fetal acidosis, including the appropriate use of vasopressor agents to minimize maternal hypotension, intravenous fluid loading, maternal positioning and shortening of the uterine incision-delivery interval. However, the impact of these measures on neonatal acid-base status and blood gases at caesarean birth remains to be established.

There are biochemical and clinical criteria established by the American College of Obstetricians and Gynecologists Committee Opinion to assess neonates who have experienced hypoxia close to delivery. These include umbilical artery acidaemia ($pH<7.0$), an Apgar score remaining between 0 and 3 for longer than 5 min, evidence of neurological sequelae and cardiovascular, gastrointestinal, haematologic, pulmonary and renal system dysfunction, alone or in combination [2]. However, for the great majority of normal neonates born at term by caesarean delivery, none of these criteria, except for

umbilical artery acidaemia, would be applicable. In view of the rising rates of caesarean delivery [7, 10], it is important to clarify the impact of the aforementioned measures to prevent maternal hypotension on the neonatal condition at caesarean delivery under RA. A randomized controlled trial is desirable, yet it is not feasible under most circumstances. We have therefore performed a prospective study to examine Apgar scores and umbilical cord arterial and venous acid-base statuses following caesarean delivery using different modes of anaesthesia for evidence of pre-delivery hypoxia in the neonates. We hoped that the study would provide some information on whether the mode of anaesthesia could have affected cord blood acid-base status. Additionally, this study was necessary to generate data on which any potential randomized trial could be based to calculate the sample size.

Materials and methods

In a prospective cohort study conducted over a 4-month period, consecutive women with non-anomalous fetuses were recruited following informed consent at the time of admission to hospital for delivery if they satisfied the inclusion and exclusion criteria, regardless of whether they were scheduled for a caesarean section. Recruitment at this relatively early stage allowed consent to be obtained in good time from those women who eventually proceeded to emergency caesarean section. The inclusion criteria were Chinese women who understood the information sheet and could sign the consent, who were carrying a singleton pregnancy without fetal anomalies and who did not require emergency delivery for fetal or maternal conditions, such as fetal distress, fetal growth restriction or placental abruption. Exclusion criteria were women who did not understand Chinese or who had fetal or maternal conditions that would impact on the fetal acid-base status. The women who eventually underwent caesarean section after 36 completed weeks constituted the study cohort. The protocol was approved beforehand by the hospital Ethics Committee.

In the absence of clear-cut medical indications or contra-indications, the choice and administration of anaesthesia was decided by the attending anaesthetist and based entirely on their assessment and discussion with the women. Recruitment into this study did not influence the choice of the mode of anaesthesia. For GA, the women were put in a left lateral tilt of 15–30° and pre-oxygenated with 100% oxygen until end-tidal oxygen reached >70%. Rapid sequence induction was then performed using thiopentone at 4–5 mg/kg and suxamethonium at 2 mg/kg. After successful intubation, atracurium at 0.5 mg/kg was administered as a muscle relaxant and anaesthesia was maintained with isoflurane, oxygen and nitrous oxide. For women being administered SA, a standard protocol with intravenous fluid loading using 500 mL Hartmann solution was adopted. Spinal anaesthesia was performed in a left lateral position with the spinal needle inserted at the L3/4 level, and 2 mL 0.5% heavy bupivacaine, 15 μg fentanyl and 0.2 mg morphine then injected into the subarachnoid space. For EA, the women were put in a left lateral tilt, and 0.75% ropivacaine and 50–100 μg fentanyl were injected into the epidural space in divided doses until loss of cold sensation was achieved bilaterally up to T4 dermatome. Continuous fetal heart monitoring was performed during the procedure of EA. Maternal blood pressure was kept within 20% of usual pressure using intravenous phenylephrine, but ephedrine was administered instead if maternal bradycardia (<60 bpm) was noted. Fetal heart rate was checked before anaesthesia and after anaesthesia was achieved. Immediately after delivery of the baby, the placental side of the divided umbilical cord was doubly clamped, and then blood was drawn from the umbilical vein and one of the umbilical arteries using pre-heparinized syringes. The syringes were then labeled and sent in an ice-filled kidney dish for acid-base analysis using the Bayer RapidLab 855 and 865 systems (Siemens). The results were printed and collected for analysis.

Maternal demographics, pre-existing maternal conditions and antenatal complications were retrieved from antenatal records. Apgar scores at birth and any admissions to neonatal intensive care units were recorded.

Statistical methods

The subjects were analyzed in three groups according to the mode of anaesthesia, namely SA, EA and GA, using an χ^2-test for categoric and one-way ANOVA methods for continuous variables. The three groups were compared for maternal demographics, obstetric complications, mean gestational age, mean birth weight, admission to neonatal intensive care unit, Apgar score and fetal acid-base analysis. One-way ANOVA was used to compare the three groups with post-hoc analysis using the Dunnett test (two-sided). Further analysis of differences between the EA and SA groups was performed by independent samples *t*-test. The calculations were performed using SPSS, version 14.0, a commercially available statistical package.

Table 1 Maternal and newborn characteristics among the three groups.

	EA	SA	GA	P-value
Maternal age (years)	31.1±4.2	32.6±5.3	32.8±4.3	NS
Gravidity	1.8±1.2	2.3±1.2	3.0±1.5	0.029
Gravidity>1 (%)	47.2	73.1	88.9	NS
Parity	0.3±0.7	0.7±0.8	0.9±0.9	0.001
Parity>0 (%)	19.4	55.2	72.2	NS
Height (cm)	157.7±5.0	155.9±7.8	157.3±5.4	NS
Weight at booking (kg)	57.8±11.3	56.9±9.5	57.7±8.3	NS
Delivery gestational (weeks)	39.6±1.5 (39.1–40.1)	38.7±1.4 (38.4–38.9)	38.2±1.5 (37.5–39.0)	<0.001
Birth weight (g)	3281±545 (3097–3465)	3211±515 (3124–3300)	3114±339 (2946–3283)	NS
Apgar score 1st min	**8.94 (8.66–9.22)	**9.05 (8.93–9.17)	8.11 (7.48–8.75)	<0.001
Apgar score 5th min	**9.94 (9.87–10.00)	**9.96 (9.92–9.99)	9.72 (9.44–10.00)	0.003

EA=epidural anaesthesia, SA=spinal anaesthesia, GA=general anaesthesia. Results expressed in mean±SD, mean±SD (95% CI of mean) for gestational age and birth weight, and mean (95% CI of mean) for Apgar scores, or in % where indicated.
Dunnett test (two-sided): **P<0.01 compared with GA.

Table 2 Obstetric complications, in numbers and percentage of total.

	EA	SA	GA	Total
Hypertension	6 (3.2%)	8 (4.3%)	1 (0.5%)	15 (8.0%)
Gestational diabetes	3 (1.6%)	16 (8.5%)	3 (1.6%)	22 (11.7%)
Anaemia	2 (1.1%)	15 (8.0%)	1 (0.5%)	18 (9.6%)
Prelabour rupture of membranes	4 (2.2%)	8 (4.3%)	2 (1.1%)	14 (7.4%)
Genital colonisation	5 (2.7%)	11 (5.9%)	1 (0.5%)	17 (9.0%)
Antepartum haemorrhage	3 (1.6%)	15 (8.0%)	5 (2.7%)	23 (12.3%)
Placenta praevia	0	10	5	15
Unknown origin	3	5	0	8

EA=epidural anaesthesia, SA=spinal anaesthesia, GA=general anaesthesia.

Results

A total of 196 recruited women were included in the study, but six were excluded from the analysis because umbilical venous blood samples were either not collected or clotted, and another two were excluded due to antepartum haemorrhage associated with placental abruption. The final number of women in the analysis was 188, with 134 (71%), 36 (19%) and 18 (10%) receiving SA, EA and GA, respectively. There was no significance difference in age, maternal height or weight at booking (Table 1). Whereas there were differences in the mean gravidity and parity (P<0.01) among the three groups, there was no significant difference in incidence of gravidity >1 (P=0.478) or parity >0 (P=0.067). There was also no significant difference in the mean birth weight, although there was a significant difference in the mean gestational age (P<0.001). Apgar scores at the first (P<0.001) and fifth min (P=0.003) were slightly but significantly higher in the groups receiving EA and SA, compared with the group receiving GA. However, the number of neonates with Apgar scores <7 at the first minute was 1, 1 and 2 for EA, SA and GA, respectively, whereas none had a fifth minute Apgar score <7. There was no significant difference in admissions to NICU (P=0.65) among the three groups, the incidences being 25%, 19.4% and 11.1%, respectively.

There was no difference in obstetrics complications, including hypertension, gestational diabetes mellitus, anaemia, prelabour rupture of membranes and positive genital tract colonisation, but a difference was noted in placenta praevia without antepartum haemorrhage and antepartum haemorrhage at the time of delivery (P<0.001) (Table 2).

For the umbilical arterial samples (Table 3), there was no difference in the pH but significant differences were found for all blood gas parameters, with PCO_2 and HCO_3 being significantly lower in both EA and SA groups, whereas PO_2 and base excess were significantly lower with EA compared with GA. When EA was compared with SA, the umbilical arterial base deficit was noted to be greater in the EA group but did not reach statistical significance (P=0.062).

For umbilical venous samples, all were significantly different (Table 3). The pH was higher with lower PO_2 and PCO_2 in both EA and SA groups, and HCO_3 was lower in the EA group. No difference was observed for base excess. Further analysis comparing EA and SA, using an independent samples *t*-test, showed that base deficit was found to be significantly greater in the EA group (P=0.009).

Table 3 Umbilical cord blood acid-base analysis in mean (95% CI of mean).

	EA	SA	GA	P-value
Umbilical arterial blood				
pH	7.29 (7.28–7.31)	7.29 (7.28–7.30)	7.27 (7.25–7.29)	0.215
PO_2	2.49 (2.18–2.81)*	2.64 (2.49–2.79)	3.12 (2.66–3.57)	0.049
pCO_2	6.82 (6.35–7.20)*	7.16 (6.96–7.35) *	7.96 (7.46–8.46)	0.003
HCO_3	**24.31 (23.55–25.06)*	25.49 (25.13–25.84)*	26.91 (25.97–27.86)	<0.001
Base excess	–2.82 (–3.48 to –2.17)*	–1.87 (–2.27 to –1.48)	–1.35 (–2.44 to –0.26)	0.035
Umbilical venous blood				
pH	7.32 (7.31–7.34)*	7.33 (7.32–7.34)*	7.29 (7.27–7.31)	0.002
PO_2	3.27 (2.95–3.59)*	3.68 (3.44–3.91)*	4.59 (3.86–5.33)	0.003
pCO_2	5.92 (5.59–6.26)*	6.14 (5.99–6.29)*	7.03 (6.59–7.46)	<0.001
HCO_3	**22.59 (21.84–23.34)*	23.80 (23.48–24.11)	24.78 (23.98–25.59)	<0.001
Base excess	**–3.36 (–4.01 to –2.70)	–2.33 (–2.67 to –1.99)	–2.67 (–3.43 to –1.90)	0.018

Dunnett *t*-test (two-sided): *P<0.05 compared with GA, **P<0.05 compared with SA.
EA=epidural anaesthesia, SA=spinal anaesthesia, GA=general anaesthesia.

Discussion

Minimizing fetal hypoxia and acidosis before birth to reduce the likelihood of fetal hypoxic injury is the aim for every delivery, especially in fetuses with limited reserves, such as in pregnancies complicated by placental insufficiency, fetal growth restriction and chorioamnionitis. However, accurate and objective assessment of the status of newborn infants is clinically difficult, as Apgar scores are subjective and correlate poorly with the actual acid-base status. Direct measurement of the umbilical cord blood acid-base parameters provides a superior and more objective assessment. Umbilical venous blood represents placental function, whereas umbilical arterial blood best represents the fetal condition. Among the acid-base parameters, base excess is the best indicator of pre-existing acidosis and predictor of neonatal outcome. Firstly, it is independent of respiration and, thus, a better index of the metabolic component and key to evaluating the recent prenatal environment. Furthermore, a base deficit of 12 mmol/L is associated with moderate to severe newborn encephalopathies.

In this study, maternal demographics were comparable, and only small differences in mean gravidity and parity were noted. This could be related to the fact there were more mothers undergoing labour for the first time who were more likely to require EA for pain relief, resulting in more patients with lower gravidity or parity continuing with EA when caesarean delivery was eventually required. The groups were also comparable in terms of major obstetric complications apart from antepartum haemorrhage, probably because EA was not adopted for use in patients with placenta praevia and placental abruption. As for infant outcomes, despite a slight difference in the mean gestational age, there was no difference in birth weight. There was no difference in the incidence of a low Apgar score, which was uniformly good for all groups, although with regards to the mean Apgar score, EA and SA were slightly but significantly superior. This finding agrees with the opinion of the Cochrane review [1].

In our study, it was observed that general anaesthesia was associated with a higher incidence of lower pH in both the umbilical artery and umbilical vein. Base excess in the umbilical artery was lowest in fetuses born under general anaesthesia. Nevertheless, PO_2 was highest when compared with spinal or epidural anaesthesia. This could be related to pre-oxygenation that the mothers received before they were anaesthetized. Umbilical venous PCO_2 was noted to be higher in the GA group.

Cord blood analysis indicated a different picture. Despite the apparent similarity in infant conditions at birth, both EA and SA were associated with significantly lower umbilical arterial PO_2, PCO_2, and HCO_3, which reflected fetal condition. This suggests that the conscious mothers were probably hyperventilating involuntarily during the operation because of anxiety, thus blowing off CO_2, which in turn reduced the HCO_3 in the fetus and manifested in cord arterial blood. As for PO_2, the higher value with GA was most likely the result of maternal pre-oxygenation. This could also have contributed to the higher PCO_2 associated with GA, as it has been postulated that maternal hyperoxia could cause hypoventilation and consequent CO_2 retention in the mother and placental vasoconstriction [5]. Furthermore, it has been shown that there is greater free radical activity in neonates born to mothers breathing oxygen enriched air [6], and this may have an important bearing on the outcome of compromised term and preterm babies. Of note, base deficit was significantly greater in the EA group, although the result was normal. It is likely that, despite the precaution measures, some degree of maternal hypotension and/or hypoperfusion of the uterus occurred with EA, which then increased slightly the base deficit of the fetus. On the other hand, higher pH was found in the umbilical venous samples for the EA and SA groups, which suggests that there was better placental perfusion and exchange resulting in more normal pH values. Similar to the arterial values, the patterns of PO_2, PCO_2, HCO_3 and base deficit values in the venous samples were also significantly lower for EA and SA groups, and the underlying explanation is likely to be similar. Taken together, the results suggest that GA is associated with better fetal oxygenation but higher pH and HCO_3, EA is associated with lower CO_2 and HCO_3 but a higher base deficit and SA is in the middle with the best venous base deficit values. Thus, SA appears to provide the most optimal *in utero* environment for the fetus prior to caesarean delivery.

In clinical application, SA also appears to be superior, as the time for onset of anaesthetic effect is shorter with a weighted mean difference of 7.91 min less [11], and there was no difference in failure rate, conversion to GA, maternal satisfaction, need for additional intra-operative analgesia, need for post-operative pain relief and need for neonatal intervention compared with EA, although there was increased need for treatment for hypotension. Overall, comparing RA with GA [1], there was no difference in terms of Apgar scores of ≤ 6 at the first minute and ≤ 4 at the fifth minute. Indeed, GA was shown to depress Apgar scores, although it is reversible and rarely significant at the fifth minute [3, 4]. A recent study also reported that GA was associated with a higher incidence of fetal acidaemia and a lower Apgar score at 1 min when compared with fetuses born under neuraxial anaesthesia [17]; however, umbilical arterial PO_2 and oxygen saturation was higher.

Our findings are in contrast with those of a meta-analysis which showed that SA for caesarean sections was associated with lower cord blood pH and greater base deficit than either GA or EA, but this was dependent on the ephedrine dose [14]. In a more recent study [17], EA was associated with the lowest incidence of fetal acidaemia, whereas SA was associated with the highest incidence of maternal hypotension and the use of ephedrine when compared with GA, as well as the highest incidence of acidotic but vigorous newborns. As a decrease in maternal systolic pressure was a significant factor in umbilical arterial pH, but not in base deficit [12], it is clear that the skill of the anaesthetist in maintaining maternal blood pressure and preventing hypotension would ensure optimal fetal outcome, and as changes in blood pressure tend to be short-lived, SA should not be considered less preferable on account of the possibility of transient maternal hypotension. As well, ephedrine has been shown to be associated with more severe umbilical arterial acidosis than is phenylephrine

[8]. Therefore, substituting phenylephrine for ephedrine as the first-line medication for maintaining maternal blood pressure was the protocol used in our study unless there was maternal bradycardia.

As discussed, we tried to exclude fetal or maternal conditions in the study that would have an impact on fetal acid-base status. The main limitation of this study is that the number of women who underwent elective caesarean delivery during the study period was not large enough to allow further subgroup analysis to exclude possible confounding effects in emergency delivery. Further studies involving larger study populations with a focus on elective caesarean delivery may reveal a clearer picture.

In conclusion, in contrast with recent findings in the literature, our results indicated that SA appeared superior to both GA and EA for caesarean delivery with respect to fetal acid-base balance. This factor should be an important consideration in the delivery of compromised fetuses, such as those with fetal growth restriction, placental insufficiency and chorioamnionitis. Additionally, the other advantages associated with SA, such as being easier to perform than EA and avoiding airway management and complications, are especially valuable in cases of emergency caesarean delivery, whereas post-operative analgesia can also be delivered by SA.

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