Maternal and umbilical cord oxygen content and acid-base balance in relation to general, epidural or subarachnoid anesthesia for term elective cesarean section

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Summary

Purpose: To compare maternal and neonatal oxygenation and acid-base status after elective cesarean section (CS) under different anesthetic techniques. *Materials and Methods:* Three hundred and eighty parturients undergoing elective cesarean section were randomly assigned to receive general (GA, n =140), epidural (EA, n = 117) or subarachnoid anesthesia (SA, n =123). Blood gases, oxygen content, and acid-base status parameters were measured in maternal artery and umbilical cord vessels. Neonatal Apgar scores were also recorded. *Results:* Umbilical artery pH, HCO_3^-, and actual base excess (ABE) were significantly higher in the GA compared to SA group ($p < 0.001$, $p < 0.05$, and $p < 0.05$, respectively). Umbilical vein ABE was lower in the SA compared to GA and EA groups ($p < 0.05$). Oxygen content in maternal artery was higher in the GA and EA groups compared to the SA group ($p < 0.05$). Neonatal oxygen content in both cord vessels was higher in the GA group compared to EA and SA groups ($p < 0.05$). Umbilical venous-arterial difference of PO_2, oxygen content, and Apgar scores did not differ significantly among groups. *Conclusion:* Neonatal oxygenation and acid-base status values were better preserved when GA was administered for elective CS compared to regional modalities. Apgar scores and neonatal outcomes were not affected by the anesthetic technique.

Key words: Anesthesia; Cesarean section; Fetal oxygenation; Fetal acid-base status.

Introduction

Regional anesthesia is considered the technique of choice for cesarean deliveries in normal and complicated pregnancies and has replaced general anesthesia (GA) in the majority of cases [1]. Nevertheless, regional anesthesia cannot always be provided, even in elective cesarean deliveries, as in cases of maternal refusal, inability to cooperate, coagulation disorders, infection at site of injection, and true allergy to local anesthetics.

General and regional anesthetic techniques have potential advantages and disadvantages. Advantages of GA include rapid induction of anesthesia, decreased incidence of hypotension, and superior ventilation control. Epidural (EA) and subarachnoid anesthesia (SA) minimize the risk of maternal aspiration and maternal death due to a difficult airway, while avoiding neonatal depression. On the other hand, regional techniques may cause maternal hypotension, due to an extended sympathetic blockade [2].

The impact of the anesthetic technique on neonatal outcome is essential. Umbilical cord acid-base status is a reliable indicator of fetal oxygenation and well being at birth; moreover it has been associated with long-term outcome as well [3]. For most clinicians it is the gold standard for the assessment of uteroplacental function and it may exclude the diagnosis of birth asphyxia in approximately 80% of depressed newborns at term [4]. The findings regarding the impact of anesthetic technique on umbilical cord blood gas values are contradictory [5-8]. Moreover, only few studies associate maternal oxygenation and blood gas values to the cord acid-base status and neonatal outcome parameters [9, 10].

The present study was designed to investigate the influence of GA, EA, and SA on neonatal blood gas values and acid-base status. The authors' hypothesis was that the anesthetic technique for elective cesarean section (CS) has no effect on fetal oxygenation and acid-base status.

Materials and Methods

After obtaining approval from the Institutional Review Board, 380 parturients scheduled for elective CS gave written informed consent to participate in the study. Women received randomly GA, EA, or SA by the use of sealed envelopes describing group allocation. All cesarean deliveries were performed in the morning. In all cases, anesthesia was provided by an experienced consultant anesthesiologist.

One hundred and forty parturients (37%) received GA, 117 (31%) received EA, and 123 (32%) received SA. Exclusion criteria were gestational age < 38 weeks, cardiotocographic abnormalities, obstetric or medical complications, oxytocin for labor stimulation, neonatal congenital malformations, predicted or known difficult airway, and parturient's request for a specific type of anesthesia.

All women received ten mg of metoclopramide and 50 mg of ranitidine intravenously 15 minutes before anesthesia. Standard monitoring was applied (electrocardiogram, non-invasive blood pressure measurement, pulse oximetry), and a capnograph was additionally used in the GA group. Parturients were breathing 50% oxygen via a Venturi facemask at 15 l/min, according to manufacturer.

In the GA group, after rapid sequence induction, anesthesia was maintained with one percent sevoflurane and 50% N_2O/oxygen mixture. Neuromuscular blockade was achieved

Revised manuscript accepted for publication July 30, 2012

with vecuronium 0.1 mg kg^{-1}, while opioids were avoided before delivery. Mechanical ventilation was adjusted to maintain an end-tidal CO_2 (ET-CO_2) 30-35 mmHg.

In regional anesthesia groups, hydroxyethyl starch (6%) 500 ml was administered preoperatively. Epidural anesthesia was performed with a 18G Tuohy needle at L_2-L_3 or L_3-L_4 intravertebral space and an epidural catheter was inserted. A test dose of 2.5 ml lidocaine two percent was followed by ropivacaine 0.75% in incremental doses of six ml, along with fentanyl one μg kg^{-1} targeting to a sensory block up to T_4 dermatome.

Subarachnoid anesthesia was performed with a 27G pencil – point needle at L_2- L_3 or L_3-L_4 intravertebral space and 1.6 - 2.0 ml of 0.5% isobaric levobupivacaine was administered, based on mother's body weight and height. Additionally, one μg kg^{-1} of fentanyl in a volume of 10 ml normal saline was administered epidurally. Ephedrine 2.5 mg was given immediately after intrathecal levobupivacaine to prevent hypotension.

In all women, arterial blood pressure was measured every minute until delivery and ephedrine was given in 2.5 mg increments if hypotension occurred. The total amount of ephedrine administered to each parturient was recorded. Hypotension was defined as systolic blood pressure below 100 mmHg or a decrease of more than 30 mmHg from the baseline value (measurement before any intervention). Skin incision-to-delivery and uterus incision-to-delivery time intervals were also recorded.

All parturients were placed in the supine position with a right hip wedge during operation. At delivery, maternal arterial blood sample from radial artery, as well as umbilical arterial and venous blood samples were withdrawn from a doubly-clamped cord segment. Blood gases, pH, HCO_3^- and actual base excess (ABE) were determined in an ABL-300 gas analyzer. Oxygen content (CTO_2) was also calculated for all blood samples according to the formula: $CTO_2 = (0.03 \times PO_2) + (1.31 \times Hb \times SO_2\ \%)$. Apgar scores were recorded five minutes after delivery by a neonatologist. Oxygen administration to the neonate, tracheal intubation, transfer to intensive care unit, and neonatal deaths were recorded as parameters of the neonatal outcome.

Statistical analysis was performed with SPSS (Statistical Program for Social Science). Analysis of variance or the non-parametric Kruskal Wallis test were used where appropriate. Before each analysis assumptions, such as normality and homogeneity of variance were checked. Multiple comparisons tests were performed between means using a Bonferroni test when appropriate. The 95% confidence interval was at a significance level of 0.05; p values were two-tailed and a $p < 0.05$ was considered significant.

Results

Data from 380 parturients were analyzed. The initial number of women assessed for eligibility to participate in the study was 438. Thirty-three parturients requested a specific type of anesthesia, while 11 of the EA group and 14 of the SA group were excluded due to inadequate anesthetic block.

Maternal characteristics, delivery times, and ephedrine doses are shown in Table 1. Maternal and umbilical cord blood gases are presented in Table 2. Maternal pH was significantly lower in the GA group ($p < 0.001$), while maternal ABE did not differ among three groups. Maternal PaO_2 and $PaCO_2$ were significantly higher in the GA vs EA and SA groups. Maternal CTO_2 was significantly higher in GA and EA compared to SA group.

Table 1. — *Maternal and cesarean section (CS) characteristics in the general anesthesia (GA), epidural anesthesia (EA), and subarachnoid anesthesia (SA) group.*

	GA (n = 140)	EA (n = 117)	SA (n = 123)
Parity			
1	76	70	66
2	54	43	51
3	10	4	6
Maternal weight (kg ± SD)	65 ± 14	71 ± 12	71.5 ± 13
Cause of CS			
Previous CS	81	70	72
Other (IVF, fetal position)	59	47	51
Gestational age (weeks ± SD)	39 ± 1	38.9 ± 0.7	38.6 ± 0.4
Skin incision to delivery time (min), (mean, range)	7 (5-8)	8 (5-9)	7 (6-9)
Uterus incision to delivery time (sec), (mean, range)	75 (52-184)	78 (50-177)	82 (58-163)
Total dose of ephedrine (mg ± SD)	0*,†	5.80 ± 6.26*,‡	9.10 ± 6.26*,†

*statistical significance ($p < 0.05$) for comparisons between GA and EA groups.
† statistical significance ($p < 0.05$) for comparisons between GA and SA groups.
‡ statistical significance ($p < 0.05$) for comparisons between EA and SA groups.

Table 2. — *Blood gas/acid base measurements in the general anesthesia (GA), epidural anesthesia (EA), and subarachnoid anesthesia (SA) group. Values are expressed as mean ± SD.*

	GA (n = 140)	EA (n = 117)	SA (n = 123)
MA-PO_2	224.56 ± 86.77*,†	151.28 ± 38*	157.36 ± 53.51†
MA-PCO_2	35.03 ± 3.88*,†	29.25 ± 5.05*	29.64 ± 4.16†
MA-pH	7.38 ± 0.03*,†	7.43 ± 0.02*	7.43 ± 0.05†
MA-ABE	-3.74 ± 1.42	-3.53 ± 2.52	-3.56 ± 1.83
MA-CTO_2	15.52 ± 0.18†	15.75 ± 0.30‡	14.92 ± 0.35†,‡
UA-PO_2	15.6 ± 5.48	9.29 ± 4.41	9.2 ± 4.06
UA-PCO_2	53.3 ± 5.02	53.2 ± 8.44	55.29 ± 8.33
UA-pH	7.29 ± 0.02†	7.27 ± 0.03	7.26 ± 0.06†
UA-HCO_3^-	25.50 ± 1.7†	24.75 ± 2.8	24.25 ± 1.8†
UA-ABE	-1.71 ± 1.3†	-2.5 ± 2.3	-3.45 ± 2.6†
UA-CTO_2	3.67 ± 0.57*,†	1.61 ± 0.39*	1.43 ± 0.29†
UV-PO_2	27.7 ± 7.66*,†	21.43 ± 6.55*	23.05 ± 6.72†
UV-PCO_2	46.2 ± 4.83	43.8 ± 7.54	43.9 ± 5.59
UV-pH	7.33 ± 0.02	7.35 ± 0.04	7.33 ± 0.04
UV-HCO_3^-	23.84 ± 1.5†	23.52 ± 2.3‡	23.14 ± 1.9†,‡
UV-ABE	-2.15 ± 1.0†	-2.06 ± 1.70‡	-3.35 ± 2.2†,‡
UV-CTO_2	9.68 ± 1.01*,†	6.97 ± 1.37*	7.51 ± 0.90†
$U_{V\text{-}A}$-PO_2	12.45 ± 6.23	11.57 ± 4.30	14.91 ± 5.98
$U_{V\text{-}A}$-PCO_2	-7.08 ± 3.27*,†	-9.20 ± 3.90*	-11.89 ± 4.7†
$U_{V\text{-}A}$-CTO_2	5.98 ± 0.82	5.36 ± 1.13	6.08 ± 0.77

* $p < 0.05$ for comparisons between GA and EA groups.
† $p < 0.05$ for comparisons between GA and SA groups.
‡ $p < 0.05$ for comparisons between EA and SA groups.
MA: maternal artery; UA: umbilical artery; UV: umbilical vein; $U_{V\text{-}A}$: umbilical venous-arterial difference; ABE: acutal base excess; CTO_2: oxygen content.
Units of measurements: ABE (mEq $litre^{-1}$); HCO_3^- (mEq $litre^{-1}$); PO_2 (mmHg); PCO_2 (mmHg); and CTO_2 (ml O_2/dl blood).

Umbilical artery pH, HCO_3^-, and ABE values differed significantly between the GA and SA groups ($p < 0.001$ for pH, $p < 0.05$ for HCO_3^-, and ABE). Umbilical artery PO_2 and CTO_2 were higher in the GA compared to both regional modalities ($p < 0.001$). Umbilical vein pH did not differ among groups, but umbilical vein PO_2 and CTO_2 were significantly higher in the GA group ($p < 0.05$). Umbilical vein HCO_3 and ABE were significantly lower in the SA group.

The umbilical venous-arterial difference of PO_2 and CTO_2 were similar in all groups, while the umbilical ve-

Table 3. — *Neonatal outcome parameters in the general anethesia (GA), epidural anesthesia (EA), and subarachnoid anesthesia (SA) group.*

	GA (n = 140)	EA (n = 117)	SA (n = 123)
Apgar score at 5th min < 7	12 (8.5%)	8 (6.8%)	10 (8.1%)
Oxygen administration to the neonate	17 (12.1%)	13 (11.1%)	15 (12.2%)
Mask ventilation of the neonate	0	0	0
Endotracheal intubation	10 (7.1%)	7 (6%)	9 (7.3%)
Transfer to a special unit for further treatment	0	0	0
Neonatal deaths	0	0	0

* Statistical significance ($p < 0.05$) for comparisons between GA and EA groups.
† Statistical significance ($p < 0.05$) for comparisons between GA and SA groups.
‡ Statistical significance ($p < 0.05$) for comparisons between EA and SA groups.
No statistical significance was found among the three groups.

nous-arterial difference of PCO_2 was higher in the GA group compared to the EA ($p < 0.05$) and SA group ($p < 0.001$).

Fetal acidemia (umbilical artery pH < 7.20) was found only in the groups of regional modalities; four cases (3.4%) were found in the EA and nine cases (7.5%) in SA group. However, none of these newborns presented Apgar score < seven at five minutes. Apgar scores and outcome variables did not differ among the groups (Table 3).

Discussion

The results in this study showed that GA for elective CS was associated with better maternal and fetal oxygenation and also a favorable umbilical cord acid-base status. Although short-term neonatal outcomes were not clinically affected, regional anesthesia, particularly SA, was associated with impaired acid-base status and oxygenation. Also, previous reports [5, 6, 10, 11] have implicated regional modalities in neonatal hypoxemia and acidemia, but with no correlation to maternal oxygenation and acid-base status.

The significance of fetal oxygenation at delivery has attracted the interest of many investigators [12-14]. Ramanathan *et al.* have shown that maternal hyperoxygenation (up to 100%) improved fetal oxygen stores during CS under EA [14]. Oxygen administration in laboring women during fetal distress has long been used to improve fetal oxygen saturation [12]. However, high maternal-inspired oxygen fraction (FiO_2: 0.5) in CS under regional anesthesia may increase free radical activity and lipid peroxidation in both mother and fetus [13]. On the contrary, administration of 100% oxygen to parturients undergoing elective CS under GA improves fetal oxygenation without increasing free radical activity and lipid peroxidation compared to lower FiO_2 (0.3 and 0.5) [15]. The clinical significance of all these findings remains, to date, unclear.

The authors calculated CTO_2 in maternal and umbilical cord blood samples for a most accurate evaluation of oxygenation. They maintained maternal FiO_2 stable (0.5) in the three groups and found a better maternal CTO_2 in the GA and EA groups compared to the SA group. Impaired pulmonary function tests with a restrictive ventilatory defect have been described in parturients undergoing CS under SA [16]. In the present study, maternal arterial pH was lower in the GA group than in the regional anesthesia groups, perhaps due to the higher maternal $PaCO_2$, as ABE was similar among groups. Dyer *et al.* have also reported higher maternal $PaCO_2$ in pre-eclamptic parturients receiving GA compared to those receiving SA [5]. The higher $PaCO_2$ values during GA are probably due to mechanical ventilation in this group and the lack of adaptation of their pregnancy-induced hyperventilation. The powerful adrenergic stimuli of intubation could be an additional or alternative reason. Apart from physiological, psychological, and emotional factors may also account for parturients' hyperventilation during CS, resulting in further $PaCO_2$ decrease in regional anesthesia groups.

In the GA group, CTO_2 in both umbilical vessels was significantly higher vs regional anesthesia groups. These results are similar to those reported in previous studies [10, 11]. A new finding of this present study is that the EA may aggravate fetal oxygen transfer, according to the lower CTO_2 in the umbilical vein, although maternal CTO_2 was similar in the GA and EA groups. This finding is supported by previous results suggesting that fetal intrapartum oxygen saturation was affected after initial or top-up epidural analgesia [17]. In this case, a high maternal FiO_2 may be quite significant in improving fetal oxygenation. The FiO_2 in the present study was 0.5 in all groups, but Ramanathan *et al.* found that PO_2 in the umbilical vein was improved when parturients under EA breathed high-oxygen concentrations up to 100% [14].

The umbilical venous-arterial PO_2 and CTO_2 difference was found similar among groups, indicating that metabolism, fetal oxygen consumption, and fetal cardiac output are not influenced by the anesthetic technique, or ephedrine administration, at least at the doses given in the present study (mean dose < 10 mg). Ephedrine produces α- and β-sympathomimetic effects and has been associated with fetal acidosis [18], especially when administered at high-bolus doses ≥ 10 mg [19]. Ephedrine has been associated with fetal acidosis by increasing fetal oxygen demand and CO_2 production due to β-adrenergic stimulation [20]. The present results do not indicate this mechanism, since oxygen consumption as assessed by CTO_2 and umbilical artery PCO_2 did not differ significantly among the groups. It should be noted though, that in the present study, the mean total dose of ephedrine administered in the SA group was quite small [19, 21].

Another finding of the present study was a higher difference of umbilical venous-arterial PCO_2 in the GA compared to the EA and SA groups. This difference was possibly due to an increased umbilical venous PCO_2 because of the higher maternal $PaCO_2$ found.

The HCO_3^- and ABE values in both umbilical vein and artery of the GA and EA groups did not differ, as in previous studies [7, 22]. However, there was a significant difference in HCO_3^- and ABE concentrations in the umbilical vein and artery between the GA and SA groups, indicating an ''acidotic'' tendency of metabolic nature in the latter. A higher incidence of fetal acidemia occurs in

cesarean deliveries under regional – especially subarachnoid – vs general anesthesia [6-8, 10, 19]. Maternal arterial hypotension is the most common cause of fetal acidemia, as uteroplacental circulation has not adequate autoregulatory mechanisms and uteroplacental blood flow is decreased [6, 10].

The duration and severity of maternal hypotension due to subarachnoid blockade is of particular importance. Fetal bradycardia may occur when hypotension persists for more than four minutes [23], while hypotension lasting even less than two minutes may cause fetal academia [24]. It has also been found that the maximum reduction of maternal systolic blood pressure significantly affects umbilical arterial pH [18], although Robson *et al.* did not show a direct correlation between the severity of hypotension and fetal acidemia after birth [23]. Maayan-Metzger *et al.* found retrospectively that term neonates tolerate quite well short periods of hypotension (three to five min) during CS under regional anesthesia, without perinatal complications [2]. It should be noted that maternal blood pressure cannot be used as a predictor of fetal outcome; hence, usually it is treated promptly and the vast majority of hypotensive episodes during CS are of short duration. However, reductions of maternal cardiac output representing a great risk for the fetus do not necessarily manifest as a maternal blood pressure decrease, because of the changes in peripheral vascular resistance. The maximum percentage change in maternal cardiac output and umbilical artery pulsatility index correlated with umbilical artery pH [25].

Subarachnoid anesthesia has been associated with a decrease in cardiac output even in the absence of hypotension [25], while the epidural administration of local anesthetics in divided doses reduces this risk [22]. Thus, it not surprising that a decrease of maternal cardiac output with an increase of umbilical artery pulsatility index, indicating a reduced uteroplacental blood flow, is found after SA but not after EA [25, 26]. Roberts *et al.* found severe fetal acidemia (pH ≤ 7.19) in 12% of patients after EA, 18% after combined spinal-epidural, and 24% after SA [10]. A lower incidence of fetal acidemia was found in the present study (3.3% after EA and 7.3% after SA), probably because of close monitoring and prompt treatment of hypotension.

In the present study the authors found no difference among the groups regarding uterus incision-to-delivery time intervals. Prolonged uterine incision-to-delivery interval has been found to significantly affect umbilical arterial pH and standard base excess, while induction-to-delivery and skin incision-to-delivery intervals were not significant predictors of neonatal acid-base status [18]. The authors also found no significant differences in immediate neonatal outcomes among the three anesthetic groups, as evaluated by five-min Apgar scores or the need for oxygen administration to the neonate or mask assisted ventilation. This finding is consistent with previous reports [27, 28]. However, there is significant controversy regarding this area. Several studies report a higher incidence of low one min Apgar scores in neonates exposed to GA, as compared with regional techniques [5, 7, 10]. Nevertheless, the adverse effects of general anesthesia on Apgar score, if present, are usually short-lived, and easily managed [19], while hypotension has also been associated with low Apgar scores at one min [29]. In either case, it should be noted that Apgar scores correlate poorly with neurologic outcome and as a subjective measure has limited diagnostic value in fetal asphyxia. Although fetal pH alone cannot serve as a prognostic index for neurologic outcome, it reflects the status of the neonate at delivery and as an objective parameter is more preferred for this purpose [6]. Routine determination of umbilical cord blood gases in every birth has been proposed by Thorp *et al.* more than 20 years ago, for medical and legal reasons [30].

A limitation of the present study is the randomization of parturients to receive general or neuraxial anesthesia, since regional techniques are on the whole safer for the mothers. Regarding this issue, the present study was approved by the Institutional Review Board and the complications of both anesthetic techniques were discussed with the parturients before their written informed consent was obtained. Also, parturients requesting a specific type of anesthesia were excluded from the study. Moreover, all cases were elective CS of the morning list, had no morbidities or predicted/known difficult airway, and anesthetics were administered by an experienced anesthesiologist. The authors consider that in this setting, the parturients who received general anesthesia were not exposed to a higher risk.

In conclusion, the current results suggest that the type of anesthesia does not significantly influence the early neonatal outcome in elective cesarean deliveries. However, maternal and fetal oxygenation and umbilical cord acid-base status appear to be superior when GA is administered compared to regional modalities, especially SA. Finally, differentiations in fetal oxygen consumption or indications for changes in fetal cardiac output were not observed with regards to anesthetic techniques.

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