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Oxygen utilization in newborns at delivery

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Abstract

Aims: To evaluate the arteriovenous (AV) pH difference in cord blood as a possible indicator of fetal O_2-utilization at delivery. Furthermore to examine which maternal, fetal and obstetrical factors lead to elevated O_2-utilization.
Methods: In this retrospective study all singleton live births, delivered within a four-month period at the University Hospital in Innsbruck, Austria, were analyzed. In total 491 deliveries were evaluated. Arterial and venous cord blood samples were collected at birth and analyzed by using a Radiometer ABL 510.
Results: Spontaneous deliveries showed a highly significant elevation in AV-difference (pH 0.10) as compared to cesarean sections (pH 0.05). In spontaneous births, the AV-difference was high in the case of low arterial cord blood pH ($P<0.01$), as well as in nuchal cord ($P<0.01$), high parity ($P<0.01$), very short labor ($P<0.05$) and elevated birth size and weight ($P<0.05$).
Conclusions: As a result of increased fetal stress at birth, spontaneous delivery leads to higher O_2-utilization than cesarean section, which is detectable in an elevated AV-difference. The AV-difference in combination with absolute pH-values can be used for the objective evaluation of fetal O_2-utilization and consecutively the fetal stress at birth.

Keywords: Arteriovenous difference; cord blood; neonate; oxygen demand; oxygen utilization; pH.

Introduction

Cord blood pH measurements are an objective marker for the evaluation of the acid base status as well as the oxygen supply of the newborn [1, 4]. Currently, the main focus is directed toward absolute pH-values, whereas the difference between arterial and venous cord blood pH (AV-difference) is not routinely used in clinical practice. In this study, 491 deliveries at the University Hospital Innsbruck were evaluated in regard to the AV-difference to determine the significance of this parameter concerning the condition of the newborn.

The fetus depends on the mother for placental exchange of oxygen and carbon dioxide. Disruption of adequate maternal blood gas concentrations, uterine blood supply, placental transfer and fetal gas transport can cause fetal hypoxia, which may lead to acidemia (high hydrogen ion concentration in the blood) or acidosis (high hydrogen ion concentration in the tissue) [2].

The affinity of oxygen to fetal hemoglobin (HbF) depends on the pH-value, which is reflected in the oxygen dissociation curve. A rise in pH leads to an increased affinity of HbF to oxygen. Conversely, when the pH-value falls, this causes a decrease in oxygen affinity of HbF. This phenomenon is called the Bohr effect [3, 7].

There is a highly significant correlation between the oxygen saturation and the pH-value in the arterial as well as in the venous cord blood [15]. According to the Bohr effect, we conclude that transfer of O_2 to tissue results in a decrease of the arterial pH or in other words in an increase of the AV-difference. Whereas the arterial cord blood pH indicates the oxygen demand of the newborn, the venous pH mainly reflects maternal oxygen supply. Accordingly, the difference between these two parameters (=AV-difference) can be considered as an indicator for O_2-utilization.

The aim of this study was to establish which fetal, maternal and obstetrical factors lead to elevated oxygen utilization and to investigate if the AV-difference can be used to determine the extent of fetal stress during delivery.

Methods

This retrospective study included all deliveries at the University Hospital in Innsbruck, Austria in a four-month period (January–April 2006). A total of 568 deliveries took place. Only live births with complete arterial and venous pH-values were included. Multiple births ($n=15$) were also excluded. All neonates with an AV-difference lower than pH 0.02 ($n=10$) were excluded to avoid the inclusion of false measurements. Double-cannulization of the same umbilical cord vessel and interchanging the venous and the arterial value are possible reasons for false measurements [18]. Consequently, 491 deliveries were included in the data analysis.

All blood samples were collected by cannulization of the vessels of the umbilical cord with a heparinized injection cannula immediately postpartum. The blood gas analysis was done with a Radiometer ABL 510 (Radiometer Medical A/S, Copenhagen) in <5 min after delivery.

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Statistical analysis of the data was performed using SPSS Version 14 (SPSS Inc., Chicago, IL). All values were expressed as median, interquartile range (IQR) and minimum and maximum values.

In a first step data were analyzed in total and in four subgroups according to mode of delivery [spontaneous vaginal delivery (SVD), vacuum extraction (VAE), elective cesarean section (ECS), non-elective cesarean section (NCS)].

As the data were not normally distributed, bivariate correlation was checked with the Spearman correlation coefficient. A strong interdependent correlation was found between the variables head circumference – birth weight, Apgar 1′ – Apgar 5′ – Apgar 10′ and week of gestation – birth weight. For that reason, the variables Apgar 1′, Apgar 10′ and week of gestation were not considered in the analysis.

In the next step, univariate variance analysis was carried out to detect significant correlations in relation to the target variable AV-difference. A cut-off point of $P \leq 0.05$ was set as significant and $P \leq 0.01$ as highly significant level, respectively.

Mann-Whitney *U*-test and Kruskal-Wallis *H*-test were utilized to analyze the basic population. A linear regression model was created for spontaneous deliveries: variables were included stepwise in terms of improving the model in the following order: arterial cord blood pH, nuchal cord, parity, duration of labor, birth size. Apgar 5′ was excluded due to non-significant correlation. Because of interdependent correlation of birth size and birth weight, birth weight was not considered in this regression model, but analyzed in an additional analysis (Mann-Whitney *U*-test).

Results

The median age of the mothers was 30 years (IQR 25–34 years). Median values of gravidity and parity were 2 (IQR 1–3) and 1 (IQR 1–2), respectively. A total of 87.7% of all women did not have any pregnancy associated risk factors. The most frequent risk factor was previous premature delivery (8.8%). The median gestational week at birth was the 39th week (IQR 38th–40th week). The male-female ratio was 54/46. The median birth weight was 3270 g (IQR 2910 g–3600 g) in all deliveries, the median size at birth was 49 cm (IQR 48 cm–51 cm) and the median head circumference was 35 cm (IQR 34 cm–36 cm). The median placenta weight was 520 g (IQR 460 g–600 g). A total of 1.8% of the newborns showed any kind of malformation.

A total of 273 (55.6%) of the 491 included births were spontaneous deliveries, 59 (12%) VAEs, 89 (18.1%) elective sections and 70 (14.3%) non-elective sections.

Abnormal cardiotocographic (CTG) readings were present in 39.7% of all births (Table 1). Oligohydramnious, polyhydramnious or meconium stained amniotic fluid was identified in 23.4% and a nuchal cord in 20.5% of all deliveries. The median Apgar scores (1′/5′/10′) were 9/10/10. Apgar at 5′ ≤7 was found in 3.1% of all deliveries (Table 1).

The median AV-difference was pH 0.08 in all deliveries (IQR 0.05–0.12; range 0.02–0.33). The median arterial pH was 7.28 (IQR 7.23–7.32; range 7.03–7.44), the median venous pH 7.37 (IQR 7.33–7.40; range 7.09–7.55). The median AV-difference was significantly increased in spontaneous vaginal deliveries (pH 0.10) as compared to elective (pH 0.05) and non-elective (pH 0.05) cesarean sections ($P<0.01$). The median AV-difference in VAEs (pH 0.09) was similar to the AV-difference in SVDs ($P=0.06$) (Tables 2 and 3).

The median arterial cord blood pH was low in VAEs (pH 7.24), and SVDs (pH 7.27). Significantly higher arterial pH-values were found in NCSs (pH 7.29) and ECSs (pH 7.32, Tables 2 and 3).

The median venous cord blood pH-value was elevated in SVDs (pH 7.38) and in ECSs (pH 7.37), whereas VAEs (pH 7.35) and NCSs (pH 7.34) showed significantly lower values (Tables 2 and 3).

A linear regression analysis with stepwise exclusion procedure, carried out for spontaneous deliveries demonstrated an inverse relation between arterial cord blood pH and AV-difference. When the arterial pH was ≤7.2 the median AV-difference was pH 0.14. If the arterial pH is >7.2, it was clearly lower at just pH 0.09 (median, $P<0.001$).

In case of nuchal cord, the AV-difference was elevated. Median AV-differences in deliveries with and without nuchal cord were pH 0.13 and pH 0.09, respectively ($P<0.001$).

Table 1 Apgar scores, CTG and amniotic fluid in regard of delivery mode.

	10–8					7–4					≤3				
	TOT	SVD	VAE	ECS	NCS	TOT	SVD	VAE	ECS	NCS	TOT	SVD	VAE	ECS	NCS
Apgar 1′	87.8	93.8	88.1	78.7	75.7	10.6	5.5	11.9	20.8	17.1	1.6	0.7	0.0	1.1	7.1
Apgar 5′	96.9	98.1	94.9	96.6	94.3	2.9	1.5	5.1	3.4	5.7	0.2	0.4	0.0	0.0	0.0
Apgar 10′	99.6	99.6	100	100	98.6	0.4	0.4	0.0	0.0	1.4	0.0	0.0	0.0	0.0	0.0

	Non-pathologic					Pathologic				
	TOT	SVD	VAE	ECS	NCS	TOT	SVD	VAE	ECS	NCS
CTG	60.3	67.3	24.6	79.2	47.5	39.7	32.7	75.4	20.8	52.5
Amniotic fluid	76.6	77.4	72.9	82.9	72.7	23.4	22.6	27.1	17.1	27.3

All values are expressed in percent.
TOT = all deliveries, SVD = spontaneous vaginal delivery, ECS = elective cesarean section, NCS = non-elective cesarean section, VAE = vacuum extraction, CTG = cardiotocography.

Table 2 AV-difference, arterial and venous cord blood pH-values by different variables.

	AV-difference	Arterial cord blood pH	Venous cord blood pH	n
Mode of labor				
TOT	0.08 (0.05–0.12)	7.28 (7.23–7.32)	7.37 (7.33–7.40)	491
SVD	0.10 (0.07–0.14)	7.27 (7.22–7.31)	7.38 (7.33–7.41)	273
VAE	0.09 (0.06–0.12)	7.24 (7.20–7.30)	7.35 (7.30–7.38)	59
ECS	0.05 (0.04–0.07)	7.32 (7.29–7.34)	7.37 (7.35–7.39)	89
NCS	0.05 (0.04–0.07)	7.29 (7.25–7.32)	7.34 (7.31–7.37)	70
Arterial cord blood pH				
≤7.20	0.14 (0.08–0.21)	7.16 (7.11–7.18)	7.31 (7.23–7.36)	53
>7.20	0.09 (0.07–0.13)	7.29 (7.25–7.33)	7.38 (7.34–7.42)	220
P-value	<0.001	<0.001	<0.001	
Nuchal cord				
Yes	0.13 (0.09–018)	7.23 (7.18–7.28)	7.38 (7.33–7.43)	99
No	0.09 (0.06–0.13)	7.28 (7.23–7.32)	7.37 (7.33–7.41)	384
P-value	<0.001	<0.001	0.538	
Duration of birth (h)				
<3	0.11 (0.08–0.16)	7.28 (7.24–7.31)	7.40 (7.36–7.43)	73
3–7	0.10 (0.07–0.15)	7.27 (7.22–7.31)	7.38 (7.33–7.42)	123
>7	0.08 (0.06–0.11)	7.26 (7.20–7.30)	7.34 (7.30–7.39)	73
P-value	0.001*	0.085*	<0.001*	
Parity				
1 delivery	0.08 (0.06–0.13)	7.26 (7.21–7.30)	7.35 (7.315–7.395)	117
2 deliveries	0.10 (0.07–0.15)	7.29 (7.23–7.32)	7.38 (7.345–7.42)	93
≥3 deliveries	0.12 (0.10–0.17)	7.26 (7.23–7.30)	7.39 (7.36–7.45)	63
P-value	<0.001**	0.483**	<0.001**	
Birth size (cm)				
≤46	0.09 (0.06–0.12)	7.27 (7.23–7.31)	7.36 (7.32–7.41)	44
≥52	0.13 (0.08–0.15)	7.27 (7.21–7.30)	7.37 (7.33–7.41)	45
P-value	0.008	0.213	0.559	
Birth weight (g)				
<3085	0.09 (0.07–013)	7.28 (7.21–7.31)	7.36 (7.32–7.41)	68
>3610	0.11 (0.08–0.15)	7.23 (7.17–7.29)	7.36 (7.32–7.40)	67
P-value	0.022	0.027	0.736	

Values are expressed as median (interquartile range). The Mann-Whitney *U*-test was used with $P<0.05$ considered as significant.
*Correlation compared deliveries <3 h vs. deliveries >7 h.
**Correlation compared 1 delivery vs. ≥3 deliveries.
TOT=all deliveries (not subdivided), SVD=spontaneous vaginal delivery, ECS=elective cesarean section, NCS=non-elective cesarean section, VAE=vacuum extraction.

Parity shows a highly significant correlation with AV-difference ($P<0.001$). The median AV-difference increases with every child born and was in women with 1, 2, and 3 or more deliveries pH 0.08, 0.10 and 0.12, respectively.

The shorter the duration of delivery, the higher is the median AV-difference ($P<0.05$). The median AV-difference was in deliveries taking <3 h (<25th percentile) pH 0.11 and in deliveries taking >7 h (>75th percentile) pH 0.08 ($P<0.01$).

Size of the neonates at birth and median AV-difference are positively correlated. Neonates with a size of ≤46 cm showed a median AV-difference of pH 0.09 compared to pH 0.13 in neonates measuring 52 cm and larger.

Spontaneous delivered newborns with <3085 g (which is the 25th percentile of all spontaneous delivered neonates) have a median AV-difference of pH 0.09 as compared with pH 0.11 in neonates of >3610 g (75th percentile) ($P<0.05$).

Discussion

Oxygen supply to the fetus depends on maternal as well as fetal factors. Impairment of maternal oxygenation, perfusion of the placenta and delivery of oxygenated blood from the placenta to the fetus can diminish oxygen supply to fetal tissue. Fetal hypoxia leads to acidemia and acidosis [2].

For this reason cord blood pH measurements immediately after delivery are used to evaluate oxygen supply during birth. Arterial cord blood pH reflects fetal oxygen demand and venous cord blood pH indicates maternal oxygen supply. The difference between these parameters (AV-difference) is an indicator of oxygen utilization. As fetal stress increases oxygen utilization we hypothesize that the AV-difference is increased in fetuses at stress. This is supported by our study.

In neonates after SVD the AV-difference was significantly higher, the arterial cord blood pH significantly lower, and

Table 3 Comparison of modes of delivery and correlations with regard to AV-difference, arterial pH and venous pH.

	P-value			
	SVD vs. ECS	SVD vs. NCS	SVD vs. VAE	ECS vs. NCS
AV difference	<0.001	<0.001	0.059	0.901
Arterial cord blood pH	<0.001	0.034	0.069	<0.001
Venous cord blood pH	0.373	<0.001	<0.001	<0.001

The Mann-Whitney *U*-test was used with $P<0.05$ considered as significant.
SVD = spontaneous vaginal deliveries, ECS = elective cesarean section, NCS = non-elective cesarean section, VAE = vacuum extractions.

the venous cord blood pH not significantly different compared to neonates after ECS. These parameters indicate that SVD is more stressful to the neonate than delivery by ECS. Maternal respiration is equally efficient in both modes of delivery. These findings of our study add additional evidence to the fact that cesarean section is generally acknowledged as exerting less stress on the fetus [12, 13, 17] than vaginal delivery.

Similar findings are found in increased fetal size, which usually implies a more difficult delivery with elevated fetal stress. The cord blood AV-difference is increased and arterial cord blood pH is decreased in heavier newborns. This corresponds well to the results of Herbst et al. [6], who found acidemia more frequently in large newborns.

Impaired fetal circulation, as it is seen in nuchal cord [9], forces the fetus to utilize a larger amount of oxygen delivered by the mother. We found that the AV-difference is significantly increased and the arterial cord pH is significantly lower in newborns with nuchal cord compared to those without nuchal cord. This is a sign that the pathological condition is on the fetal side. Several studies [5, 9, 16] have also demonstrated that nuchal cord particularly affects arterial cord blood pH.

We found significantly lower venous cord blood pH-values at the same AV-difference in NCSs as compared to ECSs. This indicates that in NCSs the mother oxygenates the blood to a lesser extent. However, according to the present data the neonate does not utilize more oxygen in NCSs than in ECSs. Accordingly, NCS seems to be a highly stressful event for the mother, which can easily be understood.

Prolongation of labor is a well-acknowledged stress factor at birth. Hence, our observation is surprising that shorter duration of the delivery leads to higher AV-difference. Firstly, this correlation was especially robust for precipitated labor, in which acidemia is observed frequently [6]. Secondly, the correlation is explained more clearly when considering the absolute pH-values: the AV-difference and the venous pH differed significantly between neonates after short and long duration of labor whereas the arterial pH stayed approximately at the same level. Maternal respiration appeared to become insufficient in prolonged deliveries. In this case, maternal blood is insufficiently oxygenated, and correspondingly less oxygen is transported by the cord blood [14].

Similar results are seen when analyzing the impact of parity on the AV-difference. The AV-difference and the venous cord blood pH-values are significantly higher in spontaneous deliveries in women with three or more births than in primiparas whereas the arterial pH remains unchanged. We suspect that this could possibly be the result of more effective respiration in multiparas due to lower maternal stress.

Divergent AV-differences may stem from variation in the size of the placental exchange surface. However, no causal relationship was found between placental weight and AV-difference. Our findings are underscored by Roemer [14], who found no correlation between placental weight and pCO_2-values in venous cord blood. This finding may be explained by the fact that placental weight was within normal ranges in the majority of our cases.

Of all variables the arterial blood cord pH showed the strongest influence on the level of the AV-difference, which increases steeply when the arterial cord blood pH is <7.25, whereas it shows only a low rise up to this value (Figure 1). This indicates that (pre)acidotic children utilize a lot of O_2

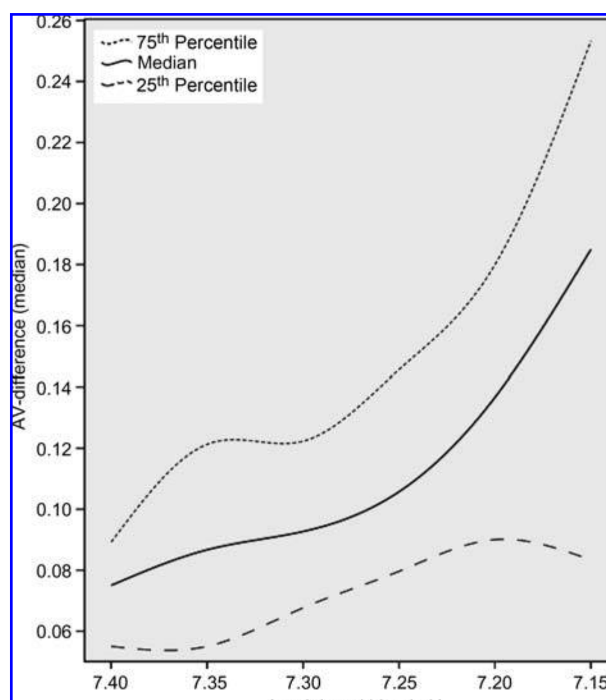

Figure 1 Dependence of the AV-difference on the arterial cord blood pH-value. Shown as median with 25[th] and 75[th] percentile.

and/or return a lot of CO_2 into the blood to counteract the threatening asphyxia and/or to maintain sufficient cerebral oxygenation [8].

Apgar score, amniotic fluid findings and CTG did not show any correlation with AV-difference. This is not surprising, as these three parameters are interpreted subjectively [10, 11].

Based on analysis of the AV-difference, we cannot make definite statements about the condition of a neonate. This parameter did not prove to be a suitable extension of the Apgar score. The AV-difference can rather be regarded as an indicator of the physiological adaptability of the newborn to different stressors at delivery. When neonatal stress is low, for example in case of an ECS, the newborn uses only little oxygen. In the case of elevated stress, the newborn adapts to these circumstances by utilizing a larger fraction of the oxygen supplied. Therefore, AV-difference is suitable for the estimation of the fetal stress at birth.

However, AV-difference must always be interpreted in the context of arterial and venous cord blood pH-values. On the one hand, there is a possibility of false interpretation. On the other, the analysis of the absolute pH-values can provide valuable additional information. The venous pH enables conclusions about the maternal ability to oxygenate the blood. The arterial pH allows interpretation of the extent at which the newborn actually utilizes the oxygen supplied.

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