Original Article

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Could the Umbilical Cord Suggest the Method of Anesthesia?

Umblikal Kord Anestezi Yöntemini Gösterebilir Mi?

Enes ÇELİK[1], Ömer TAMMO[2]

[1]Derik State Hospital, Operating Theater, Mardin, Turkey
[2]Mardin Training and Research Hospital, Clinic of Gynecology and Obstetrics, Mardin, Turkey

ABSTRACT

Objective: We aimed to investigate changes in aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), creatine kinase-myocardial band (CK-MB), and troponin I levels, which were biochemical parameters that gave an idea regarding clinical conditions such as tissue damage and asphyxia, according to the anesthesia type, to compare their levels in mothers who gave birth with normal spontaneous vaginal delivery (NSVD) and to investigate whether the type of anesthesia applied caused a change in biochemical parameters.

Methods: Of the 90 patients included in the present study, 30 (33.3%) underwent general anesthesia, while 30 (33.3%) underwent spinal anesthesia, and 30 (33.3%) gave birth with NSVD. AST, ALT, LDH, CK-MB, and troponin I levels were measured in all pregnant women before they were taken to the operating room or delivery room. After the baby was delivered, a blood sample was taken from the umblical artery to measure AST, ALT, LDH, CK-MB, and troponin I levels. The APGAR scores, the need for oxygen, positive pressure ventilation, and intubation after delivery of the newborns were recorded.

Results: Statistically significant increases were found in AST, ALT, LDH, and troponin I levels in umblical artery in all groups when compared with their levels in pregnant women before delivery.

Conclusion: An increase in umbilical artery CK-MB and ALT levels was observed in the NSVD group. Due to the increase in umbilical artery CK-MB and ALT levels in the NSVD group, it was found that it was not appropriate to evaluate the effects of anesthesia on the newborn with these markers.

Keywords: Umbilical cord, lactate dehydrogenases, parturition, anesthesia

ÖZ

Amaç: Doku hasarı, asfiksi gibi klinik durumlar hakkında fikir veren biyokimyasal parametreler olan aspartat aminotransferaz (AST), alanin aminotransferaz (ALT), laktat dehidrogenaz (LDH), kreatin kinaz-miyokardiyal bant (CK-MB) ve troponin 1 değerlerinin anestezi tipine göre farklılığını araştırmayı amaçladık. Bu parametreleri genel anesteziyle, spinal anesteziyle ve normal spontan vajinal doğum (NSVD) doğum yapan gebelerde karşılaştırmayı ve uygulanan anestezi tipinin biyokimyasal parametrelerde değişikliğe neden olup olmadığını araştırmayı amaçladık.

Yöntemler: Çalışmaya dahil edilen 90 gebenin 30'una (%33,3) genel anestezi, 30'una (%33,3) spinal anestezi uygulandı ve 30'u (%33,3) NSVD ile bebek sahibi oldu. Tüm gebelerde ameliyathaneye veya doğuma alınmadan önce kan AST, ALT, LDH, CK-MB ve troponin 1 düzeyleri ölçüldü. Bebek doğduktan sonra umblikal arterden kan numunesi alındı ve AST, ALT, LDH, CK-MB ve troponin 1 düzeyleri ölçüldü. Yenidoğanların doğumundan sonra APGAR skorları, oksijen ihtiyacı, pozitif basınçlı ventilasyon ve entübasyon ihtiyacı not edildi.

Bulgular: Tüm gruplarda gebelerin doğumdan önceki kan değerleriyle karşılaştırıldığında umblikal arter AST, ALT, LDH ve troponin 1 düzeylerinde istatistiksel olarak anlamlı artışlar tespit edildi.

Sonuç: Normal spontan vajinal doğum grubunda umbilikal arter CK-MB ve ALT düzeylerinde artış gözlendi. NSVD grubunda umblikal arter CK-MB ve ALT düzeylerindeki artış nedeniyle anestezinin yenidoğan üzerindeki etkilerini bu belirteçlerle değerlendirmenin doğru olmadığı görüldü.

Anahtar Sözcükler: Umblikal kord, laktat dehidrogenaz, doğum, anestezi

Address for Correspondence: Enes ÇELİK, Derik State Hospital, Operating Theater, Mardin, Turkey
E-mail: anestezistenescelik@gmail.com **ORCID ID:** orcid.org/0000-0002-5546-4924

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Introduction

The rate of cesarean section has increased gradually worldwide and in our country in the last twenty years (1-4). In the Turkish Statistical Institute, Child with Statistics, 2020 bulletin, it was revealed that while the rate of cesarean deliveries in live births was 51.1% in 2014, it was 54.4% in 2019 (4).

The increase in the number of cesarean sections and the impacts of spinal and general anesthesia on the mother and fetus have been compared and investigated in many studies. General and spinal anesthesia techniques used in cesarean sectionare known to have pros and cons peculiar to them. Advantages of general anesthesia include rapid induction, less hypotension, decreased cardiovascular depression, good airway, and respiratory control. Prominent advantages of regional anesthesia, which has been preferred more frequently in recent years, are that the patient is conscious, the risk of aspiration is minimal, and it does not lead to respiratory depression in the newborn.

Although first, fifth, and tenth-minute APGAR scores are the most commonly used method in the evaluation of the clinical condition of the neonate, it has been suggested that umbilical cord blood gases are more reliable as they are not correlated with temporary intrapartum and late neurological injuries and are impacted by various factors (4,5). Although pH has been reported to be the parameter that best indicates fetal status from umbilical cord artery blood gas values, studies have revealed that lactate concentration is more valuable, especially regarding fetal distress (5).

In our study, we investigated the changes in aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), creatine kinase myocardial band (CK-MB), and troponin I levels according to the anesthesia method. We evaluated the change in the levels of the same blood parameters of the fetus with anesthesia method, APGAR score, placental separation time, age and gestational week.

Methods

Pregnant women who gave birth with the diagnosis of term pregnancy between January 2021 and December 2021 were prospectively included in the present study. This study was conducted in accordance with the Declaration of Helsinki. After obtaining the ethics committee approval, this study was started prospectively (number: E-37201737-806.02.02) on 60 healthy pregnant women who were expecting a single baby, were between the ages of 18-40, had the American Society of Anesthesiologists score II, and were between 35-41 weeks of gestation, with an indication for elective cesarean section in gynecology and obstetrics clinic and on 30 pregnant women who were planned for normal spontaneous vaginal delivery (NSVD). Pregnant women were informed about this study, and their written and verbal consents were obtained. Patients who underwent emergency cesarean section or NSVD, pregnant women with HELLP, preeclampsia, eclampsia, liver disease, renal disease, cardiovascular disease or any other pregnancy-related disorder, pregnant women with multiple pregnancies, and pregnant women with abnormally high biochemical parameters in blood samples were excluded from the study. Pregnant women with Rh incompatibility, expected fetal anomaly, risk of meconium aspiration, or placental location or adhesion anomaly were excluded from this study.

The AST1, ALT1, LDH1, CK-MB1 and troponin II levels were measured in all pregnant women before they were taken to the operating room or delivery room. Vascular access was established with a 20 G angiocath from the back of the hand or antecubital region in all pregnant women, and crystalloid fluid (0.9% NaCl) infusion was started. The pregnant women included in the present study were divided into three groups: Group G (Group under general anesthesia, n=30), Group S (Group with spinal anesthesia, n=30), and Group V (Group with NSVD n=30). Group randomization was performed according to the preferences of the pregnant women and the evaluation of the obstetrician and gynecologist. Electrocardiography, heart rate, systolic arterial pressure, diastolic arterial pressure, mean arterial pressure, and peripheral oxygen saturation (SpO_2) were monitored in all groups following they were placed on the operating table. In Group G, anesthesia was induced with 2 mg/kg propofol and 0.6 mg/kg rocuronium. After muscle relaxation was achieved, the pregnant women were intubated. Patients were provided with volume-controlled ventilation to achieve a tidal volume of 6-8 mL/kg, respiratory frequency of 10-12/min, PEEP: 4 cm H_2O, and I:E 1/2. 50% oxygen-50% air mixture and 1 minimum alveolar concentration. Sevoflurane was administered for maintenance of anesthesia. When necessary, 0.15 mg/kg rocuronium was added. After the baby was delivered and the umbilical cord was clamped, 1 mcg/kg fentanyl was administered intravenously to the pregnant women as an analgesic.

In the Group S, the pregnant women were placed in a sitting position and the puncture site was wiped with povidone-iodine poly iodine complex and covered with a perforated sterile drape. After sterile conditions were achieved, the subarachnoid space was entered slowly with a 25 G (25 G Quincke) spinal needle from the midline of the L3-4 or L4-5 vertebral space in the intervention area. After the clear cerebrospinal fluid was seen to come, 2.0-2.4 mL (10-12 mg) of 0.5% hyperbaric bupivacaine (Busacain Spinal Heavy 4 ml-Haver, Istanbul, Turkey) was slowly administered into the subarachnoid space. The operation was allowed upon the sensory and motor block were at an adequate level.

After the baby was delivered and the umbilical cord was clamped, a sterile sample was taken from the umbilical artery by the same Gynecologist. AST2, ALT2, LDH2, CK-MB2, and Troponin I2 levels were measured in the blood samples taken.

The newborns were evaluated by a pediatrician. The APGAR score at the 1st and 5th minutes, the need for oxygen, positive pressure ventilation, and intubation after delivery of the newborns were recorded.

In Group V, the umbilical cord was clamped by midwives, and blood samples were taken from the umbilical artery immediately after the birth of the fetus in the delivery room.

Statistical Analysis

The software of SPSS 15.0 for Windows was used for statistical analysis. Descriptive statistics were expressed as numbers and percentages for categorical variables, while they were expressed as mean, standard deviation, minimum, maximum, median, and interquartile range for numerical variables. Comparisons of numerical variables in more than two independent groups were made with the one-way ANOVA test when the normal distribution condition was met in the groups and with the Kruskal-Wallis test when the condition was not met. Subgroup analyses were conducted via the Mann-Whitney U test and interpreted with Bonferroni Correction. Correlations between numerical variables were determined by Spearman Correlation Analysis since the parametric test condition was not met. Statistical alpha significance level was considered to be $p<0.05$.

Results

Of the 90 patients included in the present study, 30 (33.3%) underwent general anesthesia, while 30 (33.3%) underwent spinal anesthesia, and 30 (33.3%) had NSVD. The mean age of the Group V was significantly lower than the Group G and Group S (general vs. NSVD p=0.042 spinal vs. NSVD p=0.021). The removal duration of placenta in the Group G was significantly longer than the Group S (p<0.001). A significant difference was found between the APGAR scores of the groups (p=0.023). The APGAR score of the Group G was significantly lower than the Group V (p=0.007).

A significant difference was determined between the AST1 and AST2 levels of the all groups (p=0.042). In all groups, the sample taken from the mother before the birth and the sample taken from the umbilical cord after the birth were evaluated and the increase in the AST level was found to be significant (p=0.001, p=0.039 and p<0.001). The AST level of the Group G was higher than the Group S (p=0.016). A significant decrease was found in the ALT level of the Group S, whereas a significant increase was found in the Group V (p=0.001 and p=0.016). It was found that there was a significant difference in the ALT2 level, difference, and % change of the all groups (p=0.001, p=0.001 and p<0.001, respectively) (Table 1).

No significant difference was determined between the groups regarding troponin 1 levels (p=0.780). The increase in troponin levels was significant for all groups (p=0001, p<0.001 and p=0.010, respectively). A significant difference was found in the troponin II level, difference, and % change of the all groups (p<0.001 for all). troponin II, difference, and % change levels were significantly higher in the Group S than the Group G and V (p<0.001 for all) (Table 1).

A significant difference was found in LDH 1 levels of the groups (p=0.007). LDH 1 level was higher in the Group V than the Group S (p=0.002). The increase in LDH levels of all groups was statistically significant (p<0.001 for all) (Table 2). Similarly, in our study, a significant difference was found between the groups' umbilical artery LDH values (LDH 2) and maternal LDH levels (LDH 1) (p<0.001 and p=0.038, respectively). The difference between maternal and umbilical artery LDH levels in the Group G was significantly higher than in the Group S (p<0.001, p=0.001 and p=0.013) (Tables 1, 2).

No significant difference was found between the groups concerning CK-MB1 levels (p=0.053). Difference and % change were higher in the Group V than Group G and Group S,. whileCK-MB2 level was higher in the Group V compared to the Group G (p<0.001, p=0.004, p=0.006 and p=0.012, respectively). A significant difference was found between the groups regarding the CK-MB2 level, difference, and % change (p=0.001, p=0.012 and p=0.033, respectively) (Table 1).

A significant positive correlation was found between duration of placental removal and LDH2 level in all groups (p=0.020). In our study, a significant positive correlation was found between duration of placental removal and LDH2 level in all groups (p=0.012 and p=0.020, respectively), while the duration of placental removal in the Group G was significantly longer than in the Group S (p<0.001) (Table 3).

None of the neonates needed intubation or respiratory support. None of the pregnant women needed respiratory support and intensive care after delivery.

Discussion

The superiority of general and spinal anesthesia administered in pregnant patients during cesarean delivery, which has become one of the most frequently performed surgical procedures today, to each other could not be shown in studies (6-8). With the increase in the number of cesarean sections performed, how the newborn is impacted by anesthesia has been investigated. Although there are many studies on this issue, the effects of anesthesia type on the newborn still attracts attention. In the evaluation of the newborn, the blood sample taken from the umbilical cord has been studied with a great variety of parameters (9-11). It has been revealed that umbilical artery blood gas values are guiding in determining hypoxemic and acidic newborns (9,10).

There are many studies investigating the effects of umbilical cord blood gas values and anesthesia on the newborn and the effects of bupivacaine on the umbilical artery (5,11,12). Maternal hypotension caused by regional anesthesia may affect uteroplacental blood flow, resulting in fetal acidosis, asphyxia, and low Apgar scores (12,13). By measuring umbilical artery LDH levels, it is supported that LDH is a sensitive marker in showing stress in the intrapartum period (14). It has also been demonstrated that it can be a marker of hypoxic-ischemic encephalopathy (HIE) in the first 12 hours after birth, and the relationship between severity of HIE and LDH levels in newborns is promising (15-17). Reddy et al. (18) reported in their study that LDH was the most accurate test in the first 72 hours to distinguish asphyxia in newborns. Likewise, in our study, LDH2 level was found to be significantly increased compared to LDH1 in all groups. However, since LDH level is affected by various factors and its level increases with hemolysis, its use in evaluating the effects of anesthesia on the newborn is limited.

Crawford et al. (14) have suggested that the most significant factor that can affect the oxygenation and acid-base status of the fetus at birth is the duration between uterine incision and delivery. In our study, a significant positive correlation was found between duration of placental removal and LDH2 level in all groups. The duration of placenta removal of the Group G was significantly longer than the Group S. We are of the opinion that the reason for the higher elevation in LDH2 level in the Group G is due to the length of duration for placental removal in pregnants undergoing the cesarean section under general anesthesia.

Although AST and ALT may increase due to many reasons in the fetus, they may also increase idiopathically (19). In our study, it was observed that ALT2 level decreased compared to ALT1 level in Group S, while an increase was found in Group V, which did not receive anesthesia. Therefore, we think that spinal anesthesia may not have a direct effect on the change in ALT levels.

The CK-MB and troponin I levels can be affected by various pathological conditions, such as HIE and asphyxia (20,21). Wan et al. (20) reported that there was a significant correlation between

Table 1. Change according to anesthesia method

	Group G	Group S	Group V	p*
AST1	25.3±8.4	20.7±7.1	22.2±6.8	0.042
AST2	38.6±18.7	29.8±17.8	33.1±11.4	0.063
Difference	12 (0-21.5)	3 (-5-18.25)	8 (3-18)	0.256
P	0.001*	0.039*	<0.001*	
% change	48.7 (0.0-146.3)	11.7 (-19.7-111.5)	40.4 (14.3-107.3)	0.426
ALT1	15.4±7.7	14.0±6.5	11.4±5.5	0.039
ALT2	16.3±8.4	10.0±5.1	14.8±6.2	0.001
Difference	1.5 (-5-6.5)	-3.5 (-5.75- -0.75)	2.5 (-1-7)	0.001
P	0.459*	0.001*	0.016*	
% change	13 (-31.3-52)	-25.6 (-45.8- -6.3)	22.6 (-9.1-90.6)	<0.001*
TROP1	0.0035±0.0016	0.0064±0.0133	0.0038±0.0041	0.780
TROP2	0.0051±0.0021	0.0384±0.1112	0.0044±0.0021	<0.001*
Difference	0.0011 (-0.00015-0.0035)	0.0049 (0.0027-0.0088)	0.0007 (0-0.0024)	<0.001*
P	0.001*	<0.001*	0.010*	
% change	33.1 (-3.6-140.9)	203.6 (93.6-634)	26.5 (0.0-93.4)	<0.001*
LDH1	290.6±82.5	247.1±64.8	307.1±78.5	0.007
LDH2	495.1±147.1	387.3±197.8	475.8±126.9	<0.001*
Difference	179.5 (100-313.5)	111 (64.75-144.75)	165 (93.75-251)	0.038
P	<0.001#	<0.001#	<0.001*	
% change	68.1 (34.2-123.2)	47.4 (25.7-77.6)	52.8 (29.0-88.1)	0.384
CK-MB1	1.90±0.99	1.73±1.01	2.33±1.06	0.053
CK-MB2	1.97±2.14	2.17±2.20	3.87±2.78	0.001
Difference	0 (-1-0.25)	0 (-1-1)	1 (0-3.25)	0.012
P	0.484#	0.612#	0.002#	
% change	0.0 (-50-25)	0.0 (-33.3-100)	66.7 (0.0-100)	0.033

*P-value <0.05 is considered as statistically significant difference
AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, CK-MB: Creatine kinase myocardial band

Table 2. The amount of change according to anesthesia method

	AST difference	ALT difference	TROP difference	LDH difference	CK-MB difference
	p	p	p	p	p
Group G vs Group S	0.156*	0.0167*	<0.001*	0.013*	0.393
Group G vs Group V	0.668	0.446	0.515	0.451	0.006*
Group S vs. Group V	0.167*	<0.001*	<0.001*	0.082	0.028
	AST change	ALT change	TROP change	LDHD change	CK-MB change
Group G vs Group S	0.304	0.013*	<0.001*	0.174	0.273
Group G vs Group V	0.882	0.222	0.535	0.379	0.012*
Group G vs Group V	0.220	<0.001*	<0.001*	0.631	0.103

Mann-Whitney U test Bonferroni correction p<0.017
*P-value <0.05 is considered as statistically significant difference.
AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, CK-MB: Creatine kinase-myocardial band

Table 3. Clinical features

	Age		Gestational week		Duration of placenta removal		APGAR	
	r	p	R	p	r	p	R	p
AST1	0.094	0.381	0.115	0.282	0.162	0.215	-0.002	0.984
AST2	-0.011	0.917	0.015	0.888	0.233	0.074	-0.024	0.823
AST difference	-0.065	0.542	-0.077	0.473	0.125	0.341	0.000	0.996
AST change	-0.085	0.424	-0.069	0.518	0.104	0.428	0.017	0.877
ALT1	0.167	0.116	0.051	0.632	0.217	0.096	-0.157	0.140
ALT2	-0.098	0.360	0.097	0.361	0.224	0.085	-0.188	0.076
ALT difference	-0.123	0.246	0.012	0.912	0.035	0.789	-0.027	0.803
ALT change	-0.164	0.123	0.004	0.970	0.061	0.646	-0.048	0.652
TROP1	0.212	0.045*	0.004	0.970	0.322	0.012*	0.079	0.458
TROP2	0.195	0.066	-0.055	0.607	-0.230	0.077	0.043	0.689
TROP difference	0.020	0.851	-0.032	0.763	-0.299	0.020*	0.072	0.503
TROP change	0.012	0.914	0.000	0.999	-0.321	0.012*	0.065	0.545
LDH1	0.142	0181	0.087	0.413	0.097	0.460	-0.194	0.067
LDH2	-0.092	0.386	0.001	0.994	0.261	0.044*	-0.010	0.928
LDH difference	-0.164	0.122	-0.040	0.705	0.198	0.129	0.100	0.348
LDH change	-0.196	0.064	-0.034	0.749	0.140	0.285	0.181	0.087
CK-MB1	-0.065	0.541	-0.025	0.812	-0.010	0.938	0.120	0.262
CK-MB2	-0.143	0.179	-0.218	0.039*	0.063	0.630	0.131	0.219
CK-MB change	-0.095	0.373	-0.205	0.053	0.063	0.634	0.054	0.614
CK-MB difference	-0.093	0.383	-0.196	0.065	0.073	0.580	0.079	0.462

*P-value <0.05 is considered as a statistically significant difference.
AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, CK-MB: Creatine kinase-myocardial band

umbilical cord CK-MB and troponin I levels and neonatal HIE (NHIE). In addition, Sanjay et al. (21) revealed that CK-MB in the first eight hours and LDH levels in the first 72 hours in newborns could help to distinguish between asphyxiated and non-asphyxiated newborns.

In our study, however, no pathological levels were found in the effects of anesthesia and operation/delivery on the fetus with CK-MB and troponin I evaluation. The change in CK-MB2 levels was higher in the Group V than the Group G. However, as in other biochemical markers we studied, CK-MB and troponin I levels were impacted by many pathological conditions, such as HIE and asphyxia. Moreover, we think that it is not appropriate to use anesthesia alone to assess the effects of anesthesia on the neonate since there is a higher increase in the Group V than in the Group G.

Study Limitations

Since the mean duration to placenta removal was 7.37±0.49 minutes even in the general anesthesia group, the inability to analyze whether this duration was adequate to make an assessment with biochemical parameters constituted the limitations of our study, in which we tried to evaluate the effects of anesthesia on the neonate. Another limitation of the study was the fact that our study was conducted in a single center and with a small sample size.

Conclusion

In our study, it was observed that ALT2 level was decreased compared to ALT1 in Group S, while an increase was found in Group V, which did not receive anesthesia. Therefore, we think that spinal anesthesia may not have a direct effect on the change in ALT levels.

Due to the increase in CK-MB2 and ALT2 levels in the Group V, it was found that it was not appropriate to evaluate the effects of anesthesia on the newborn with these markers. We need more specific markers to evaluate the effects of anesthesia on the fetus at an early time.

Ethics

Ethics Committee Approval: After obtaining the ethics committee approval, this study was started prospectively (number: E-37201737-806.02.02).

Informed Consent: A consent form was completed by all participants.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: E.Ç., Ö.T., Concept: E.Ç., Ö.T., Design: E.Ç., Data Collection or Processing: E.Ç., Ö.T., Analysis or Interpretation: Ö.T., Literature Search: E.Ç., Ö.T., Writing: E.Ç.

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