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The Effect of Blood Base Deficit on Neonatal Convulsions and Amplitude Electroencephalography Measurements in Perinatal Asphyxia

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Abstract

Objective: To determine the effect of blood pH levels and base deficit on neonatal convulsions and amplitude electroencephalography measurements in patients with perinatal asphyxia.

Methods: This study included 102 patients monitored in the neonatal intensive care unit for perinatal asphyxia. Amplitude electroencephalography measurements and convulsions were recorded from all patients for 80 hours. Blood samples were taken in the umbilical artery for the pH analysis and calculation of base deficit.

Results: The mean gestational age was 38.13±1.30 weeks with 66/36 (64.7% / 35.3%), male/female ratio. Fifty-seven (55.9%) babies were delivered by normal spontaneous vaginal delivery, while 45 patients (44.1%) had a history of cesarean delivery. There were significant differences between the mean base deficit and amplitude electroencephalography recordings at the first 24th, 48th, and 72nd hours (KW=32.819, p<0.001; KW=23.687, p<0.001, and KW=24.992, p<0.001, respectively). Sixty-five (63.7%) of the patients had neonatal convulsions. The mean base deficit was 20.64±4.70 mmol/L and 17.48±2.92 mmol/L in patients with and without seizures, respectively. The mean base deficit was significantly higher in patients with neonatal seizures (Z=3.912; p=0.001).

Conclusion: Our study showed patients with abnormal amplitude electroencephalography findings and epileptic electrical activity were found to have higher base deficits at the time of diagnosis. It suggests that high base deficit levels may have a negative effect on the neurodevelopmental process in the neonatal period.

Keywords: Amplitude electroencephalography, base deficit, convulsion, perinatal asphyxia

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Perinatal Asfikside Baz Açığının Yenidoğan Konvülzyonları ve Amplitüd Elektroensefalografi Ölçümleri Üzerine Etkisi

Öz

Amaç: Perinatal asfiksi hastalarında kan pH düzeyi ve baz açığının yenidoğan konvülzyonları ve amplitüd elektroensefalografi ölçümleri üzerine etkisini araştırmak.

Yöntemler: Bu çalışmaya yenidoğan yoğun bakım ünitesinde perinatal asfiksi tanısıyla takip edilen 102 hasta dahil edildi. Tüm hastalardan 80 saat boyunca amplitüd elektroensefalografi ölçümleri ve konvülzyonlar kaydedildi. Tüm olgulardan pH ve baz açığı için göbek arterinden kan örnekleri alındı.

Bulgular: Ortalama gebelik yaşı 38,13±1,30 hafta olup erkek/kadın oranı 66/36 (%64,7 / %35,3) idi. Bebeklerin 57'si (%55,9) normal spontan vajinal yolla doğarken, 45'inde (%44,1) sezaryen doğum öyküsü vardı. İlk 24, 48 ve 72. saatlerdeki baz açığı ve amplitüd elektroensefalografi kayıtları ortalamaları arasında anlamlı fark vardı (sırasıyla KW=32,819, p<0,001; KW=23,687, p<0,001 ve KW=24,992, p<0,001). Hastaların 65'inde (%63,7) yenidoğan nöbeti vardı. Ortalama baz açığı, nöbet geçiren ve nöbet geçirmeyen hastalarda sırasıyla 20,64±4,70 mmol/L ve 17,48±2,92 mmol/L idi. Yenidoğan nöbeti geçiren hastalarda baz açığı ortalaması anlamlı derecede yüksekti (Z=3,912; p=0,001).

Sonuç: Çalışmamız anormal amplitüd elektroensefalografi bulguları ve epileptik elektriksel aktivitesi olan hastaların tanı anında baz açığı daha yüksek olduğunu gösterdi. Yüksek baz açığı düzeylerinin yenidoğan döneminde nörogelişimsel süreç üzerinde olumsuz etki yaratabileceğini düşündürmektedir.

Anahtar kelimeler: Amplitüd elektroensefalografi, baz açığı, konvülziyon, perinatal asfiksi.

INTRODUCTION

Perinatal asphyxia(PA) develops with arterial hypoxemia and hypercarbia due to deterioration of oxygen-carbon dioxide exchange as a result of inadequate gas exchange in the placenta or deterioration of ventilation at the pulmonary level as a result of postnatal events[1,2]. Hypoxemia leads to an increase in lactic acid and base deficit (BD) levels and a decrease in pH levels, leading to disruption of normal metabolic activity and the development of metabolic acidosis[3]. These metabolic abnormalities that develop in mature and premature babies are the most important cause of neurological morbidity that may develop later[4]. Neuroimaging and neurophysiological examination are important in predicting prognosis in babies with PA[5,6]. Amplitude electroencephalography (aEEG) allows the evaluation of brain functions. It has been stated that aEEG can be used to predict neurodevelopmental outcomes in asphyxiated infants. It has been reported that mildly distorted and normal traces in amplitude-integrated EEG are associated with better long-term outcomes, while severely distorted traces are associated with worse long-term outcomes[7,8]. In asphyxia babies, aEEG allows the diagnosis of convulsions and monitoring of the effects of anticonvulsant drugs[9]. It has been determined that mortality is increased in newborns suffering from convulsions and that there is an increase in negative neurodevelopmental outcomes in surviving cases. Convulsions in newborns are the hallmark manifestation of neurological diseases and are associated with worse neurodevelopmental outcomes, regardless of the severity of hypoxic-ischemic brain injury[10].

We aim to investigate the effect of pH and BD values at the time of diagnosis on neonatal convulsions and aEEG findings in patients followed by a diagnosis of PA.

METHODS

Design

This case-control study was conducted in the tertiary neonatal intensive care unit between January 2020 and June 2023. 102 cases who were followed up and treated with a diagnosis of perinatal asphyxia were included. Ethics Committee approval was obtained before the study (decision no: 25, session no: 09, date 28.12.2023).

Participants

This study comprises of 102 neonates with perinatal asphyxia. Patients had a gestational age of ≥ 36 weeks, born within ≤6 h, having pH≤7.00 or BD ≥ 16 mmol/L in the fetal cord blood gas obtained within one hour after delivery, 10-minute Apgar scores <5 or requiring constant resuscitation, and demonstrating intermediate or patients who underwent resuscitation and had moderate or severe encephalopathy findings according to Sarnat criteria were included. Babies with gestational age <36 weeks, more than 6-hour time-lapse after birth, birth weight <2000g, having congenital metabolic disease, family history of energy deficiency and other disorders leading to early encephalopathy, severe cranial parenchymal bleeding, fatal coagulopathy, presence of chorioamnionitis in the mother, chromosomal anomalies and multiple organ pathologies were excluded[11,12].

Collection and analysis of blood samples and an aEEG recording

For blood gas analysis, 2-milliliter fetal blood samples were taken into the umbilical artery in all cases under anaerobic conditions. The needle tips were bent and covered with plastic caps after sampling to prevent fetal blood from contacting oxygen. Blood gas parameters were analyzed in the first 30 minutes under cold chain conditions.

aEEG waves were recorded with Olympic CFM Brainz Monitor (Natus Newborn Care, USA) for 80 hours. Needle electrodes sized 12x29mm (C3, C4, P3, P4, and COM) were used for recording. Of the five electrodes, purple and black colored C3 and P3 electrodes were placed in the left parietal area of the scalp, while the purple and black colored C4 and P4 electrodes were placed in the right parietal area, and the white reference electrode (COM) was settled to the middle at the frontal region. aEEG recordings were evaluated according to the "Pattern classification system" (Table 1)[13-15]. In the aEEG, epileptic seizure activities are usually seen as a sudden rise in the minimum amplitudes, usually accompanied by simultaneous elevations in the maximum amplitudes, and often followed by a short period of decreased amplitude. Epileptic seizures include single seizures, recurrent seizures (≥3 seizure patterns in 30 minutes), and status epilepticus (SE) "sawtooth pattern" It was classified as[16].

Table I: Definitions of the aEEG patterns

aEEG pattern	Definition
Continuous Normal Voltage (CNV)	Continuous background activity with minimal amplitude 5–10 μV and maximal amplitude 10–50 μV
Discontinuous Normal Voltage (DNV)	Discontinuous background activity with a minimum amplitude below 5μV and maximum amplitude >10 μV
Burst suppression (BS)	Discontinuous background with the lowest magnitude without variability at 0–2 μV intermixed with bursts of higher amplitude
Low Voltage(LV)	Continuous background with a very low voltage around or below 5 μV
Inactive, flat trace (FT)	Isoelectric background activity <5 μV
Seizure activity SZ	Single or repetitive ictal activity on a CNV/DNV background

Statistical Analysis

Statistical analysis was performed using SPSS version 24.0 software. Kruskal Wallis test was used to compare the normal non-distributed numerical variables of 4 independent groups; Adjusted p values were evaluated for post-hoc analysis. The Friedmann test was used to evaluate the three dependent groups, and the marginal homogeneity method was chosen as the post hoc method. The results were added as frequency, mean, percentage, and standard deviation (SD). Fisher Exact and Mann-Whitney U tests were used for categorical variables in the study. P values <0.05 were considered significant.

RESULTS

The gestational age of the cases was 38.13±1.30 weeks. The mean birth weights were 3187±491 grams, and the male/female ratio was 66/36 (64.7%/35.3%). 57 cases (55.9%) were delivered by the normal spontaneous vaginal route, and 45 (44.1%) by cesarean section (C/S). The blood gas analysis revealed that the mean baseline pH and BD values were 6.89±0.13 and 19.50±4.40 mmol/L, respectively. According to Sarnat's criteria, 47 (%46.1) patients had moderate and 55 (%53.9) cases had severe encephalopathy in the clinical evaluation of the cases. The aEEG recordings at the 24th, 48th, and 72nd hours during the hypothermia treatment periods were significantly different from each other. The number of patients with continuous normal voltage (CNV) and discontinuous normal voltage (DNV) increased, while those having burst suppression (BS) and low voltage (LV) reduced over the period (Figure 1).

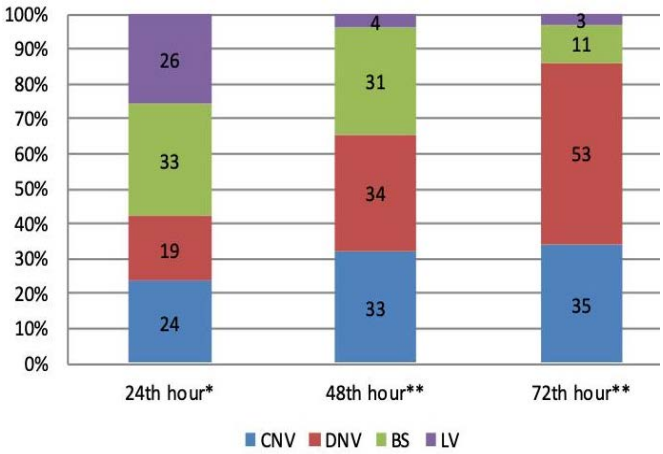

Figure 1: aEEG findings recorded in patients over the 0-72 hour period.

*CNV: Continuous Normal Voltage, DNV: Discontinuous Normal Voltage, BS: Burst suppression, LV: Low Voltage, FT: Inactive, flat trace, MH: Marginal homogeneity. Friedmann Test results:p:<0.001 *24h vs. 48h. MH=6.188; p<0.001. **48h vs. 72h. MH=3.207; p:0.001. ***24h vs. 72h. MH=6.902; p:<0.001*

There was a significant difference in BD values according to aEEG findings in all periods. However, differences in mean pH were only significant in aEEG measurements at 72nd hours (Table II).

Table II: Mean base deficit (BD) and pH values classified with EEG findings at different time points

		n	Mean	SD	95% CI		KW	p-value*
					Lower	Upper		
	24h							
Base deficit	CNV	24	16.83	2.023	15.98	17.68	32.819	**<0.001**
	DNV	19	18.24	3.321	16.64	19.84		
	BS	33	18.86	3.189	17.73	19.99		
	LV	26	23.68	5.174	21.59	25.78		
	Total	102	19.50	4.402	18.63	20.37		
pH	CNV	24	6.93	0.099	6.89	6.97	3.973	0.264
	DNV	19	6.91	0.110	6.86	6.96		
	BS	33	6.90	0.118	6.86	6.94		
	LV	26	6.84	0.176	6.77	6.91		
	Total	102	6.89	0.132	6.87	6.92		
	48h							
Base deficit	CNV	33	17.19	2.284	16.38	18.00	23.687	**<0.001**
	DNV	34	18.96	3.775	17.64	20.27		
	BS	31	22.01	5.013	20.17	23.85		
	LV	4	23.65	6.232	13.73	33.57		
	Total	102	19.50	4.402	18.63	20.36		
pH	CNV	33	6.92	0.106	6.88	6.96	4.482	0.214
	DNV	34	6.89	0.122	6.85	6.94		
	BS	31	6.88	0.150	6.83	6.94		
	LV	4	6.75	0.198	6.43	7.06		
	Total	102	6.89	0.132	6.87	6.92		
	72h							
Base deficit	CNV	35	17.31	2.644	16.40	18.21	24.992	**<0.001**
	DNV	53	19.55	3.554	18.57	20.53		
	BS	11	22.55	4.893	19.26	25.83		
	LV	3	33.00	1.732	28.70	37.30		
	Total	102	19.50	4.402	18.63	20.36		
pH	CNV	35	6.92	0.103	6.88	6.96	9.186	0.027**
	DNV	53	6.90	0.116	6.87	6.94		
	BS	11	6.85	0.185	6.72	6.97		
	LV	3	6.57	0.023	6.52	6.63		
	Total	102	6.89	0.132	6.87	6.92		

**: Kruskal Wallis test was used.*

There was a significant relationship between the level of AEEG abnormality and the frequency of convulsions. It was found that cases with BS and LV at the 24th-hour aEEG record had more frequent convulsions compared to patients with CNV and DNV (Fisher exact test = 67.011; p: <0.001) (Figure 2).

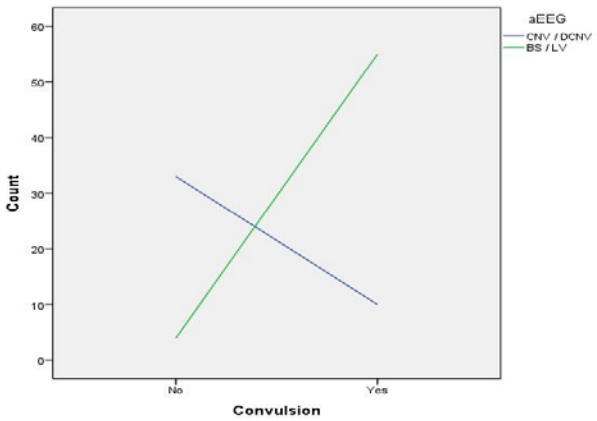

Figure 2: aEEG abnormality and the frequency of convulsions

65 patients (63.7%) experienced convulsion. The mean BD in patients with and without convulsions was 20.64±4.70 and 17.48±2.92, respectively (Z=3.912; p=0.001). The mean pH levels were 6.88±0.145 mmol/L and 6.92±0.103 mmol/L in patients with and without convulsions, respectively and there was no significant difference in terms of the pH levels between them (Z=0.899; p=0.369).

DISCUSSION

Indicators of metabolic acidosis are pH levels and the degree of BD. pH levels < 7.00 mmol/L measured in the fetal cord blood suggests significant fetal acidemia, BD levels BD >16 mmol/L points out in severe hypoxia5. In our study, it was determined that blood gas analysis mean baseline pH: 6.89 ± 0.13 and BD: 19.50 ± 4.40 mmol / L. The cases included in our study were moderate in 46.1% of cases and severe encephalopathy in 53.9% of cases according to Sarnat's criteria. This study revealed that there is a relationship between BD and neonatal convulsion and aEEG findings in patients admitted to the neonatal intensive care unit with a diagnosis of PA.

Amplitude-EEG has a very sensitive early predictive value in estimating prognosis[17]. Amplitude-EEG has been used as a tool for monitoring brain function throughout the treatment period[18,19]. Hallberg et al.20 reported that asphyctic infants treated with hypothermia who had an aEEG abnormality that persisted beyond 24 hours of delivery showed poor neurological outcomes at the end of one year. Chandrasekaran et al.[8] suggested that the effect of six-hour aEEG was inadequate in predicting the prognosis of asphyxia. The authors state that favorable outcomes could be achieved despite an abnormal early aEEG and a persistent abnormal aEEG at 48 hours or later was also associated with a negative neurodevelopmental outcome. Amplitude-EEG has been used as a tool to monitor brain function throughout the treatment period[18,19]. Hallberg et al.[20] reported that asphyxiated infants with aEEG abnormalities lasting more than 24 hours showed poor neurological outcomes at the end of one year. Chandrasekaran et al.[8] suggested that the effect of six-hour aEEG was inadequate in predicting the prognosis of asphyxia. The authors state that favorable outcomes could be achieved despite an abnormal early aEEG and a persistent abnormal aEEG at 48 hours or later was also associated with a negative neurodevelopmental outcome. In our study, a continuous normal voltage (CNV) was observed in 23.3% of the patients and 76.7% of the patients displayed abnormal aEEG findings in the first 24 hours of the hypothermia treatment. On the other hand, abnormal aEEG findings were observed in 68% of the patients for 48 hours.

It has been reported that the hypoxic birth of the baby with BD 12-16 mmol / L, BD> 16 mmol / L is associated with severe hypoxia of the baby, and BD> 20-25 m mol / L is associated with poor prognosis[5,21]. Hellström-Westas L et al.[14] determined that children demonstrating CNV or DNV on an aEEG show a favorable prognosis with a relatively lower risk of sequelae, while patients with BS, CLV, or FT on aEEG have a higher risk of mortality or morbidity. Peliowski A. et al.[22] too, have shown that background abnormalities in aEEG, including BS, LV, and CLV patterns, were associated with a significantly increased morbidity and mortality risk. In our study, we found that patients with LV and BS patterns in AEEG records had higher BD at the time of diagnosis. Qian J et al.[23] In their study, a close correlation was found between brain damage and pH. However, In our study, the differences in the mean pH were significant only for the aEEG measurements at 72nd hours.

Newborn convulsions are the most common symptom of brain injury in newborns and are suggestive of deterioration in brain function. In our study, 65 patients (63.7%) experienced

convulsions. Shellhaas et al.[24] reported that aEEG can provide sufficient information to detect seizures and changes caused by acute events. Besides, Akçay et al.[25] proposed aEEG monitoring in the follow-up of electrophysiological changes and electrographic seizures in newborns with acute brain injury. In the study of Fang Luo et al.[26] a significant relationship was found between epileptic electrical activity and prognosis, as well as aEEG pattern and prognosis. In our study, a relationship was found between aEEG and epileptic electrical activity. High BD levels at the time of diagnosis in PA cases are associated with poor prognosis[4]. In our study, the mean BD in patients with and without convulsions was 20.64 ± 4.70 and 17.48 ± 2.92 mmol / L, respectively. We detected significantly higher BD at the time of diagnosis in patients with convulsions (p = 0.001). There was no significant difference in patients with and without mean pH levels convulsion. Thorp et al; stated that routine umbilical cord pH monitoring is an objective criterion indicating the acid-base balance of the fetus, and it is sufficient to look only at pH from cord blood values. Qian J et al.[23] It was found that there was a close correlation between low brain pH in arterial cord blood between brain damage. In our study, there was no significant difference in patients with and without mean pH levels convulsion.

CONCLUSION

In this study, patients with abnormal aEEG findings and epileptic electrical activity were found to have higher BD at the time of diagnosis. We suggest that healthcare professionals dealing with perinatal asphyxia should be informed that the high BD levels at the time of diagnosis could affect neurodevelopmental prognoses such as abnormal aEEG findings and epileptic electrical activity.

Ethics Committee Approval: This study conformed to the principles of the 2008 Declaration of Helsinki and was approved by the local ethics committee of Harran University, Medical Faculty, Turkey (Approval date/number: 07.01.2019/190102).

Conflict of Interest: The authors declared no conflicts of interest.

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