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The efficacy of early S100B and aEEG in predicting the onset of brain injury in preterm infants and neurological outcome at hospital discharge

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Abstract: *To analyse the efficacy of early S100B and aEEG in predicting the occurrence of brain injury in preterm infants and neurological outcome at discharge. Eighty-five preterm infants admitted to the neonatology department of our hospital from June 2022 to June 2023 were selected for this study. 80 children were divided into three groups according to the clinical symptoms and imaging findings, i.e., the group with no brain injury, the group with periventricular-intraventricular haemorrhage, and the group with periventricular white matter softening. Comparison of the three groups of patients. Comparing the baseline data of the three groups of patients, the difference was not statistically significant, P>0.05. Comparing the postnatal blood gases and inflammatory indexes of the three groups of patients, it can be seen that the PH and BE of the periventricular-intraventricular haemorrhage group and periventricular white matter softening group were higher than those of the no-injury group, and the periventricular white matter softening group had the highest, P<0.05. The PCT and CRP of the three groups of patients were not statistically significant, and the differences were not statistically significant, P<0.05. In comparison with CRP, the difference was not statistically significant, P>0.05, and the relationship between S100B, aEEG and neurological outcome of preterm infants discharged from the hospital with brain injury has not been clearly established. S100B, aEEG indexes can help to predict early brain injury when preterm infants are discharged from the hospital, which effectively reduces the probability of brain injury in preterm infants, and is worth to be further promoted and applied in the clinic.*

Keywords: *S100B; aEEG; brain injury in preterm infants; neurological outcome*

1. Introduction

Neonatal brain injury is the outcome after brain injury caused by multiple pathological factors, which occurs on the basis of the original disease, causing the normal structure of brain cells to be destroyed and brain function to be abnormal. Clinically, it shows impaired consciousness, altered behavioural ability, abnormal muscle tone, loss of primitive reflexes, convulsions and brainstem symptoms can occur, and in severe cases, it can even be life-threatening. Regarding the etiology of neonatal brain injury, the most familiar is neonatal hypoxic-ischemic encephalopathy (HIE). Various other pathological factors can also trigger acute brain injury, such as inflammatory encephalopathy, hypoglycemic encephalopathy, bilirubin encephalopathy, metabolic encephalopathy, convulsive encephalopathy, and so on. Monitoring of brain injury can help predict the occurrence of brain injury in newborns and assess the severity and prognosis of brain injury [1].

In recent years, researchers have gradually explored reliable biomarkers of brain injury in preterm infants. It has been shown [2] that biomarkers such as S100B protein, NSE, neurofilament protein light chain and glial fibrillary acidic protein can help in the early screening of brain injury in preterm infants, in monitoring the progression of brain injury as well as in evaluating the efficacy of clinical neuroprotective treatments. In addition, alpha-II haemoglobin cleavage products, chemokines, melatonin and urinary metabolomics have been found to be closely associated with the diagnosis and prognostic assessment of brain injury in preterm infants, and are considered to be new biomarkers for the diagnosis of early brain injury. Currently, S100B protein, NSE and MBP have been widely used in the clinical diagnosis of brain injury in preterm infants because of their simple detection method and mature detection technology [3]. In contrast, the neonatal amplitude-integrated electroencephalogram (aEEG) is a brain function monitoring device that compresses and integrates the waveforms of the

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original EEG and displays them in a simplified form. The device can be operated and recorded at the crib side with video recording. It can be used for diagnosis and prognosis of neonatal brain injury, evaluation of neonatal brain development, and monitoring of neonatal convulsions. It is an important electrophysiological tool for evaluating neonatal brain function. Some studies have shown that the severity of aEEG is positively correlated with the degree of brain injury in the early and late stages of brain injury and its corresponding aEEG monitoring graphs, and that early aEEG monitoring has a high predictive value for the long-term prognosis of brain injury. Therefore, in the long-term prognosis of neonates, especially preterm infants, regular and periodic brain function monitoring is necessary [4]. However, other biomarkers have not yet been widely used in the clinic because of the high cost of detection and unclear pathophysiological mechanisms. Therefore, the aim of this study was to analyse the effectiveness of early S100B and aEEG in predicting brain injury in preterm infants.

2. Information and methods

2.1 Inclusion and exclusion criteria

Inclusion criteria: (1) birth gestational age <37 weeks, admitted to the hospital within 24 hours after birth and hospital stay ≥2 weeks; (2) perfect clinical data; (3) stable vital indicators. Exclusion criteria: (1) chromosomal abnormalities; (2) serious complications; (3) neurological malformations; (4) family members' refusal of the study; (5) midway withdrawal.

2.2 Research Methods

The newborns were grouped according to their brain imaging examinations. Cranial ultrasound was performed at 2-3 days, 1 week, 2 weeks, 3 weeks and 4 weeks after birth, and cranial MRI and video-EEG were performed before discharge from the hospital or when the gestational age was corrected to 40 weeks. Cranial ultrasound was used to classify PVH-IVH into 4 grades according to the Papile grading method, namely, echogenic phase, relatively normal phase, cystic cavity formation, and cystic cavity disappearance. If no abnormality was found on cranial ultrasound, it was considered normal. Cranial MRI suggesting foci of white matter softening, diffuse high or low signal and poor myelination may be present with white matter damage. Video EEG records background brain activity by amplification and filtering. The groupings were based on expert consensus on clinical application and the findings of head ultrasound and MRI, and were divided into the group with no brain damage, the group with periventricular-intraventricular haemorrhage, and the group with periventricular white matter softening. The periventricular-intraventricular haemorrhage group refers to the head ultrasound and MRI did not see obvious abnormal signals in the white matter area, and the periventricular white matter softening group refers to the B-mode ultrasound examination showing local or extensive strong echoes around bilateral ventricles.

2.3 Observation indexes

Comparison of the baseline data of the three groups of patients, comparative analysis of blood gases as well as inflammatory indexes of the three groups of patients after birth, and the relationship between early S100B, aEEG and neurological outcome of preterm infants with brain injuries at the time of discharge from the hospital

2.4 Statistical methods

Data were analysed using SPSS26.0 software; measurement data were expressed as ±s, using t-test; counts were expressed as percentages, using X2 test; and comparisons between multiple groups were made using the Z test, and differences were considered statistically significant if P>0.05.

3. Results

3.1 Comparison of baseline data of three groups of patients

Comparison of the baseline data of the three groups of patients, the difference is not statistically significant, P>0.05. As shown in Table 1.

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Table 1: Comparison of baseline data of three groups of patients

groups	number of examples	Gender		Gestational age (weeks)
		male	female	
brain injury-free group	44	21	23	29.87±1.36
Periventricular-intraventricular haemorrhage group	28	15	13	30.43±1.43
Periventricular white matter softening group	13	7	6	30.21±1.56
Z-value		0.573		3.124
P-value		0.214		0.047

3.2 Comparative analysis of blood gases and inflammatory indexes of the three groups of patients after birth

Analysing the data in the following table and comparing the blood gases and inflammatory indexes of the three groups of patients after birth, it can be seen that the PH and BE of the periventricular-intraventricular haemorrhage group and periventricular white matter softening group were higher than those of the group with no brain damage, and the periventricular white matter softening group was the highest, $P<0.05$; and the differences in the PCT and CRP of the three groups of patients were not statistically significant, $P>0.05$. As shown in table 2.

Table 2: Comparative analysis of postnatal blood gas and inflammatory indexes of the three groups of patients

groups	number of examples	PH	BE(mol/L)	PCT(ug/L)	CRP(mg/L)
brain injury-free group	44	6.97±0.05	2.34±0.38	8.02±3.57	31.25±9.16
Periventricular-intraventricular haemorrhage group	28	7.13±0.06	3.87±0.45	8.56±4.45	32.65±7.08
Periventricular white matter softening group	13	7.25±0.08	5.46±0.51	9.54±3.02	33.71±8.21
Z-value		2.541	2.273	1.780	1.374
P-value		0.042	0.036	0.052	0.061

3.3 Relationship between early S100B, aEEG and neurological outcome of preterm infants discharged from hospital with brain injury

Currently, it is widely recognised by scholars that neurodevelopmental deficits in brain-injured preterm infants may be related to inflammatory immune responses. Inflammatory exposure in utero can initiate an inflammatory immune response in the foetus, leading to an increase in pro-inflammatory cytokines, which can impair brain development, interfere with neuronal differentiation and apoptosis, as well as activate microglia to release inflammatory and cytotoxic mediators, and affect the integrity of the blood-brain barrier. Studies have shown that levels of pro-inflammatory cytokines increase shortly after birth, increasing the incidence of neonatal cerebral palsy and adversely affecting neurological prognosis. Thus, systemic inflammation has been identified as an important factor affecting the nervous system and neurodevelopmental disorders. In order to assess neurological prognosis, an initial assessment can be made by quantifying cytokines and chemokines.

4. Conclusions

Rapid advances in perinatal medicine have led to a significant increase in the survival rate of preterm infants; however, these preterm infants face short- and long-term impacts and threats to their quality of life from brain injury, which severely affects the growth and development of preterm infants and imposes a significant burden on the community and families [5]. In the United States, about 63,000 very low birth weight infants are born each year, accounting for 1.5% of live births, of which 25% to 50% will develop cognitive, behavioural, attentional, and social adjustment disorders, and 5% to 10% will develop movement disorders (e.g., cerebral palsy). In the past, it was believed that the main cause of brain injury in preterm infants was perinatal hypoxia-ischemia, and its classical pathological forms were periventricular-intraventricular hemorrhage (PVI-IVH) and periventricular white matter softening (PVL) [6]. With the accumulation of clinical epidemiological data and the development of clinical

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neuroimaging and developmental biology in recent years, there has been great progress in the understanding of both the etiology, pathogenesis, and neuropathological alterations of brain injury in preterm infants, and in particular, the important mechanism of perinatal intrauterine infection/inflammation that leads to white matter injury and the subsequent disruption of brain development leading to adverse neurological outcomes has attracted widespread attention. How to effectively prevent and reduce brain injury in preterm infants has become a social challenge of great concern. Finding ways to be able to diagnose the relevant indicators at an early stage can provide timely intervention and treatment for the affected children, which is the key to improving clinical symptoms, obtaining a good prognosis, improving the quality of life of preterm infants, and promoting the development of medicine [7].

Currently, imaging is the main method to diagnose brain injury in preterm infants, including headultrasound (HUS) head magneticresonanceimaging (MRI), etc[8]. Therefore, the search for serological markers of early brain injury with high specificity and easy operation has gradually become a research hotspot. Studies have shown that serological markers such as S100B protein, neuroflament (Nf), glial fibrillary acidic protein (GFAP) are helpful in the early clinical screening and monitoring of brain injury in preterm infants. Brain injury in preterm infants, to monitor the progression of brain injury and to assess the neurological prognosis.

S100B (relative molecular mass 21 000) is an acidic calcium-binding protein produced mainly by glial cells, and is most abundant in the nervous system (90.9 per cent), with small amounts also distributed in tissues such as muscle (7.1 per cent) and fat (1.77 per cent). Immediately after the onset of brain injury, S100B is released from damaged glial cells into the peripheral circulation and subsequently excreted via the kidneys (98%) with a half-life in the blood of about 1.5 h. Therefore, it can be used as a biomarker for acute brain injury. In addition, aEEG technology has been widely used in clinical practice for half a century since its invention, and its practical value of diagnosis and monitoring has been recognised by academics[9].

The diagnosis of neonatal brain injury needs to be based on birth history, clinical manifestations, cranial ultrasound and MRI and other factors, but the existing clinical detection methods are not only generally sensitive, but also have obvious lagging effect.The study of metabolite-related biomarkers, such as S100B, aEEG, etc., can not only provide clinical work with high sensitivity and specificity, but also help to deepen the understanding of the pathology and physiology of brain injury [10]. However, at present, the biomarkers of brain injury mainly focus on neonatal brain injury such as NE, and there are fewer studies on preterm infants, and there are shortcomings such as single-centre, small sample sizes, and lack of thresholds, etc. A large number of multi-centre clinical studies are still needed to draw reliable conclusions on the types of diseases, sampling times and concentration thresholds.

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