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Color Doppler ultrasound evaluation of asphyxial neonatal left ventricular function and its correlation with target organ damage

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ABSTRACT

Objective: To study the color Doppler ultrasound parameters of asphyxial neonatal left ventricular function and the correlation with target organ damage. **Methods:** Normal neonates, mildly asphyxial neonates and severely asphyxial neonates born in our hospital between January 2014 and December 2015 were selected as the control group (n = 46), mild asphyxia group (n = 37) and severe asphyxia group (n = 23) respectively. On the 1st day after birth, color Doppler ultrasound was used to evaluate left ventricular function, and serum was collected to determine myocardial tissue injury, brain tissue injury and brain tissue metabolism indexes. **Results:** Color Doppler ultrasound parameters cardiac output (CO), ejection fraction (EF) and left ventricular fraction shortening (FS) as well as serum folate and vitamin B12 content of mild asphyxia group and severe asphyxia group were significantly lower than those of control group ($P<0.05$) while serum creatine kinase isoenzyme (CK-MB), troponin I (cTnI), troponin T (cTnT), S100B, neuron-specific enolase (NSE), creatine kinase BB (CK-BB), glycogen phosphorylase BB (GPBB), and homocysteine (Hcy) content were significantly higher than those of control group ($P<0.05$); CO, FS and EF as well as serum folate and vitamin B12 content of severe asphyxia group were significantly lower than those of mild asphyxia group ($P<0.05$) while serum CK-MB, cTnT, cTnI, S100B, NSE, CK-BB, GPBB and Hcy content were significantly higher than those of mild asphyxia group ($P<0.05$). **Conclusions:** Color Doppler ultrasound can accurately assess asphyxial neonatal left ventricular function damage degree and is closely related to myocardial tissue injury and brain tissue injury degree.

1. Introduction

Neonatal asphyxia is a common clinical cause of neonatal death and disability, and the asphyxia-induced hypoxemia can cause acidosis and hypoxia, which further increases the risk of damage in multiple viscera[1–2]. The heart and brain are with active metabolism and large oxygen consumption, and they are very sensitive to anoxia. The risk of heart and brain tissue damage is big after neonatal asphyxia, and early diagnosing tissue ischemia hypoxia and providing corresponding treatment and intervention are the key measures to improve the prognosis of neonatal asphyxia[3–4]. Myocardial injury caused by ischemia hypoxia will directly affect the left ventricular pump function, and color Doppler ultrasound is an important auxiliary examination method to assess ventricular function. In the following study, the left ventricular function of asphyxial newborn was evaluated by the color Doppler ultrasound and the correlation between ultrasound parameters and target organ damage was analyzed.

2. Materials and methods

2.1. Research subjects

The neonates born in our hospital between January 2014 and December 2015 were selected, the medical records were reviewed, and according to the Apgar score, normal neonates, mildly asphyxial neonates and severely asphyxial neonates were selected as research subjects. Normal neonates (n = 46) were the control group, were with Apgar score 8–10 points and (9.12±0.99) points in average, included 27 male cases and 19 female cases and were

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with gestational age of (38.5±5.2) weeks; mildly asphyxial neonates (n = 37) were the mild asphyxia group, were with Apgar score 4–7 points and (6.23±0.67) points in average, included 22 male cases and 15 female cases and were with gestational age (37.6±4.5) weeks; severely asphyxial neonates (n = 23) were the severe asphyxia group, were with Apgar score 0–3 points and (2.32±0.35) points in average, included 13 male cases and 10 female cases and were with gestational age of (37.6±4.2) weeks. The three groups of neonates were not statistically significant in general information.

2.2. Neonatal color Doppler ultrasound evaluation methods

On the 1st day after birth, the Vivid E9 color Doppler diasonograph from American GE Company was used for cardiac color Doppler ultrasonography. Left sternal border left ventricular long axis and chordae tendineae horizontal section were selected to get a clear image, and then the left ventricular cardiac output (CO), ejection fraction (EF) and left ventricular fraction shortening (FS) were measured. Each index was measured for three times in three different cardiac cycles, and then the average was calculated.

2.3. Serum sample collection and index detection methods

On the 1st day after birth, 3 mL of peripheral venous blood was collected from two groups of neonates and centrifuged to get serum, and then the enzyme-linked immunosorbent assay kits were used to determine creatine kinase isoenzyme (CK-MB), troponin I (cTnI), troponin T (cTnT), S100B protein and neuron-specific enolase (NSE) as well as creatine kinase BB (CK-BB), glycogen phosphorylase BB (GPBB), homocysteine (Hcy), folate and vitamin B12 content.

2.4. Statistical analysis

SPSS20.0 software was used to input and analyze data, measurement data ($\bar{x}\pm s$) comparison among three groups was by variance analysis, pair-wise comparison was by $LSD-t$ test, the correlation between two measurement data was by Pearson test and $P<0.05$ indicated statistical significance in differences.

3. Results

3.1. Ultrasound parameters of left ventricular function

Analysis of ultrasound parameters CO, FS and EF of left ventricular function among three groups of neonates is as follows: CO, FS and EF of mild asphyxia group and severe asphyxia group were significantly lower than those of control group ($P<0.05$); CO, FS and EF of severe asphyxia group were significantly lower than those of mild asphyxia group. Differences in pair-wise comparison of ultrasound parameters CO, FS and EF of left ventricular function were statistically significant among three groups of neonates ($P<0.05$) (Table 1).

Table 1
Comparison of ultrasound parameters of left ventricular function among three groups of neonates ($\bar{x}\pm s$).

Groups	n	CO (L)	FS	EF
Control group	46	0.87±0.11	35.13±5.52	68.65±8.32
Mild asphyxia group	37	0.73±0.08[a]	30.57±4.46[a]	61.34±5.67[a]
Severe asphyxia group	23	0.61±0.07[ab]	24.16±3.28[ab]	54.42±6.71[ab]
F		7.829	7.283	6.993
P		<0.05	<0.05	<0.05

[a]: compared with control group, $P<0.05$; [b]: compared with mild asphyxia group, $P<0.05$.

3.2. Serum myocardial tissue injury indexes

Analysis of serum myocardial tissue injury indexes CK-MB, cTnT and cTnI among three groups of neonates is as follows: serum CK-MB, cTnT and cTnI content of mild asphyxia group and severe asphyxia group were significantly higher than those of control group ($P<0.05$); serum CK-MB, cTnT and cTnI content of severe asphyxia group were significantly higher than those of mild asphyxia group ($P<0.05$). Differences in pair-wise comparison of serum CK-MB, cTnT and cTnI content were statistically significant among three groups of neonates ($P<0.05$) (Table 2).

Table 2
Comparison of serum myocardial tissue injury indexes among three groups of neonates($\bar{x}\pm s$) .

Groups	n	CK-MB (U/L)	cTnT (ng/mL)	cTnI (ng/mL)
Control group	46	23.46±4.21	0.41±0.06	1.35±0.16
Mild asphyxia group	37	36.53±5.24[a]	0.78±0.09[a]	1.83±0.22[a]
Severe asphyxia group	23	81.35±9.37[ab]	1.13±0.15[ab]	3.72±0.51[ab]
F		14.598	12.951	18.862
P		<0.05	<0.05	<0.05

[a]: compared with control group, $P<0.05$; [b]: compared with mild asphyxia group, $P<0.05$.

3.3. Serum brain tissue injury indexes

Analysis of serum brain tissue injury indexes S100B, NSE, CK-BB and GPBB among three groups of neonates is as follows: serum S100B, NSE, CK-BB and GPBB content of mild asphyxia group and severe asphyxia group were significantly higher than those of control group ($P<0.05$); serum S100B, NSE, CK-BB and GPBB content of severe asphyxia group were significantly higher than those of mild asphyxia group ($P<0.05$). Differences in pair-wise comparison of serum S100B, NSE, CK-BB and GPBB content were statistically significant among three groups of neonates ($P<0.05$) (Table 3).

3.4. Serum brain tissue metabolism indexes

Analysis of serum brain tissue metabolism indexes Hcy, folate and vitamin B12 among three groups of neonates is as follows: serum

Table 3
Comparison of serum brain tissue injury indexes among three groups of neonates ($\bar{x}\pm s$, ng/mL).

Groups	*n*	S100B	NSE	CK-BB	GPBB
Control group	46	0.49±0.06	35.58±5.52	53.42±7.81	4.58±0.67
Mild asphyxia group	37	0.73±0.08[a]	56.26±7.81[a]	64.45±9.34[a]	7.15±0.88[a]
Severe asphyxia group	23	1.14±0.15[ab]	93.42±10.24[ab]	113.56±13.42[ab]	11.35±1.42[ab]
F		11.582	17.856	10.974	13.453
P		<0.05	<0.05	<0.05	<0.05

[a]: compared with control group, $P<0.05$; [b]: compared with mild asphyxia group, $P<0.05$.

Hcy content of mild asphyxia group and severe asphyxia group were significantly higher than that of control group ($P<0.05$) while folate and vitamin B12 content were significantly lower than those of control group ($P<0.05$); serum Hcy content of severe asphyxia group was significantly higher than that of mild asphyxia group ($P<0.05$) while folate and vitamin B12 content were significantly lower than those of mild asphyxia group ($P<0.05$). Differences in pair-wise comparison of serum Hcy, folate and vitamin B12 content were statistically significant among three groups of neonates ($P<0.05$) (Table 4).

Table 4
Comparison of serum brain tissue metabolism indexes among three groups of neonates ($\bar{x}\pm s$).

Groups	*n*	Hcy (μmol/L)	Folate (nmol/L)	Vitamin B12 (nmol/L)
Control group	56	4.52±0.68	17.87±2.21	0.63±0.08
Mild asphyxia group	42	7.68±0.91[a]	13.03±1.67[a]	0.50±0.06[a]
Severe asphyxia group	23	14.45±1.78[ab]	10.31±1.32[ab]	0.37±0.05[ab]
F		23.282	7.698	9.187
P		<0.05	<0.05	<0.05

[a]: compared with control group, $P<0.05$; [b]: compared with mild asphyxia group, $P<0.05$.

3.5. Correlation analysis results

The Pearson test analysis of the correlation between color Doppler ultrasound parameters CO, FS, EF of left ventricular function and serum indexes CK-MB, cTnT, cTnI, S100B, NSE, CK-BB, GPBB, Hcy, folate, vitamin B12 showed that CO, FS and EF levels were negatively correlated with serum CK-MB, cTnT, cTnI, S100B, NSE, CK-BB, GPBB and Hcy content, and positively correlated with serum folate and vitamin B12 content.

4. Discussion

The most prominent pathological physiological changes of neonatal asphyxia are hypoxemia and metabolic acidosis, which can cause the heart, brain and other important viscera damage and increase the morbidity and mortality of the disease[5]. Hypoxic-ischemic damage will affect the cardiac diastolic function, and accurate assessment of neonatal cardiac function can provide the basis for neonatal asphyxia condition judgment[6-8]. Color Doppler ultrasound is the most convenient and intuitive way for clinical evaluation of the cardiac morphology and function, and in recent years, with the development of ultrasonic inspection instruments and inspection technique, color Doppler ultrasound is increasingly used in neonatal cardiac function evaluation[9]. In the study, color Doppler ultrasound assessment of asphyxial neonatal and normal neonatal left ventricular function showed that CO, FS and EF of mild asphyxia group and severe asphyxia group were significantly lower than those of control group ($P<0.05$); CO, FS and EF of severe asphyxia group were significantly lower than those of mild asphyxia group ($P<0.05$). This means that asphyxia will affect the neonatal left ventricular function, which is characterized by the decreased volume ejection and ejection fraction as well as worsened ventricular compliance.

Myocardial tissue is with active metabolism and extremely sensitive to the hypoxia caused by asphyxia, and hypoxia-induced myocardial tissue damage can lead to cell rupture and cause the CK-MB, cTnT, cTnI and other metabolic enzymes and structural proteins in the cytoplasm released into the blood[10-12]. In the study, the comparison and analysis of serum myocardial tissue damage indexes between asphyxial neonates and normal neonates showed that serum CK-MB, cTnT and cTnI content of mild asphyxia group and severe asphyxia group were significantly higher than those of control group ($P<0.05$); serum CK-MB, cTnT and cTnI content of severe asphyxia group were significantly higher than those of mild asphyxia group ($P<0.05$). This means that the neonatal asphyxia can cause the damage and rupture of myocardial cells, and the release of metabolic enzymes and structural proteins in the cytoplasm into the blood circulation. Further analysis of the correlation between color Doppler parameters of left ventricular function and myocardial tissue damage indexes showed that CO, FS and EF levels were negatively correlated with serum CK-MB, cTnT and cTnI content. Thus it confirms that the cardiac color Doppler parameters can not only assess the left ventricular function of asphyxial newborn, but are also closely related to the myocardial hypoxic-ischemic damage degree.

Hypoxemia can not only cause myocardial tissue damage, but can also cause anoxic injury to brain tissue. In addition, cardiac output decrease will further affect the blood perfusion of brain tissue and aggravate the injury caused by ischemia hypoxia. S100B is the structural protein in brain tissue glial cells and is involved in the regulation of cellular structure stability. NSE, CK-BB and GPBB are the three types of key enzymes in brain tissue that adjust the

energy metabolism, and NSE can adjust the transformation between phosphoenolpyruvic acid and 2-phosphoglyceric acid, promote the glycolytic pathway and increase the energy supply; CK-BB can regulate and promote the energy metabolism of neurons and glial cells[13-14]; GPBB can regulate glycogenolysis, promote glycogen mobilization and supply energy under ischemic-hypoxic condition[15]. In the study, the comparison and analysis of serum brain tissue damage indexes between asphyxial neonates and normal neonates showed that serum S100B, NSE, CK-BB and GPBB content of mild asphyxia group and severe asphyxia group were significantly higher than those of control group (P<0.05) and negatively correlated with CO, FS and EF levels. It confirms that neonatal asphyxia will cause brain tissue injury and cardiac color Doppler parameters are closely related to the degree of cerebral hypoxic-ischemic injury.

In recent years, study of neonatal asphyxia and neonatal hypoxic-ischemic encephalopathy shows that Hcy metabolic disorders are closely associated with hypoxia-induced neonatal brain tissue injury. Hcy is the intermediate of methionine cycle, and its metabolism uses folate and vitamin B12 as coenzymes; in the case of folate and vitamin B12 deficiency, Hcy goes through metabolic disorder and accumulates in the body, causing the brain tissue damage[16]. Hcy damage to brain tissue is mainly done by way of endothelial dysfunction, and the endothelial dysfunction caused by Hcy can aggravate the microcirculation disturbance and cerebral ischemia hypoxia[17]. In the study, the analysis of brain Hcy metabolism indexes showed that serum Hcy content of mild asphyxia group and severe asphyxia group were significantly higher than that of control group (P<0.05) and negatively correlated with CO, FS and EF levels while folate and vitamin B12 content were significantly lower than those of control group (P<0.05) and positively correlated with CO, FS and EF levels. This means that the neonatal asphyxia can cause the metabolic disorders and abnormal accumulation of Hcy, and cardiac color Doppler parameters are closely related to the metabolic disorder degree of Hcy.

The study results show that color Doppler ultrasound can accurately assess asphyxial neonatal left ventricular function damage degree and is closely related to myocardial tissue injury and brain tissue injury degree.

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