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Correlation between the umbilical artery flow ultrasound parameters of intrauterine fetal distress and fetal ischemic hypoxic damage

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ABSTRACT

Objective: To study the correlation between the umbilical artery flow ultrasound parameters of intrauterine fetal distress and fetal ischemic hypoxic damage. **Methods:** A total of 158 puerperae who gave birth in our hospital between July 2016 and June 2017 were selected and divided into the intrauterine distress group (Apgar<7 points) and normal pregnancy group (Apgar≥7 points) according to the neonatal Apgar score, the umbilical artery flow ultrasound parameters at 24-30 weeks, 31-36 weeks and 37-41 weeks of gestation were determined, and the umbilical arterial blood gas parameters and oxidative stress molecule levels were determined. **Results:** At 24-30 weeks, 31-36 weeks and 37-41 weeks of gestation, umbilical arterial RI, PI and S/D of intrauterine distress group were significantly higher than those of normal pregnancy group; umbilical arterial pH and PaO_2 of intrauterine distress group were significantly lower than those of normal pregnancy group and negatively correlated with RI, PI and S/D while $PaCO_2$ and lactic acid levels were significantly higher than those of normal pregnancy group and positively correlated with RI, PI and S/D; SOD, GSH-px and CAT levels in umbilical artery of intrauterine distress group were significantly lower than those of normal pregnancy group and negatively correlated with RI, PI and S/D while MDA and 8-OHdG levels were significantly higher than those of normal pregnancy group and positively correlated with RI, PI and S/D. **Conclusion:** Umbilical artery flow ultrasound characteristics of intrauterine fetal distress are characterized by the increased resistance and decreased blood flow and are correlated with the degree of fetal hypoxia and oxidative stress.

1. Introduction

Fetal intrauterine distress, also known as fetal intrauterine hypoxia, is the fetal acute or chronic hypoxia in uterus of pregnant women caused by different pathological factors, which will cause adverse effects on the fetal and maternal health and safety. Fetal intrauterine hypoxia can increase the incidence of neonatal asphyxia and affect newborn health and life safety[1,2]. Epidemiological study has reported that 20%-30% of perinatal infant deaths are associated with fetal intrauterine distress[3]. Therefore, it is necessary to early predict the risk of fetal intrauterine distress and conduct effective prevention and intervention in clinical practice. Umbilical cord abnormality is the most common cause of fetal intrauterine distress, and the overturning of the cord blood vessels, the spiral absence and other abnormal factors can cause the blocked umbilical cord blood and the fetal ischemia hypoxia; the fetal distress caused by factors such as placental abruption and placenta previa can also be combined with abnormal blood flow in the umbilical cord. Ultrasonography can quantitatively evaluate the umbilical cord blood flow parameters[4], and we analyzed the correlation between the umbilical artery flow ultrasound parameters of intrauterine fetal distress and fetal ischemic hypoxic damage in the following study.

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2. Subjects and methods

2.1 Research subjects

A total of 158 puerperae who gave birth in our hospital between July 2016 and June 2017 were selected as the research subjects, all women received regular antenatal examination, and those with gestational hypertension disease, placenta previa, placental abruption, abnormal fetal position and fetal anomaly were eliminated. According to the neonatal Apgar score, the 158 puerperae were divided into the intrauterine distress group and normal pregnancy group. Intrauterine distress group were with neonatal Apgar score < 7 points, included 48 cases, were 25-37 years old and (29.2±4.4) years old in average, and were with gestational age of (38.6±5.5) weeks at delivery; normal pregnancy group were with neonatal Apgar score ⩾7 points, included 110 cases, were 24-35 years old and (28.7±4.7) years old in average, and were with gestational age of (38.9±5.8) weeks at delivery. There was no significant difference in general information between the two groups of puerperae (P>0.05).

2.2 Umbilical artery flow ultrasound evaluation

At 24-30 weeks, 31-36 weeks and 37-41 weeks of pregnancy, umbilical artery flow ultrasound parameters were determined during antenatal examination, and the method was as follows: Philips IU22 type of color Doppler diasonograph was used to determine umbilical artery flow ultrasound parameters, the probe frequency was set to 3.5 MHz, the blood flow diagram was obtained after the position of the umbilical artery was confirmed, five continuous diastolic and systolic blood flow diagrams were monitored, software was used to determine resistance index (RI), pulsatility index (PI), diastolic velocity (Vd) and systolic velocity (Vs), and the S/D ratio was calculated.

2.3 Umbilical arterial blood collection and index detection

Immediately after delivery of baby, about 15 cm of the umbilical cord was clipped with vessel clamp before the neonatal first cry, heparinized syringe needle was used to puncture umbilical artery and extract the umbilical arterial blood, and blood gas analyzer was used to test the pH, arterial partial pressure of oxygen (PaO_2) and arterial partial pressure of carbon dioxide ($PaCO_2$) as well as lactic acid content immediately; radioimmunoprecipitation kit from Nanjing Jiancheng Bio Company was used to detect superoxide dismutase (SOD), glutathione peroxidase (GSH-px), catalase (CAT), malondialdehyde (MDA) and 8-hydroxy-2-deoxyguanosine (8-OHdG) contents in umbilical arterial blood.

2.4 Statistical methods

SPSS 21.0 software was used to statistically process experimental data, measurement data analysis between two groups was by t test, correlation analysis was by Pearson test and P<0.05 indicated statistical significance in differences.

3. Results

3.1 Umbilical artery ultrasound parameters

At 24-30 weeks, 31-36 weeks and 37-41 weeks of gestation, umbilical arterial RI, PI and S/D of intrauterine distress group were significantly higher than those of normal pregnancy group, and differences in RI, PI and S/D were significant between the two groups (P<0.05).

3.2 Umbilical arterial blood gas analysis parameters

Analysis of umbilical arterial blood gas analysis parameters pH, PaO_2, $PaCO_2$ and lactic acid between intrauterine distress group and normal pregnancy group was as follows: umbilical arterial pH and PaO_2 of intrauterine distress group were significantly lower than those of normal pregnancy group while $PaCO_2$ and lactic acid levels were significantly higher than those of normal pregnancy group (P<0.05).

Table 1.

Comparison of umbilical artery ultrasound parameters between two groups of puerperae.

Groups	n	Gestational age	RI	PI	S/D
Intrauterine distress group	48	24-30 weeks of gestation	0.85±0.12*	1.32±0.18*	3.81±0.55*
		31-36 weeks of gestation	0.81±0.11*	1.29±0.17*	4.14±0.71*
		37-41 weeks of gestation	0.77±0.09*	1.35±0.20*	4.06±0.62*
Normal pregnancy group	110	24-30 weeks of gestation	0.61±0.04	0.87±0.11	3.11±0.48
		31-36 weeks of gestation	0.63±0.09	0.75±0.04	3.02±0.41
		37-41 weeks of gestation	0.59±0.07	0.79±0.09	3.06±0.46

*: comparison between intrauterine distress group and normal pregnancy group at the same gestational age, P<0.05.

Table 2.

Comparison of umbilical arterial blood gas analysis parameters between two groups of puerperae.

Groups	n	pH	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	Lactic acid (mmol/L)
Intrauterine distress group	48	6.92±0.92	35.22±5.72	62.41±8.79	4.49±0.87
Normal pregnancy group	110	7.29±0.87	54.19±8.25	36.38±5.63	2.31±0.42
T		7.928	8.571	9.274	8.928
P		<0.05	<0.05	<0.05	<0.05

Table 3.

Comparison of oxidative stress injury molecule levels in umbilical artery between two groups of puerperae.

Groups	*n*	Anti-oxidant enzyme levels (U/mL)			Oxidation product levels (μmol/L)	
		SOD	GSH-px	CAT	MDA	8-OHdG
Intrauterine distress group	48	38.51±5.56	52.67±7.83	29.22±4.47	7.49±0.91	11.25±1.75
Normal pregnancy group	110	83.26±9.58	121.24±19.82	68.64±8.59	4.28±0.67	5.52±0.89
T		13.584	11.372	18.028	8.294	10.947
P		<0.05	<0.05	<0.05	<0.05	<0.05

3.3 Oxidative stress injury molecule levels in umbilical artery

Analysis of oxidative stress injury molecules SOD, GSH-px, CAT, MDA and 8-OHdG levels in umbilical artery between intrauterine distress group and normal pregnancy group was as follows: SOD, GSH-px and CAT levels in umbilical artery of intrauterine distress group were significantly lower than those of normal pregnancy group while MDA and 8-OHdG levels were significantly higher than those of normal pregnancy group (P<0.05).

3.4 Correlation between ultrasound parameters and umbilical artery indexes

Pearson correlation analysis showed that umbilical artery flow RI, PI and S/D were negatively correlated with umbilical arterial pH and PaO_2 as well as SOD, GSH-px and CAT levels in umbilical artery, and positively correlated with $PaCO_2$ and lactic acid levels as well as MDA and 8-OHdG levels in umbilical artery.

Table 4.

Correlation analysis results between ultrasound parameters and umbilical artery indexes.

Parameters	RI		PI		S/D	
	r	*P*	*r*	*P*	*r*	*P*
pH	-0.682	<0.05	-0.539	<0.05	-0.624	<0.05
PaO_2	-0.715	<0.05	-0.610	<0.05	-0.695	<0.05
$PaCO_2$	0.618	<0.05	0.768	<0.05	0.728	<0.05
Lactic acid	0.653	<0.05	0.498	<0.05	0.526	<0.05
SOD	-0.705	<0.05	-0.627	<0.05	0.691	<0.05
GSH-px	-0.592	<0.05	-0.653	<0.05	-0.426	<0.05
CAT	-0.526	<0.05	-0.689	<0.05	-0.579	<0.05
MDA	0.637	<0.05	0.741	<0.05	0.717	<0.05
8-OHdG	0.694	<0.05	0.776	<0.05	0.774	<0.05

4. Discussion

Fetal distress was the high risk factor causing neonatal asphyxia and perinatal fetal death, and the survived newborn will have neural function damage and sequelae under the influence of long-term intrauterine hypoxia[5,6]. In the clinical practice, early prediction of the risk of fetal distress is helpful to early prevention and intervention, thus reducing the fetal distress damage to the mother and the newborn[7]. Abnormal umbilical cord blood is the pathological factor closely related to fetal intrauterine distress, abnormal umbilical cord will directly affect the umbilical artery flow state, and abnormal placental factors and maternal factors will be complicated by abnormal umbilical artery flow[8,9]. Therefore, the evaluation of umbilical artery flow characteristics can provide a reference for diagnosis, prediction and evaluation of fetal distress. Color Doppler ultrasound is a routine method for prenatal examination, which can not only evaluate fetal growth and development, but also quantitatively measure the parameters of umbilical artery flow. In the study, the analysis of the ultrasonic parameters of umbilical artery flow in normal pregnant women confirmed that the RI, PI and S/D of the umbilical artery gradually decreased with the extension of gestational week. The changes of umbilical arterial ultrasound features are associated with vascular resistance decrease, lumen expansion and blood flow increase, which also reflect that the blood perfusion of fetus and placenta are increasing with the process of pregnancy.

During the development of fetal distress, the abnormal umbilical artery flow caused by different pathological factors can affect the blood supply of the fetus and result in ischemic hypoxic injury. In order to define the changes of the umbilical artery flow ultrasound parameters of puerperae with fetal intrauterine hypoxia, the differences in umbilical artery flow ultrasound parameters were analyzed between puerperae with fetal intrauterine distress and puerperae with normal pregnancy, and the results showed that the RI, PI and S/D of intrauterine distress group were significantly higher than those of normal pregnancy group at different stages of pregnancy. This means that the umbilical artery flow resistance increases significantly while the blood flow decreases significantly in puerperae with intrauterine hypoxia, which will enhance the fetal ischemia hypoxia and anaerobic glycolysis process and cause local lactic acid accumulation[10,11]. In the study, the umbilical arterial blood gas analysis was used to further reflect the umbilical artery flow state and the fetal hypoxia, and the results showed that umbilical arterial pH and PaO_2 of intrauterine distress group were significantly lower than those of normal pregnancy group and negatively correlated with RI, PI and S/D while $PaCO_2$ and lactic

acid levels were significantly higher than those of normal pregnancy group and positively correlated with RI, PI and S/D. This indicates that the ultrasonic parameters of umbilical artery flow are correlated with the changes of umbilical arterial blood gas parameters caused by fetal uterine distress. The ultrasonic parameters can be used to evaluate the degree of umbilical artery flow decrease and fetal hypoxia.

Oxidative stress response activation is an important pathological link for intrauterine distress to cause fetal tissue and organ injury, oxygen free radical generation significantly increases under the hypoxia condition, and the biological structures of tissues and organs react with oxygen free radicals and develop oxidative damage. The oxidation reaction products of lipids and nucleic acids are MDA and 8-OHdG respectively, and the MDA and 8-OHdG can reflect the production of oxygen free radicals and the degree of oxidative stress response[12,13]. SOD, GSH-px, and CAT are native antioxidant enzymes in the body that can catalyze REDOX reaction and scavenge oxygen free radicals[14,15]. In the study, the analysis of the contents of these oxidative stress molecules in umbilical artery showed that SOD, GSH-px and CAT levels in umbilical artery of intrauterine distress group were significantly lower than those of normal pregnancy group while MDA and 8-OHdG levels were significantly higher than those of normal pregnancy group. This indicates that fetal distress can cause oxidative stress damage on the basis of ischemia hypoxia, the production of oxidative products significantly increases and the antioxidant enzymes are consumed in large quantities. Further analysis of the correlation between oxidative stress reaction and umbilical artery flow ultrasound parameters showed that SOD, GSH-px and CAT levels in umbilical artery were negatively correlated with RI, PI and S/D while MDA and 8-OHdG levels were positively correlated with RI, PI and S/D. This indicates that the ultrasonic parameters of umbilical artery flow can assess the degree of oxidative stress response induced by hypoxia.

To sum up, it is believed that Umbilical artery flow ultrasound characteristics of intrauterine fetal distress are characterized by the increased resistance and decreased blood flow and are correlated with the degree of fetal hypoxia and oxidative stress.

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