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Ultrasonic characteristics and clinical significance of umbilical cord blood flow in acute fetal distress

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ABSTRACT

Objective: To study ultrasonic characteristics of umbilical cord blood flow in acute fetal distress and its correlation with umbilical artery blood gas parameters, oxidative stress parameters, neonatal brain injury and myocardial injury.

Methods: The pregnant women delivered in Department of Obstetrics of our hospital were chosen during the period from May 2012 to August 2015. The pregnant women with acute fetal distress were included in the distress group, and the healthy pregnant women with no acute fetal distress were included in the control group. The resistance index (RI), pulsatility index (PI) and systolic/diastolic (S/D) ratio of umbilical artery were measured at 24–30 weeks, 31–36 weeks and 37–41 weeks of pregnancy. After delivery, umbilical artery blood was taken for analysis of blood gas and determination of oxidative stress parameters. The venous blood of newborns was taken to measure the myocardial injury and brain injury parameters.

Results: At 24–30 weeks, 31–36 weeks and 37–41 weeks of pregnancy, RI, S/D and PI in pregnant women of distress group were significantly higher than those in control group. The pH, contents of arterial partial pressure of oxygen, vitamin C, vitamin E, superoxide dismutase and glutathione peroxidase in umbilical artery blood in pregnant women of distress group was significantly lower than those in control group and negatively correlated with the umbilical artery RI, PI and S/D. The contents of partial pressure of carbon dioxide in artery, lactic acid and malondialdehyde in pregnant women of distress group were significantly higher than those in control group and positively correlated with the umbilical artery RI, PI and S/D. The contents of lactate dehydrogenase, hydroxybutyrate dehydrogenase, creatine kinase, creatine kinase-MB, S100B, neuron-specific enolase, creatine kinase-BB and Tau in newborns' venous blood in distress group were significantly higher than those in control group and positively correlated with the umbilical artery RI, PI and S/D.

Conclusions: The ultrasonic characteristics of umbilical cord blood flow in patients with acute fetal distress are increase of the resistance, reduction of blood flow, and significant reduction of ultrasonic parameters of RI, PI and S/D. The degree of hypoxia, oxidative stress, myocardial injury and brain injury can also be evaluated.

1. Introduction

Acute fetal distress is one of the serious complications in perinatal period and it refers to acute hypoxia of the fetus in the womb. Its pathological features are the circulatory and respiratory dysfunctions of the fetus in the womb, which will damage the heart, lung and brain of the fetus and other important visceral organs and lead to fetal death, neonatal asphyxia when it's serious. Besides, the survived fetus will leave the intrauterine nerve injury because of hypoxia for a long time[1–3]. The occurrence of fetal distress is related to various factors such as umbilical cord, placenta, maternal, fetal factors, *etc*. Hypertension during pregnancy is a common maternal factor to cause fetal distress. Placental abruption and placental previa are the common placental factors to cause fetal distress. Fetal malformation and congenital heart disease are the common fetal factors to cause fetal distress. And umbilical

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cord around the neck is the common umbilical cord factor to cause fetal distress[4,5]. At present, the fetal distress is mainly predicted and diagnosed by fetal heart rate monitoring and amniotic fluid monitoring in clinic. However, the sensitivity is not very satisfactory and it cannot detect the disease in the early phase and make intervention.

The growth, development and metabolism of fetus in the womb need umbilical cord to provide nutrition and oxygen. Under physiological conditions, the pressure differences between umbilical cord blood and maternal blood can guarantee adequate blood flow in the umbilical artery and adequate nutrition and oxygen of fetus. When the umbilical cord blood flow is reduced and the blood flow is not enough due to different pathological factors, the parent cannot provide the necessary nutrition and oxygen for the growth and development of the fetus, which can result in fetal distress[6,7]. Umbilical cord blood flow is an important channel to connect the fetus and the maternal body. Evaluating the characteristics of umbilical cord blood flow with ultrasound can provide references for the prediction and diagnosis of fetal distress[8]. In the following study, the characteristics and clinical significance of umbilical cord blood flow in patients with acute fetal distress were analyzed.

2. Materials and methods

2.1. Clinical data

Pregnant women delivering in our hospital in obstetrical department during the period of May 2012–August 2015 were selected and their medical history was reviewed. Inclusion criteria: (1) Receiving prenatal examination on a regular basis in our hospital and having complete medical history data; (2) umbilical arterial blood gas was analyzed immediately after delivery; (3) umbilical artery blood samples and peripheral blood samples of newborns were collected; (4) informed consent was obtained. Exclusion criteria: (1) Fetus with congenital heart disease or deformity; (2) with complications of placental abruption, placenta previa and premature rupture of membranes; (3) incomplete medical history data or missing clinical samples. A total of 179 pregnant women were included. Apgar score was used to determine whether they have fetal distress or not, and accordingly, they were divided into distress group and control group. There were 52 pregnant women in distress group with average age of (29.93 ± 4.78) years old. The pregnant weeks on average were (37.41 ± 5.51) weeks at delivery. There were 127 pregnant women in control group. The average age was (29.34 ± 4.25) years old. The pregnant weeks on average were (38.32 ± 5.23) weeks at delivery.

2.2. Methods

2.2.1. Detection of umbilical cord blood flow using ultrasonography

Cord blood flow ultrasound examinations were taken by using four-dimensional color ultrasonic diagnostic apparatus (GE, USA). The probe frequency was 3.5 MHz and the examinations were taken at 24–30 weeks, 31–36 weeks and 37–41 weeks of their pregnancy. Firstly, the conditions of biparietal diameter, placenta, umbilical cord, amniotic fluid and other parts were examined. Then, the ultrasound probe was placed at the ventral side of the fetus to acquire the umbilical artery blood flow signal and continuous blood flow signals of five cardiac cycles. The end-diastolic blood flow velocity and the end-systolic blood flow velocity were measured. The systolic/diastolic (S/D) ratio, resistance index (RI) and pulsatility index (PI) were calculated.

2.2.2. Analysis of umbilical cord blood gas and molecular detection

Umbilical cord arterial blood was taken to measure the pH, partial pressure of oxygen in artery (PaO_2), partial pressure of carbon dioxide in artery ($PaCO_2$) and lactic acid contents by using blood-gas analyzer. The contents of superoxide dismutase (SOD), glutathione peroxidase (GSH-pX), malondialdehyde (MDA), vitamin C (VitC) and vitamin E (VitE) were measured by radioimmunology precipitation assay kit provided by Nanjing Jiancheng Biological Company.

2.2.3. Detection of venous blood indexes of newborns

The neonatal peripheral vein blood was withdrawn and centrifuged. The contents of S100B protein, neuron specific enolase (NSE), creatine kinase-BB (CK-BB) and Tau protein in serum were determined by using ELISA, and the content of lactic dehydrogenase (LDH), α-hydroxybutyrate dehydrogenase (HBDH), creatine kinase (CK) and creatine kinase-MB (CK-MB) was measured by using automatic biochemical analyzer.

2.3. Statistical analysis

The data was input and analyzed by SPSS20.0. The measurement data was analyzed by *t*-test. The correlation analysis was carried out by Pearson test. Difference was regarded as statistical significance when $P < 0.05$.

3. Results

3.1. Umbilical artery blood flow indexes at different phases in pregnant women in the two groups

At 24–30 weeks, 31–36 weeks and 37–41 weeks of pregnancy, the values of RI, S/D and PI of pregnant women in distress group were significantly higher than those in control group (Table 1).

3.2. Parameters of umbilical arterial blood gas and oxidative stress

Analyses of umbilical arterial blood gas parameters of pregnant women in the two groups are as follows: pH (6.96 ± 0.78 *vs.* 7.21 ± 0.95) and PaO_2 [(36.53 ± 6.14) *vs.* (55.25 ± 7.85) mmHg] of umbilical artery blood of pregnant women in distress group were significantly lower than those of control group. $PaCO_2$ [(60.41 ± 9.25) *vs.* (35.42 ± 4.86) mmHg] and lactic acid [(4.51 ± 0.78 *vs.* 2.25 ± 0.33) mmol/L] were significantly higher than those of control group. Analyses of oxidative stress parameters are as follows: the contents of SOD [(69.33 ± 9.14) *vs.* (94.52 ± 11.47) IU/L], GSH-Px [(98.67 ± 11.76) *vs.* (165.65 ± 22.37) IU/L], VitC [(22.15 ± 3.52) *vs.* (35.25 ± 5.69) μg/mL], VitE [(4.68 ± 0.74) *vs.* (7.92 ± 1.03) μg/mL] of arterial blood of pregnant women in distress group were significantly

Table 1
Comparison of umbilical artery blood flow indexes in two groups at different pregnant phases (mean ± SD).

Group	RI			PI			S/D		
	24–30 weeks	31–36 weeks	37–41 weeks	24–30 weeks	31–36 weeks	37–41 weeks	24–30 weeks	31–36 weeks	37–41 weeks
Distress group (n = 52)	0.86 ± 0.11*	0.82 ± 0.09*	0.79 ± 0.10*	1.36 ± 0.18*	1.28 ± 0.15*	1.32 ± 0.16*	4.08 ± 0.62*	4.29 ± 0.80*	4.11 ± 0.58*
Control group (n = 127)	0.65 ± 0.07	0.63 ± 0.08	0.59 ± 0.05	0.83 ± 0.11	0.78 ± 0.09	0.92 ± 0.12	3.04 ± 0.49	2.49 ± 0.33	2.21 ± 0.29

*: $P < 0.05$ compared with control group.

lower than those of control group. The contents of MDA [(26.85 ± 3.58) *vs.* (14.41 ± 1.95) mmol/L] were significantly higher than those of control group (Table 2).

3.3. Parameters of neonatal venous blood myocardial injury and brain injury

Analyses of parameters of neonatal venous blood myocardial injury and brain damage of pregnant women in the two groups are as follows: the contents of LDH [(154.52 ± 20.14) *vs.* (68.52 ± 10.35) IU/L], HBDH [(188.31 ± 24.29) *vs.* (74.63 ± 14.67) IU/L], CK [(402.56 ± 54.76) *vs.* (105.75 ± 15.86) IU/L], CK-MB [(46.97 ± 6.82) *vs.* (17.85 ± 2.63) IU/L] in neonatal venous blood of distress group were significantly higher than those of control group. Analyses of parameters of brain damage are as follows: the contents of S100B [(1.42 ± 0.22) *vs.* (0.42 ± 0.06) ng/mL], NSE [(86.51 ± 10.15) *vs.* (25.42 ± 3.52) ng/mL], CK-BB [(114.52 ± 16.49) *vs.* (33.52 ± 5.64) ng/mL], Tau [(1.56 ± 0.22) *vs.* (0.59 ± 0.07) ng/mL] in neonatal venous blood of distress group were significantly higher than those of healthy group (Table 3).

3.4. The correlation of umbilical artery ultrasound parameters and the molecular indicators

Test of Pearson revealed that PI, S/D and RI of umbilical artery were negatively correlated with pH value, PaO_2, VitC, VitE, SOD and GSH-Px contents in umbilical arterial blood, and positively correlated with $PaCO_2$, lactic acid and MDA contents in umbilical artery blood, LDH, HBDH, CK, CK-MB, S100B, NSE, CK-BB and Tau in neonatal venous blood.

4. Discussion

Umbilical blood flow is an important channel connecting the fetus and maternal body where nutrients and oxygen can be delivered by umbilical artery[9,10]. When the acute fetal distress happens, influenced by maternal, placental, fetal and umbilical factors, the umbilical cord blood flow and fetal infusion are reduced, which in turn leads to circulatory and respiratory dysfunctions of fetus in the womb[11,12]. In this study, the parameters of RI, PI and S/D of umbilical blood flow were evaluated by color Doppler ultrasound. In the course of normal pregnancy, RI, PI and S/D decrease gradually with the prolongation of gestation, development of placental vascular bed, gradual expansion of lumen, gradual reduce of resistance and increase of blood flow of the umbilical artery. When the acute fetal distress happened, RI, PI and S/D of pregnant women of distress group were significantly higher than those in control group detected by color Doppler ultrasound at the pregnancy of 24–30 weeks, 31–36 weeks and 37–41 weeks. This shows that the ultrasound of umbilical cord blood flow of acute fetal distress is characterized by increased vascular resistance and decreased blood flow in blood vessels.

Table 2
Comparison of umbilical arterial blood gas and oxidative stress parameters between pregnant women in two groups (mean ± SD).

Group	Blood gas parameters				Oxidative stress parameters				
	pH	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	Lactic acid (mmol/L)	SOD (IU/L)	GSH-Px (IU/L)	VitC (μg/mL)	VitE (μg/mL)	MDA (mmol/L)
Distress group (n = 52)	6.96 ± 0.78*	36.53 ± 6.14*	60.41 ± 9.25*	4.51 ± 0.78*	69.33 ± 9.14*	98.67 ± 11.76*	22.15 ± 3.52*	4.68 ± 0.74*	26.85 ± 3.58*
Control group (n = 127)	7.21 ± 0.95	55.25 ± 7.85	35.42 ± 4.86	2.25 ± 0.33	94.52 ± 11.47	165.65 ± 22.37	35.25 ± 5.69	7.92 ± 1.03	14.41 ± 1.95

*: $P < 0.05$ compared with control group.

Table 3
Comparison of parameters of neonatal venous blood myocardial injury and brain damage between the two groups (mean ± SD).

Group	Myocardial damage (IU/L)				Oxidative stress indicators (ng/mL)			
	LDH	HBDH	CK	CK-MB	S100B	NSE	CK-BB	Tau
Distress group (n = 52)	154.52 ± 20.14*	188.31 ± 24.29*	402.56 ± 54.76*	46.97 ± 6.82*	1.42 ± 0.22*	86.51 ± 10.15*	114.52 ± 16.49*	1.56 ± 0.22*
Control group (n = 127)	68.52 ± 10.35	74.63 ± 14.67	105.75 ± 15.86	17.85 ± 2.63	0.42 ± 0.06	25.42 ± 3.52	33.52 ± 5.64	0.59 ± 0.07

*: $P < 0.05$ compared with control group.

The primary means for diagnosis of fetal distress in clinic is still fetal heart rate monitoring which has poor sensitivity. When the results of fetal heart rate monitoring appear obvious abnormalities, fetal hypoxia and ischemia mostly have already been comparably serious. The analysis of characteristics of umbilical cord blood flow in pregnant women with fetal distress in the course of pregnancy has confirmed that the changes in the umbilical artery RI, PI and S/D had emerged from the mid-trimester of pregnancy. Thus, the authors consider that parameters of umbilical artery ultrasound have predictive value for fetal distress and assessment value for disease severity. The increase of resistance of umbilical artery and decrease of blood flow can result in the enhancement of local ischemia and hypoxia and anaerobic glycolysis, which can in turn lead to the local accumulation of lactic acid[13,14]. The analysis of umbilical artery blood gas confirmed that pH and PaO_2 in pregnant women of distress group was significantly lower than those in control group and negatively correlated with the umbilical artery RI, PI, S/D. While, the contents of $PaCO_2$ and lactic acid were significantly higher than those in control group and positively correlated with the umbilical artery RI, PI, S/D. This reveals that the parameters of umbilical artery blood flow ultrasound have assessment value for local blood perfusion and the degree of hypoxia.

The hypoxia caused by the decrease of the blood perfusion in the umbilical artery can activate the reaction of oxidative stress, the reduction of ATP and increase of reactive oxygen species[15,16]. Oxygen free radical is the main form of reactive oxygen produced by oxidative stress which can attack the lipid components in the cell membrane and react with fatty acid and produce MDA and also cause cellular functional damage[17]. Under physiological conditions, the body has a variety of antioxidants. VitC and VitE are the main non enzymatic antioxidants and SOD and GSH-Px are the main antioxidant enzymes. When oxygen free radicals damage the cellular oxidation, a large number of antioxidant substances were consumed and the antioxidant contents were decreased[18,19]. The analysis of oxidative stress of umbilical artery blood confirmed that the contents of MDA of umbilical artery blood were significantly higher than those in control group and positively correlated with RI, PI and S/D. And the contents of VitC, VitE, SOD and GSH-Px were significantly lower than those in control group and negatively correlated with RI, PI and S/D. This suggests that the parameters of umbilical artery blood flow ultrasound have assessment value for oxidative stress damage in the body of pregnant women with acute fetal distress.

Acute fetal distress can cause neonatal ischemia and hypoxia. Cardiac muscle tissue and brain tissue were very sensitive and the intrauterine hypoxia can damage it[20,21]. Myocardial enzymes involved in energy metabolism of myocardial cells as enzymes highly expressed in myocardial cells. When the cells undergone hypoxic damage, the cells broke down and caused the release of the enzymes in the endochylema into the blood circulation[22]. The analysis of indexes of neonatal myocardial enzymes in the venous blood confirmed that the contents of LDH, HBDH, CK and CK-MB of neonatal venous blood in distress group were significantly higher than those in control group and positively correlated with umbilical artery RI, PI and S/D. When hypoxia injury happens in brain tissue, neurons and glial cells were damaged. Then, S100B, NSE, CK-BB and other molecules in the cells were released into the cerebrospinal fluid and entered the blood circulation via the blood brain barrier[23,24]. The analysis of nerve injury molecules in neonatal venous blood confirmed that the contents of S100B, NSE, CK-BB and Tau of neonatal venous blood in distress group were significantly higher than those in control group and positively correlated with umbilical artery RI, PI and S/D. The analysis results above reveal that the parameters of umbilical artery blood flow ultrasound has assessment value for myocardial injury and brain injury in newborns with acute fetal distress.

In conclusion, the umbilical cord blood flow ultrasound of acute fetal distress is characterized by increased resistance and decreased blood flow. Besides, the ultrasound parameters of RI, PI and S/D were reduced obviously and the degree of hypoxia, oxidative stress, myocardial injury and brain injury can be evaluated.

Conflict of interest statement

The authors report no conflict of interest.

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