

Original Article

Analysis of cardiac output in parturient women complicated with valvular heart disease and its effect on fetal umbilical cord blood

Shujing Zhou, Jing Hu, Zhenzhou He, Qionghui Zhan

Department of Anesthesia, South Campus, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Received January 25, 2016; Accepted February 10, 2016; Epub February 15, 2016; Published February 29, 2016

Abstract: Background: With the development of diagnostic techniques in pediatric and cardiothoracic surgery in recent years, more and more women with valvular heart disease (VHD) can successfully conceive. However, the combined spinal and epidural anesthesia (CSEA) and adjuvant drugs applied in conventional cesarean section may cause hemodynamic change, which would bring certain impact on the cardiac output (CO) of VHD parturient women, and further influence the oxygenation of their newborns. The fetal umbilical blood analysis is presently the main indicator of the oxygenation status of newborns; however, so far, there are few studies about the correlation between umbilical cord blood and the CO of VHD parturient women undergoing C-section with combined spinal epidural anesthesia (CSEA). Objective: Our study aimed to compare the difference of cardiac output between healthy parturient women and VHD parturient women in CSEA C-section as well as the difference in umbilical cord blood of their newborns; and to understand the hemodynamic change in VHD parturient women while undergoing CSEA C-section. Methods: 33 parturient women with VHD (VHD group) and 35 healthy parturient women (H group), undergoing elective cesarean section with CSEA, were enrolled. Heart rate (HR), arterial systolic blood pressure (SBP) and non-invasive cardiac output (CO) were monitored and recorded from entering the operation room to 10 min after CSEA. Immediately after the delivery of fetus, fetal umbilical blood was collected and analyzed. Results: 30 cases of VHD group and 31 cases of H group were statistically analyzed. There was no significant difference in maternal gestational weeks, preoperative cardiac output, operation situation, phenylephrine doses and neonatal Apgar score in two groups. The pH, BE and HCO_3^- values of umbilical cord blood in VHD group (pH: 7.29 ± 0.03 , BE: -2.32 ± 2.2 mmol/L, HCO_3^- : 21.1 ± 2.1 mmol/L) were significantly lower than that in H group (pH: 7.33 ± 0.03 , BE: -0.3 ± 2.0 mmol/L, HCO_3^- : 22.4 ± 1.3 mmol/L) ($P < 0.05$). HR (increased by 16%, $P < 0.05$) and CO (increased by 6%, $P < 0.05$) significantly increased at 2 min after CSEA in VHD group. HR (decreased by 8%, $P < 0.05$) and CO (decreased by 8%, $P < 0.05$) significantly decreased at 4 min after CSEA in VHD group. The CO value of the parturient women in both groups dropped to the lowest at 4 min after CSEA, with VHD group ($[6.47 \pm 0.27]$ L/min) significantly lower than H group ($[7.03 \pm 0.30]$ L/min, $P < 0.05$). Conclusions: In cesarean section with CSEA, VHD parturient women had a significantly lower pH, BE and HCO_3^- value of fetal umbilical artery blood and lower CO at 4 min after CSEA than normal parturient women, which may be related to the use of phenylephrine after CSEA.

Keywords: Combined spinal and epidural anesthesia, pregnancy, valvular disease of the heart, heart stroke, umbilical cord blood

Introduction

Rheumatic heart disease in pregnancy can significantly increase the incidence of maternal mortality and fetal adverse events [1-7]. In developed countries, the incidence of rheumatic heart disease has declined significantly, but in developing countries, it is still one of the important causes of maternal mortality [2, 4].

With the development of diagnostic techniques in pediatric and thoracic surgery in recent years, many women with valvular heart disease (VHD) can successfully conceive. Therefore, a better understanding of the impact of VHD on the maternal and fetal is very important.

Combined spinal and epidural anesthesia (CSEA) has been a common anesthesia used in

Analysis of fetal umbilical cord blood

Table 1. Valvular lesion types in VHD group

Valvular lesion type	n (%)
MS	15 (50)
Mitral regurgitation	8 (26.7)
MS with mitral regurgitation	3 (10)
MS with mitral regurgitation and aortic regurgitation	2 (6.7)
MS with mitral regurgitation and tricuspid regurgitation	1 (3.3)
Aortic regurgitation	1 (3.3)

caesarean operation. In C-section, maintaining sufficient placental blood perfusion is an important aspect of anesthetic management [8, 9], and understanding of intrauterine environment can reflect the condition of placental blood perfusion. Umbilical blood acid-base status and umbilical blood gas analysis could be used as an objective index to reflect the intrauterine environment. These indexes can be used to understand the situations and provide guidance for clinical diagnosis and treatment as soon as possible. In our previous study, we found pH value, BE value and HCO_3^- value of VHD women, undergoing planned C-section with CSEA, were significantly lower than those of healthy women. We believed the use of phenylephrine for maternal hypotension after CSEA may cause the decrease in heart rate and cardiac output, which decreased the placental blood perfusion and further caused the changes in the value of umbilical cord blood; however, in previous study, we did not directly monitor the maternal cardiac output, but speculated the changes in cardiac output according to the changes in maternal heart rate [10]. On the other hand, some studies indicated that there is a direct correlation between the incidence and mortality rate of fetal complications and the decrease of CO in parturient women with heart disease, but there is no related data on this aspect [11].

So far, there is little research on the cardiac output and umbilical blood acid-base status of VHD maternal. The purpose of this study was to compare the pH value of neonatal umbilical blood in VHD maternal and healthy maternal undergoing C-section with CSEA, and to monitor the cardiac output with the principle of thoracic bioimpedance. The results of this study provided evidence for clinical diagnosis and early intervention to reduce the incidence of neonatal complications.

Method

Inclusion criteria and exclusion criteria

The research was authorized by the Ethic Committee of Renji Hospital Affiliated to Shanghai Jiaotong University School of Medicine (ethical code number (2013) 100K). All the parturient women enrolled in the study underwent cesarean section with single fetus, and the anesthesia method was CSEA. They were divided into healthy maternal group (H group, 35 cases) and VHD maternal group (VHD group, 33 cases). The inclusion criteria for VHD group: parturient women who were diagnosed of VHD before pregnancy or first diagnosed as VHD during pregnancy. Exclusion criteria of both groups: parturient women combined with hypertension, congenital heart disease, cardiomyopathy, diabetes, thyroid disease and other complications; fetus with intrauterine distress; women who entered into production process; women with CSEA contradictions; maternal age < 18 etc.

The types of valvular lesions in the VHD group were shown in **Table 1**. There were 15 patients of single mitral stenosis (MS) (50%), 6 patients of MS complicated with other valve disease (20%), 8 patients of single mitral regurgitation (26.7%) and 1 patients of single aortic stenosis (3.3%). Among the 30 cases of VHD women, there were 26 women (86.7%) were diagnosed as VHD before pregnancy, and 4 (13.3%) were first diagnosed of VHD by echocardiography due to palpitation during pregnancy. There were 22 cases with pulmonary arterial hypertension in VHD group, of which 11 cases with mild pulmonary hypertension (> 25 mmHg, ≤ 40 mmHg), 9 cases with moderate pulmonary hypertension (> 40 mmHg, ≤ 70 mmHg), and 2 cases with severe pulmonary arterial hypertension (75 mmhg and 83 mmHg). All VHD parturient women were normal in the preoperative ejection fraction (EF).

Anesthesia and intraoperative monitoring

In this study, BeneView T8 monitor (Shenzhen MINDRAY Bio Medical Electronics Co., Ltd) was used to monitor the maternal cardiac output (CO), heart rate (HR) and noninvasive arterial blood pressure (BP). Four monitoring electrodes were placed on the chest wall: two were

Analysis of fetal umbilical cord blood

Table 2. Maternal general conditions and operation-related conditions

	VHD group (n = 30)	H group (n = 31)	P
Age (years)	29 ± 5	29 ± 4	0.57
Gestational age (weeks)	37 ± 2	39 ± 1	0.004
BMI (kg/m ²)	26 ± 4	28 ± 2	0.07
Cardiac function classification (NYHA)			
I	5	29	/
II	20	2	/
III	5	0	/
Prenatal heart disease medication			
None	24	31	/
β- blocker	6	0	/
T _{s-H} (min)	5 ± 1	5 ± 1	0.96
T _{H-U} (sec)	53 ± 6	51 ± 6	0.29
Fluid input volume before fetus delivery (ml)	685 ± 74	690 ± 85	0.96
Phenylephrine consumption dosage before fetus Delivery (µg)	77 ± 73	68 ± 66	0.47
pH	7.41 ± 0.06	7.42 ± 0.03	0.72
PCO ₂ (mmHg)	31.0 ± 4.2	31.1 ± 3.2	0.26
PO ₂ (mmHg)	141.8 ± 55.9	142.1 ± 58.7	0.82
BE (mmol/L)	-1.8 ± 1.3	-1.9 ± 1.5	0.23
HCO ₃ ⁻ (mmol/L)	21.1 ± 1.8	21.4 ± 1.2	0.21
Lac (mmol/L)	1.8 ± 1.3	1.6 ± 0.5	0.53

BMI: Body mass index; NYHA: New York Heart Association functional class; T_{s-H}: time from CSEA to uterine incision; T_{H-U}: time from uterine incision to umbilical cord clamping; BE: Base excess; Lac: Lactate. Results data were expressed as mean ± standard deviation, and numerals.

placed under clavicle along the midclavicle line, and the other two were placed on costal margin along the midclavicle line. The mean value of the first three (every other minute) systolic blood pressure (SBP) was recorded as the baseline value. All participants were given sodium lactate Ringer's solution via a 20G intravenous needle on the hand free of cuff manometry. The parturient women took right lateral position, and CSEA was applied in the gap of L2-3. A 16G epidural needle was placed in the epidural space using physiological saline expendable method, and a 25G spinal anesthesia puncture needle passed through the core of epidural puncture needle to reach the subarachnoid; 2 ml of 0.75% isobaric ropivacaine (Swedish AstraZeneca) solution was given into subarachnoid for 10 s after seeing cerebrospinal fluid outflow. After drug administration, indwelling a 19G tri-porous epidural catheter with top closed on the head side with depth about 4 cm. Then, all the women took supine position with uterus tilted 15 degrees to the left. The level of anesthesia before C-section should achieve T4-6, otherwise another 2% lidocaine shall be administered via epidural catheter. Electronic fetal heart monitor was

used to monitor the heart rate of fetus before and after anesthesia. Single intravenous inject of phenylephrine 100 µg while hypotension (systolic pressure < 90 mmHg or systolic pressure decreased < 80% of the baseline) occurring; Single intravenous inject of atropine 0.25-0.5 mg while heart rate decreasing (heart rate < 50 beats/min). After delivery of the fetus, clamping the umbilical cord at both ends immediately, and extracting umbilical artery and vein blood (2 mL for each) and stored in tubes pre-filled with heparin anticoagulant. At the same time, another anesthetist drew arterial blood from parturient women. All the blood samples were immediately processed for blood gas analysis after collected (i-STAT300F blood test pieces were used, Abbott Point of Care Inc. of America). Maternal age, BMI, gestational weeks, time from CSEA to uterine incision (T_{c-H}), time from uterine incision to umbilical cord clamping (T_{H-U}), total dosage of phenylephrine used from subarachnoid block to fetus delivery, and Apgar score of 1 minute and 5 minutes were carefully recorded. Maternal SBP, HR and CO were examined and recorded every 2 minutes from monitoring baseline values until 10 minutes after subarachnoid administration.

Analysis of fetal umbilical cord blood

Table 3. HR, SBP and CO in 10 min after CSEA

	Baseline value	2 min	4 min	6 min	8 min	10 min
Heart rate (beats/min)						
VHD group	92 ± 6	104 ± 7*	85 ± 8*	94 ± 5*	91 ± 8*	92 ± 7
H group	92 ± 9	107 ± 10*	90 ± 5*	93 ± 7*	95 ± 9	95 ± 8*
Systolic blood Pressure (mmHg)						
VHD group	115 ± 8	95 ± 9*	105 ± 6*	98 ± 4*	109 ± 8*	110 ± 7*
H group	119 ± 9	98 ± 12*	107 ± 6*	100 ± 5*	109 ± 6*	112 ± 7*
Cardiac output (L/min)						
VHD group	7.03 ± 0.31	7.43 ± 0.29*	6.47 ± 0.27*	7.15 ± 0.28*	7.0 ± 0.25	7.11 ± 0.32*
H group	7.14 ± 0.29	7.50 ± 0.30*	7.03 ± 0.30*	7.17 ± 0.29	7.28 ± 0.29*	7.24 ± 0.65*

The data were expressed as mean ± standard deviation. *P < 0.05 compared with baseline number, it was significantly different.

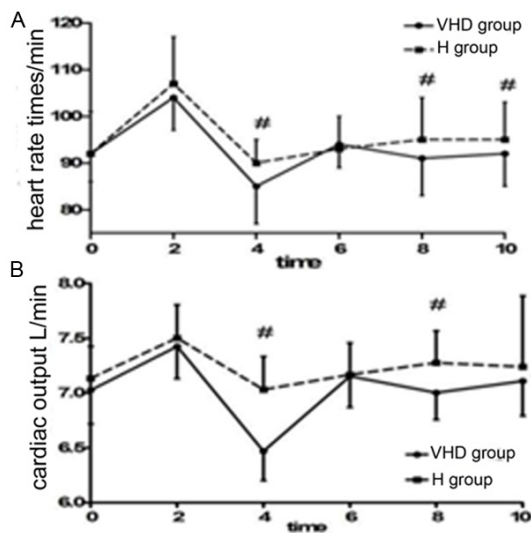


Figure 1. Changes of HR and CO in 10 min after CSEA. A: At 4 min, 8 min and 10 min after CSEA, heart rate of parturient women in VHD group was significantly lower than that of H group. B: At 4 minutes and 8 minutes after CSEA, cardiac output of parturient women in VHD group was significantly lower than that of H group. #P < 0.05: compared with H group, it was significantly different.

Statistical methods

According to our previous study [10], pH value changes in arterial blood reaching 0.03 was considered as significant difference, the sample size for each group of 30 cases were calculated by setting $\beta = 0.8$ and $\alpha = 0.05$; considering the 5% fell off of cases, each group should at least enroll 32 parturient women. The numerical results were expressed by digital, mean and standard deviation (mean ± standard deviation) or median (range). Comparison

between two groups was examined by t test. Classification variables were examined by chi-square test. Hemodynamic parameters within 10 minutes after CSEA were analyzed using repeated measurement with mixed models. Excel 2000 and SPSS 11.0 were used for all the process. A P < 0.05 (bilateral) was considered statistically significant.

Results

Enrollment

From August 1, 2013 to January 1, 2015, we enrolled 35 healthy parturient women (H group) and 33 VHD parturient women (VHD group); among them, 2 women from H group were excluded because of CSEA failure, and other 2 women from H group and 3 women from VHD group were excluded because of incomplete blood gas analysis data. At last, 30 cases in VHD group and 31 cases in H group were selected to finish the statistical analysis.

Data of maternal

There was no significant difference in age and BMI between the two groups of maternal, but the gestational age of VHD group was significantly less than H group (P = 0.004). 5 women (16.7%) in VHD group were classified as level III according to NYHA classification (Table 2) and 6 women in VHD group took β -receptor block medicine.

The anesthesia block level of all parturient women reached T4-6 before C-section, without additional injection of 2% lidocaine in any case. There was no statistical difference in T_{C-H} , T_{H-U} and volume of fluid input before fetus delivery

Analysis of fetal umbilical cord blood

Table 4. Neonatal weight, the Apgar scores of 1 minute and 5 minutes, and the umbilical blood gas values of arterial and venous blood

	VHD group (n = 30)	H group (n = 31)	P
The birth weight (kg)	3.17 ± 0.24	3.22 ± 0.20	0.000
Apgar scores			
1 min	8.9 ± 0.5	9.2 ± 0.6	0.88
5 min	9.8 ± 0.4	9.8 ± 0.4	0.81
umbilical arterial			
pH	7.29 ± 0.03	7.33 ± 0.03	0.001
PCO ₂ (mmHg)	48.6 ± 6.3	49.9 ± 9.0	0.71
PO ₂ (mmHg)	21.5 ± 6.6	22.6 ± 7.8	0.32
BE (mmol/L)	-2.32 ± 2.2	-0.3 ± 2.0	0.000
HCO ₃ ⁻ (mmol/L)	21.1 ± 2.1	22.4 ± 1.3	0.003
Lac (mmol/L)	2.5 ± 1.0	2.0 ± 0.7	0.20
pH (umbilical venous)	7.33±0.06	7.35±0.04	0.22

BE: base excess; Lac: lactate. The data were expressed as mean ± standard deviation.

in two groups (**Table 2**). The total dose of phenylephrine used in VHD group ($77 \pm 73 \mu\text{g}$) from CSEA till fetus delivery was higher than that of H group ($68 \pm 66 \mu\text{g}$), but without statistical significance ($P = 0.47$) (**Table 2**).

Compared with baseline values, heart rate (HR) of H group and VHD group all increased significantly 2 minutes after CSEA ($P < 0.05$) with an increasing rate of 16% and 13% respectively, and then significantly decreased 4 minutes after CSEA ($P < 0.05$) with a reducing rate of 2% and 8% respectively; the systolic blood pressure (SBP) of H group and VHD group decreased significantly after CSEA ($P < 0.05$); and the cardiac output (CO) of H group and VHD group also significantly increased 2 minutes after CSEA ($P < 0.05$) with an increasing rate of 5% and 6% respectively, and then remarkably decreased 4 min after CSEA ($P < 0.05$) with a reducing rate of 2% and 8% respectively (**Table 3**).

In 4 minutes after CSEA, HR and CO of VHD group were significantly lower than that of H group ($[85 \pm 8 \text{ beats/min vs. } 90 \pm 5 \text{ beats/min}]$, $[6.47 \pm 0.27 \text{ L/min vs. } 7.03 \pm 0.30 \text{ L/min}]$) ($P < 0.05$, **Figure 1**).

Data of neonatal

The weight of newborns in VHD group (3.07 ± 0.24) kg were significantly lighter than that of H

group (3.32 ± 0.20) kg ($P < 0.001$) (**Table 4**). Neonatal Apgar scores of 1 minute and 5 minutes showed no statistical difference in two groups. The pH of umbilical arterial blood of VHD group (7.29; 95% CI: 7.28 to 7.30) was significantly lower than that of H group (7.33; 95% CI: 7.32 to 7.34) ($P = 0.001$). The BE value of umbilical artery blood of VHD group (-2.32; 95% CI: -3.1 to -1.5 mmol/L) was significantly lower than that of H group (-0.3; 95% CI: -1.0 to -0.4) ($P < 0.001$). The HCO₃⁻ value of umbilical artery blood of VHD group (21.1; 95% CI: 20.3 to 21.8 mmol/L) was significantly lower than that of H group (22.4; 95% CI: 22.0 to 22.9) ($P = 0.003$). No significant difference was found in pH value of umbilical vein blood between two groups. The fetal heart rates were normal before and after CSEA. There were no newborns with congenital heart disease.

Discussion

As so far, there are few reaches on CO and umbilical blood analysis of VHD parturient women and healthy parturient women undergoing planned cesarean section with CSEA. Our results showed, under the same anesthesia method and similar surgical status, the pH value, BE value and HCO₃⁻ value of fetal umbilical artery blood of VHD parturient women were significantly lower than those of healthy parturient women. We assumed that it may relate with the decline of maternal heart rate and cardiac output.

With the progress of pediatric and cardiac surgery in recent years, most women with valvular heart disease can survive to reproductive age. At childbearing age, the main causes of female VHD patients are rheumatic heart disease, endocarditis, or congenital valve abnormalities [9]. VHD pregnant women with reflux type have a better tolerance during pregnancy, because the increase of systemic circulation capacity and decrease of peripheral circulation resistance can increase the cardiac output during pregnancy [12, 14]. However, VHD pregnant women with valvular stenosis have poor tolerance because narrow valve cannot increase cardiac output as blood volume increasing [12, 14]. MS is the most common mortality cause in VHD parturient women; the maternal mortality

Analysis of fetal umbilical cord blood

rate could reach 10% while the fetal mortality rate could reach 12 - 31% [2, 15]. In this study, the parturient women with MS accounted for 70% of VHD group (in which single MS accounted for 50%, while MS combined with other valvular lesions accounted for 20%), mitral regurgitation (MR) accounted for 26.7%, and aortic stenosis (AS), only 1 case that accounted for 3.3%. The mitral valve stenosis restricts the full filling of left ventricular diastolic, which leads to increased pressure difference on both sides of the mitral valve and increased pressure in left atrium. Such increase of pressure is more prominent when blood volume increases and in physiological tachycardia during pregnancy that ultimately promote the incidence of pulmonary edema [12, 13]. In this study, MS women accounted for a large proportion, but their pregnant weeks were 37 ± 2 weeks and most of them (83%) were at level I-II in cardiac function with normal preoperative cardiac function (7.03 ± 0.31 L/min), so, we thought the pre-operation situation of parturient women and fetal intra-uterine state in VHD group was similar to that of H group. We could exclude the influence of pre-operative maternal pathological and physiological condition on fetal umbilical cord blood value during operation.

The main results of this study showed that the pH value (7.29 ± 0.03), BE value (-2.32 ± 2.2 mmol/L) and HCO_3^- (21.1 ± 2.1 mmol/L) of fetal umbilical arterial blood in the VHD group were significantly lower than those of H group. This result was consistent with the findings of our previous study on fetal umbilical cord blood analysis of puerpera with congenital heart disease undergoing CSEA [10]. In the two studies, the time from CSEA to clipping umbilical cord was all nearly 6 min, and we thought that the maternal hemodynamic changes in 6 min after CSEA, especially cardiac output changes, would affect the placental blood perfusion, thus affect fetal umbilical artery blood acid-base status. The noninvasive cardiac output monitor was used to directly monitor the cardiac output of the parturient women in both VHD group and H group from entering the operation room to 10 min after CSEA. Compared with baseline values, maternal cardiac output (CO) in H group and VHD group was significantly increased ($P < 0.05$) 2 min after CSEA. This change resulted from the decrease of peripheral vascular resistance after CSEA, which lead

to decrease of maternal blood pressure as well as the increase of heart rate and cardiac output [16, 17]. In 4 min after CSEA, the maternal cardiac output of H group and VHD group decreased significantly ($P < 0.05$). This change was due to the use of α -adrenocceptor agonist (phenylephrine) after maternal hypotension, which caused contraction of peripheral blood vessels, increase of maternal blood pressure and reflex decrease of HR and CO [11, 12]. In 4 min after CSEA, the CO value in VHD group (6.47 ± 0.27) l/min was significantly lower than that of H group (7.03 ± 0.30 L/min) ($P < 0.05$). The CO decline rate of VHD group (8%) was higher than that of H group (2%). We believed that it was related to the higher total dosage of phenylephrine used in VHD group (77 ± 73) μg than in H group (68 ± 66) μg before fetus delivery. Dyer et al. used the same method to monitor the CO of healthy parturient women, and found the cardiac output significantly reduced (14%) after giving phenylephrine (single 80 μg) for therapeutic hypertension [16]. And phenylephrine induced CO decrease is dose-dependent, Stewart A. et al. pump injected phenylephrine with dosage of 25 g/min, 50 g/min and 100 g/min respectively to healthy parturient women undergoing planned C-section to prevent hypotension after lumbar anesthesia. The results showed that the more phenylephrine used the greater cardiac output decreased [18]. However, there was no significant difference in the neonatal Apgar scores and umbilical arterial blood gas values of those healthy parturient women. These authors suggested that the CO decline in healthy parturient women does not necessarily lead to the occurrence of neonatal adverse events, but may bring adverse outcomes to the fetus of parturient women with combined disease. In this research, the pH value, BE value and HCO_3^- value of the umbilical arterial blood of the VHD women who have relatively fixed cardiac output were significantly lower than the values of healthy parturient women; although it didn't reach the level of fetal intrauterine distress, it may increase the incidence of neonatal adverse events if the parturient women with severe heart disease [15].

Limitations and countermeasures of this study: First, the valvular lesions in VHD group were mainly MS (70%), which may lead to selection bias in the results of the present experiment. But MS is the most common type of valvular

heart disease, which is also the main reason for the MS parturient women accounting for the majority of VHD group. Second, the monitoring principle of the non-invasive cardiac output monitor (Beneview T8) used in this study is the biological impedance technique, which may be influenced by the factors such as patients' breathing, and operation etc. The cardiac output can be monitored continuously by the transesophageal ultrasonic echocardiograph, which can be repeatedly used and also can objectively reflect the change of cardiac output. In view of this, we used repeated measures analysis of variance to compare the change trend of cardiac output, and in future research we will use the transesophageal ultrasonic to monitor the cardiac output. Third, in this study, we did not directly evaluate the status of placental blood perfusion with Doppler ultrasound technology, but predicted according to the change of cardiac output; it is mainly because the application of Doppler ultrasonic technology during operation is difficult and may easily disturb the operation process.

In summary, in cesarean section with CSEA, the pH, BE and HCO_3^- values of umbilical arterial blood of VHD parturient women were significantly lower than those of healthy parturient women, which was related with cardiac output decreasing after the use of phenylephrine; although the lower pH, BE and HCO_3^- values did not reach the level of fetal intrauterine distress, it may increase the incidence of neonatal adverse events if the women with severe heart disease. At the same time, it also reminds clinical obstetric anaesthetists: the use of phenylephrine after CSEA can increase the blood pressure, but the reflex decrease in heart rate and cardiac output may influence placental blood perfusion, which may have adverse impact on the fetus of parturient women with pregnancy complications.

Declaration of conflict of interest

None.

Address correspondence to: Qionghui Zhan, Department of Anesthesia, South Campus, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China. E-mail: zhanqionghui328@163.com

References

- [1] Simpson LL. Maternal cardiac disease: update for the clinician. *Obstet Gynecol* 2012; 119: 345-359.
- [2] Malhotra M, Sharma JB, Tripathii R, Arora P and Arora R. Maternal and fetal outcome in valvular heart disease. *Int J Gynaecol Obstet* 2004; 84: 11-16.
- [3] Gomar C and Errando CL. Neuroaxial anaesthesia in obstetrical patients with cardiac disease. *Curr Opin Anaesthesiol* 2005; 18: 507-512.
- [4] Essop MR and Nkomo VT. Rheumatic and non-rheumatic valvular heart disease: epidemiology, management, and prevention in Africa. *Circulation* 2005; 112: 3584-3591.
- [5] Akhter N, Rahman F, Salman M, Anam K, Begum N, Naher S, Fatema N, Hasan Z, Rashid MA and Benerjee SK. Valvular heart disease in pregnancy: maternal and fetal outcome. *Mymensingh Med J* 2011; 20: 436-440.
- [6] Dennis A. Valvular heart disease in pregnancy. *Int J Obstet Anesth* 2016; 25: 4-8.
- [7] Bhatt AB and DeFaria Yeh D. Pregnancy and Adult Congenital Heart Disease. *Cardiol Clin* 2015; 33: 611-623.
- [8] Reynolds F, Sharma SK and Seed PT. Analgesia in labour and fetal acid-base balance: a meta-analysis comparing epidural with systemic opioid analgesia. *BJOG* 2002; 109: 1344-1353.
- [9] Chen LK, Lin CJ, Huang CH, Wang MH, Lin PL, Lee CN and Sun WZ. The effects of continuous epidural analgesia on Doppler velocimetry of uterine arteries during different periods of labour analgesia. *Br J Anaesth* 2006; 96: 226-230.
- [10] Zhan Q, Wang X, Yu J and Fan Y. Umbilical cord blood acid-base status in pregnancy with congenital heart disease. *Acta Anaesthesiol Scand* 2014; 58: 851-857.
- [11] Wald RM, Silversides CK, Kingdom J, Toi A, Lau CS, Mason J, Colman JM, Sermer M and Siu SC. Maternal Cardiac Output and Fetal Doppler Predict Adverse Neonatal Outcomes in Pregnant Women With Heart Disease. *J Am Heart Assoc* 2015; 4: e002414.
- [12] Benali Zel A, Ahmaidi H, Rachidi K and Omari D. Mitral stenosis with term pregnancy: how to manage this case? *Pan Afr Med J* 2013; 14: 144.
- [13] Hu H and Pasca I. Management of Complex Cardiac Issues in the Pregnant Patient. *Crit Care Clin* 2016; 32: 97-107.
- [14] Bowater SE and Thorne SA. Management of pregnancy in women with acquired and congenital heart disease. *Postgrad Med J* 2010; 86: 100-105.

Analysis of fetal umbilical cord blood

- [15] Ahmed N, Kausar H, Ali L and Rakhshinda. Fetomaternal outcome of pregnancy with Mitral stenosis. *Pak J Med Sci* 2015; 31: 643-647.
- [16] Dyer RA, Reed AR, van Dyk D, Arcache MJ, Hodges O, Lombard CJ, Greenwood J and James MF. Hemodynamic effects of ephedrine, phenylephrine, and the coadministration of phenylephrine with oxytocin during spinal anesthesia for elective cesarean delivery. *Anesthesiology* 2009; 111: 753-765.
- [17] Langesaeter E, Rosseland LA and Stubhaug A. Continuous invasive blood pressure and cardiac output monitoring during cesarean delivery: a randomized, double-blind comparison of low-dose versus high-dose spinal anesthesia with intravenous phenylephrine or placebo infusion. *Anesthesiology* 2008; 109: 856-863.
- [18] Stewart A, Fernando R, McDonald S, Hignett R, Jones T and Columb M. The dose-dependent effects of phenylephrine for elective cesarean delivery under spinal anesthesia. *Anesth Analg* 2010; 111: 1230-1237.