Original Article

The hemodynamic repercussions of the autonomic modulations in growth-restricted fetuses

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A R T I C L E   I N F O

A B S T R A C T

Objectives: Idiopathic fetal growth restriction is considered to be associated with hemodynamic abnormalities.

Objectives: The study was aimed to the investigation of the relationship between fetal and maternal autonomic balance, arterial and venous hemodynamic Doppler indices and CTG variables in case of normal fetal development and fetal growth restriction.

Methods: 106 patients at 32–40 weeks of gestation were enrolled in the study. 30 of them had healthy pregnancy and were involved in Group I. In Group II, 44 pregnant women with fetal growth restriction and normal umbilical hemodynamic Doppler indices were observed. 32 patients with fetal growth restriction and an absent or reversed end-diastolic umbilical flow were monitored in Group III. The curves of maximum blood flow velocity were isolated and their spectral components were determined from the umbilical Doppler spectrograms. The maternal and fetal heart rate variability, conventional CTG patterns were obtained from RR-interval time series registered from maternal abdominal wall electrocardiographically.

Results: The increased adrenergic regulation has modulated parasympathetic impact on fetal cardiovascular system. The decreased reactivity was mirrored in low LTV, lack of accelerations and an increased score of decelerations.

Results: The CTG findings were also featured by the revealed correlations demonstrated an obvious relationship between fetal and maternal hemodynamics in healthy pregnancy. It was possible to speculate that a controlling signal of 0.5 Hz has played a significant role in the umbilical venous blood flow. The decreased fetal autonomic tone and the fetal and maternal hemodynamic decoupling were found in growth-retarded fetuses.

Conclusion: Fetal heart rate pattern was influenced by maternal and fetal autonomic tone. Maternal cardiovascular oscillations were reflected in the umbilical circulation in healthy pregnancy Fetal distress was featured by sympathetic overactivity and the reduction of vagal tone. Such autonomic modulations was manifested by the decelerative pattern of CTG and deteriorated umbilical hemodynamics.

1. Introduction

HRV is known as a clinically oriented approach to the investigation of fetal neurodevelopment and maturation.[1–4] The concept of the intrauterine programming of the diseases determines a non-invasive diagnosing of fetal well-being as a prospect in perinatology. Fetal autonomic tone is found to be involved in the neurobehavioral response to different stationary conditions. Fetal heart rate captures the continual changes of the autonomic (sympatho-vagal) balance. Ultrasonic CTG is a routinely used method for the assessment of the fetal cardiovascular reactivity to the periods of wakefulness, active or calm sleep and fetal compromise.[13] But this method based on the mechanical measurement of the cardiac intervals is not absolutely specific for the diagnosing of fetal distress. The accuracy of the early detection of fetal compromise is not sufficient. The opinion that fetal electronic monitoring has contributed to an abnormally increased cesareans rate was rather

evident.[5] The extremely large complexity of the relations in the system of "mother-placenta-fetus" is known to have a dramatic impact on two main oscillators – maternal and fetal heart.[6–8] FNIECG has a complicated reputation because of low signal-to-noise ratio but provides the ability to obtain fetal cardiac rhythm tracing based on the initial myocardial bioelectrical processes.[2,5] The assessment of the morphological variables of QRS complex, p and T waves is an evident option of FNIECG.[9]

Idiopathic FGR is considered to be associated with the utero-placental and umbilical hemodynamic abnormalities.[1,10] Fetal circulatory modulations were influenced by the autonomic imbalance. The increased sympathetic and decreased parasympathetic regulation was found in FGR.[1,3,11,12] The abnormal neurodevelopment in FGR could be a reason of altered cardiovascular reactivity. Since an elevated vagal tone is known as a sign of fetal maturation the question of possible correlations between fetal autonomic tone and hemodynamic variables becomes a rather relevant issue in growth-restricted fetuses.

The study was aimed to the investigation of the relationship between fetal and maternal autonomic balance, arterial and venous hemodynamic Doppler indices and CTG variables in case of normal fetal development and FGR.

2. Materials and methods

2.1. Patients

This study was cross-sectional. The study protocol was approved by the Bioethics Committee of the Kharkiv Medical Academy of Postgraduate Education.[13] The eligible participants were informed about the methodology of the study, its aims, objectives, indications and eventual complications before inclusion in the study. All patients who met the inclusion criteria gave written informed consent to participate in the investigation. The cases of the idiopathic FGR were determined. Inclusion criteria: FGR according to ultrasonography. The FGR was in diagnosed in case of fetal weight parameters were lower than 10th percentile.[1,3] Exclusion criteria: multiple pregnancy, preexisting medical disorders like diabetes mellitus, metabolic syndrome, cardiac diseases, renal disease, thyrotoxicosis. 106 patients at 32–40 weeks of gestation were enrolled in the study. And 30 of them had healthy pregnancy and were involved in Group I. In Group II, 44 pregnant women with FGR and normal umbilical hemodynamic Doppler indices were observed. 32 patients with FGR and an absent or reversed end-diastolic umbilical flow were monitored in Group III.

2.2. Methods

Doppler ultrasonography was performed on the ultrasound system "Voluson 730" (GE Healthcare, USA). The obtained within 1 min Doppler spectrogram of the venous umbilical blood flow was subjected to further processing. The curves of maximum blood flow velocity were isolated and their spectral components were determined. The spectra were calculated by sampling step $\Delta t = 0.01$ s for a sample of 256 points. The resulting spectrum was obtained by averaging over all samples of this contingent. The maternal HRV, fetal HRV and conventional CTG patterns were obtained from RR-interval time series registered from maternal abdominal wall electrocardiographically. Fetal noninvasive computer electrocardiographic system "Cardiolab Baby Card" (Scientific Research Center "KhAI-Medica", Ukraine) was used in the study. The Ukrainian fetal ECG recordings were included in PhysioNet Database.[13] The registration was carried out over 10 min. Blind source separation, adaptive noise cancellation and Kalman filtering techniques were used to reduce artifact rate. The sampling

rate was 1000 Hz. The values TP and its spectral compounds, i.e. the VLF, the LF, the HF and LF/HF ratio or sympatho-vagal balance, were determined. The temporal characteristics of the fetal HRV: the SDNN, RMSSD, pNN50, AMo (the most frequent value of NN interval or the highest column in the histogram) – the number of NN intervals included in the pocket corresponding to the mode measured in percentages (%) and $SI = AMo(\%)/(2 \times Mo \times Var)$; $Var = NNmax - NNmin$; were calculated.[9]

2.3. Statistics

The results thus obtained were analyzed with an ANOVA test to compare data between groups. For the assessment of the difference between non-parametric variables Mann-Whitney test was used. The significance was set at p-value <0.05. For the statistical analysis of relationship between X and Y, the correlations coefficients were estimated with Spearman's test. Microsoft Office 2010 Excel software was used for statistical analysis (Washington, USA).

3. Results

3.1. Clinical characteristics of the study population

The mean age values were different in patients of Group I, Group II and Group III (Table 1). The mean values of the gestational age were not different significantly between all study groups. The body mass index values supported the absence of pre-gestational metabolic syndrome or malnutrition in the study population. The obtained data made an emphasis on the prevalence of pre-eclamptic women with first pregnancy in the Group III. The rate of the threatened preterm labor was low among all patients. The average fetal weight in patients of Group II and Group III was significantly lower than in healthy pregnancy.

3.2. Fetal HRV in FGR

The investigation of the fetal HRV and CTG variables revealed certain regularities (Table 2). The fetal autonomic tone according to obtained values of TP and SDNN was decreased in women in Group II and Group III. The markers of the sympathetic activity: LF, AMo and SI were elevated in growth-retarded fetuses. The parasympathetic tone was decreased based on revealed values of RMSSD, pNN50, HF, STV. The autonomic balance was found to be elevated in FGR. The decreased fetal heart rate reactivity was mirrored in low LTV in Group II and Group III. The CTG findings in FGR were also featured by lower number of accelerations and an increased score of decelerations.

Table 1
Clinical characteristics of the observed women.

Clinical parameter, units of measure	Group I	Group II	Group III
Age, years	23.2 ± 6,4	29.1 ± 7.2[*]	26.2 ± 5.1[*]/[**]
Gestational age, weeks	35.3 ± 3.6	35.4 ± 2.8	35.2 ± 3.2
BMI	25.6 ± 3.3	23.5 ± 4.0[*]	28.1 ± 5.4[*]/[**]
Parity	1.8 ± 0.6	2.1 ± 0.7[*]	1.1 ± 0.2[*]/[**]
Pre-eclampsia or gestational hypertension, number of cases (%)	–	2 (4.5%)	25 (78.1%)
Threatened preterm delivery, number of cases (%)	–	3 (6.8%)	1 (3.1%)
Average fetal weight percentile	54.6 ± 11.9	8.1 ± 1.6[*]	6.2 ± 2.0[*]/[**]

[*] The differences were statistically significant compared to Group I (p < 0.05).
[**] The differences were statistically significant compared to Group II (p < 0.05).