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Cerebral Hemodynamics and Fetal Behavioral States in IUGR Fetuses

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Abstract: The aim of this study was to evaluate the hemodynamic patterns in the proximal (M1) and distal (M2) portions of the middle cerebral artery (MCA) during different fetal behavioral states (FBSs) in healthy and IUGR fetuses. After identification of the FBS in 20 normal (group A) and 8 IUGR (group B) singleton pregnancies (36-40 weeks), flow velocity evaluation was performed on the M1 and M2 segment of the MCA during "quiescence" (FBS 1F) and "activity" (FBS 2F). In the group A, a statistically significant decrease of impedance to flow values was identified in both segments of the MCA during "activity". In the group B not statistically significant differences were identified in the impedance to flow values during different FBSs. For each segments of MCA it was found significant lower impedance to flow values in the group B for all FBSs. The mean fetal heart rate during "quiescience" was significantly lower than during "activity" in both groups. The results of this study provide evidences of the influence of different FBSs on fetal cerebral hemodynamic patterns. These information should be considered in the evaluation of fetal cerebral hemodynamics.

Keywords: Cerebral hemodynamics, Fetal behavioral.

INTRODUCTION

Fetal cerebral vessels are one of the most sensitive vascular districts to metabolic and gas variations.[1] Fetal cerebral hemodynamics is affected by pathological conditions leading to fetal hypoxemia.[1-4] However, physiological events can be responsible for modifications of fetal cerebral blood perfusion. Fetal "activity" is known to increase global metabolic and circulatory response, particularly in the brain, inducing cerebral vessels vasodilatation with increased brain blood perfusion. The opposite pattern is present during periods of fetal "quiescence".[5]

Specific patterns of hemodynamic changes, suggesting a reduction of vascular resistance in the fetal brain during fetal "activity", have been identified by Doppler velocimetry studies at the level of carotid artery, anterior and posterior cerebral arteries.[6-7]

On the contrary discordant results have been reported on the relationship between middle cerebral artery (MCA) hemodynamic patterns and FBSs,[8] and no satisfactory explanation has been provided to clarify the apparently discordant hemodynamic pattern of MCA.

Furthermore the MCA supplies diencephalic structures with its proximal portion and the majority of the cerebral cortex with its distal portion.[9] These different brain structures undergo preferential activation during different fetal behavioral states, that might result in different hemodynamic patterns between proximal and distal portion of the MCA. Thus during different fetal behavioral states we would not only expect changes of cerebral blood perfusion but we could also postulate different hemodynamic patterns between different portions of the vessel.

Aim of this study is to evaluate the hemodynamic patterns of MCA during different FBSs and in particular to assess the influence of different FBSs on the proximal and distal portion of the MCA in a group of normal and IUGR fetuses.

MATERIALS AND METHODS

The study includes 20 healthy pregnant women (group A) and 8 complicated by IUGR (group B) with singleton pregnancies between 36 and 40 weeks gestation. All women aged 20-35, were non smokers and with no history of drug assumption except for folic acid and iron supplementation. The gestational age-based on the last menstrual period, was confirmed by CRL measurement within 10 weeks of gestation. At the time of the study, the fetal growth was assessed by the measurements of BPD, FL and AC. Fetal growth was within the 40th and the 60th centile for the group A and below the 11 and not 20th centile for the group B, according to our reference curves. Birth-weight was within the 40th and the 60th centile for the group A and below the 11 and not 20th centile for the group B, according to Kloosterman's table adjusted for maternal parity and fetal sex.[10] No fetuses displayed structural anomalies at birth, all fetuses were delivered by uncomplicated spontaneous vaginal delivery with no signs of fetal severe hypoxia, none of the fetuses were acidotic and they had Apgar score above 8 at 5 minute.

Fetal behavioral state (FBS) was defined as "quiescence" (FBS-1F) or "activity" (FBS-2F) according to the criteria stated in Table 1.[11-12]

Table 1: Definition of the fetal behavioral states (FBSs) 1F and 2F (Modified from Nijhuis et al, Early Hum Dev, 1982)

FBS 1F: Coincidence of (for at least 3 minutes):

- No eye movements
- Quiescence, which can be interrupted by brief gross body movements, mostly startles
- Fetal heart rate pattern A (*stable heart rate pattern with a small oscillation bandwidth of less than 10 bpm, isolated accelerations do occur but are strictly related to fetal movements*)

FBS 2F: Coincidence of (for at least 3 minutes):

- Eye movements are continuously present
- Frequent and periodic gross body movements, mainly stretches and retroflexions and movements of the extremities
- Fetal heart rate pattern B (*oscillation bandwidth of more than 10 bpm, frequent accelerations during movements*)

Fetal heart rate pattern, fetal eye movements and fetal body movements were simultaneously recorded. Fetal heart rate pattern was recorded using a computerized cardiotocograph (Sonicaid 8002 system, Oxford, UK) (Fig.1).

Using a multifrequency (3.5 to 5 MHz) transabdominal curvilinear transducer with a real-time ultrasound Doppler machine (B & K 3535, Denmark), fetal eye movements were observed by sonographic visualization of the eye lens in a transverse scanning plane through the orbits; immediately after the individualization of the presence or absence of eye movements, the transducer was rotated towards a sagittal plane of the fetal trunk to evaluate the fetal body movements. Flow velocity waveform evaluation was performed only after a specific FBS persisted for at least 5 minutes. The middle cerebral artery was sampled at two levels: near its origin from the circle of Willis (MCA-M1) and near the end of the big wing of the sphenoid bone, setting the sample volume immediately before its bifurcation (MCA-M2)[13] (Fig. 2).

In all cases included in the study it was possible to identify both FBS-1F and FBS-2F and the transition between the two conditions during the same session.

All recordings were performed by the same sonographer (GC) and stored on videotape for post-procedural verification. The mean and standard deviations of the PI values in the MCA-M1 and MCA-M2, during FBS-1F and FBS-2F, were calculated. Changes in PI values of different portions of MCA related to the FBSs were statistically analyzed using the paired Student *t*-test ($p < 0.05$ was considered statistically significant). The correlation between both segments of the MCA PI values and FHR was evaluated by the coefficients and slopes of the regression lines.

The study was approved by the local Ethical Committee. No patients refused to take part to the study.

RESULTS

In the group A the mean MCA PI values were lower during FBS-2F (M1: 1.44 ± 0.17; M2: 1.53 ± 0.17) than FBS-1F (M1: 1.58 ± 0.15; M2: 2.06 ± 0.25) in both segments but this difference was particularly significant in the M2 segment ($p = 0.00000085$) in comparison with the M1 ($p = 0.0028$) (Table 2A).

In the group B there were not statistically significant changes in the impedance to flow values between different portion of the MCA during different FBSs (Table 2B).

Tables 2A and B: PI values in MCA-M1 and MCA-M2 segments during FBS-1F and FBS-2F in healthy (A) IUGR and (B) fetuses

(A)

MCA-M1 PI (mean ± SD)		*MCA-M2 PI (mean ± SD)*	
FBS 1F	**FBS 2F**	**FBS 1F**	**FBS 2F**
1.58 ± 0.15	1.44 ± 0.17	2.06 ± 0.25	1.53 ± 0.17
p = 0.02		*p* = 0.001	

(B)

MCA-M1 PI (mean ± SD)		*MCA-M2 PI (mean ± SD)*	
FBS 1F	**FBS 2F**	**FBS 1F**	**FBS 2F**
1.03 ± 0.08	1.00 ± 0.05	1.05 ± 0.07	1.01 ± 0.07
p = 0.13		*p* = 0.07	

There was a statistically significant difference in the impedance to flow values between the two groups during different FBSs in all MCA segments (Table 3) with lower values in the IUGR group.

The fetal heart rate during FBS-1F was significantly lower than in FBS-2F for both groups (group A: p = 0.004; group B: p = 0.032) (Table 4).

However, the regression analysis between the PI of both segments of the MCA and the fetal heart rate during FBS-1F and FBS-2F for each groups, showed no significant correlation (group A: M1/FHR r = 0.07; M2/FHR r = – 0.17) (group B: M1/FHR r = – 0.24; M2/FHR r = – 0.3), suggesting that the decrease of the impedance to flow values observed during the FBS-2F was not related to the increased fetal heart rate.

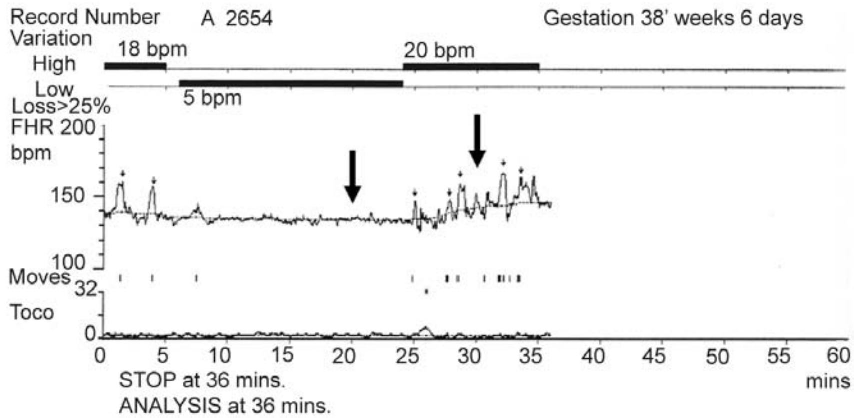

Fig. 1: Example of FHR tracing: arrows indicates when the Doppler recordings were performed according to different FHR patterns

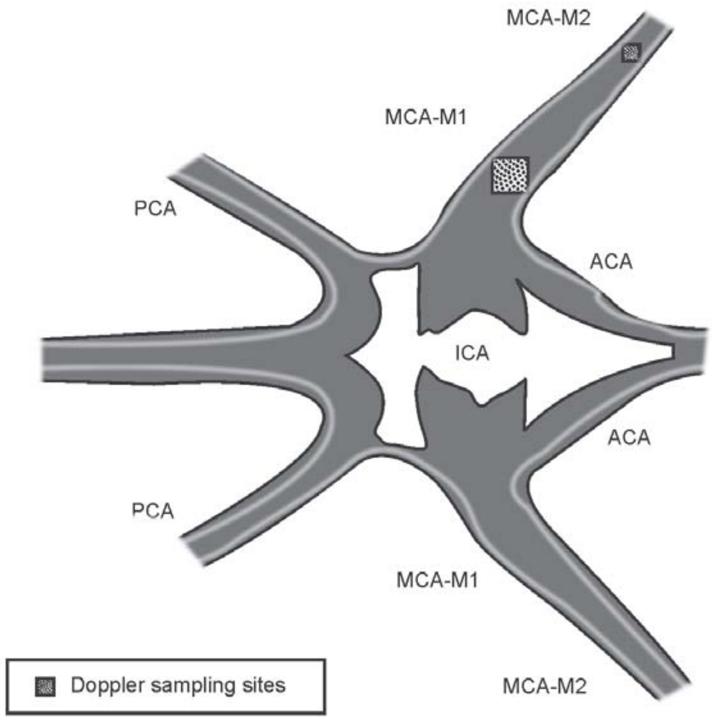

Fig. 2: Schematic representation of the Circle of Willis (ICA: Internal Carotid Artery; PCA: Posterior Cerebral Artery; ACA: Anterior Cerebral Artery; MCA–M1: Middle Cerebral Artery M1 segment; MCA–M2: Middle Cerebral Artery M2 segment) and Doppler sampling sites of different portions of the MCA

Table 3: PI values in MCA-M1 and MCA-M2 segments during FBS-1F and FBS-2F in healthy (group A) and IUGR (group B) fetuses

PI MCA-M1				*PI MCA-M2*				
FBS-1F		*FBS-2F*		*FBS-1F*		*FBS-2F*		
Group A	*Group B*	*Group A*	*Group B*	*Group A*	*Group B*	*Group A*	*Group B*	
1.58	1,03	1.44	1.00	2.06	1.05	1.53	1.01	Mean
0.15	0.08	0.17	0.05	0.25	0.07	0.17	0.07	SD
0.0001		0.0001		0.0001		0.0001		*p*

Table 4. Fetal heart rate during FBS-1F and FBS-2F in healthy (group A) and IUGR (group B) fetuses.

group A		*group B*		
FBS-1F	*FBS-2F*	*FBS-1F*	*FBS-2F*	
135	141	144	154	Mean
6.76	7.41	6.43	7.42	SD
0.004		0.032		*p*

DISCUSSION

Several studies have demonstrated the usefulness of Doppler technology in the evaluation of fetal condition during chronic hypoxemia secondary to "placental insufficiency" leading to IUGR.[1-4] It is known that fetal cerebral vessels constitute one of the vascular districts more sensitive to the metabolic and gas variations induced by pathological conditions during intrauterine fetal life.[4]

Other studies have shown that some vascular fetal districts are affected, in their velocimetric patterns, also by "physiologic" conditions.[5-8,14-18] It is well known that correct evaluation and interpretation of Doppler hemodynamic patterns depends not only on appropriate technical skills but also on the knowledge of the physical and physiological variables that can influence fetal velocity waveform profile.

The results of the present study suggest that changes in FBS is one of the parameter that should be considered when interpreting fetal hemodynamic patterns. In particular this study demonstrate that, in healthy fetuses, there is a significant difference of the impedance to flow values between the two segments of the MCA and that the hemodynamic pattern of the MCA is related to fetal behavioral states. In fact, in this group (A), active fetal state is associated with a significant decrease in impedance to flow values in the MCA. This decrease in impedance to flow appears to be more marked in the subcortical segment (MCA-M2) of the vessel rather than in the proximal portion (MCA-M1). This pattern is probably due to the cortical metabolic activation during fetal activity, inducing vasodilatation by local mechanisms (EDRF/NO, prostaglandins, pH variations, hypercapnia, hypoxia, etc.).

Furthermore, in IUGR fetuses (group B) there is a significant decrease of the impedance to flow values of both segment of the MCA, in relation to the values of the uncomplicated pregnancies. Moreover, in IUGR group there is no difference in the impedance to flow values during different FBSs.

The findings of this study provide new information on the influence of physiological fetal reactions during different FBS that should be taken in consideration when evaluating cerebral hemodynamics.

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