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Fetal response to external audial stimulation in high-risk pregnancies

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Summary

Introduction: An aim of the first phase of the present authors' prospective clinical trial was to determine the variation of pulsatile index (PI) in the median cerebral artery (MCA) in low- and in high-risk pregnancies with gestational hypertension, diabetes mellitus, intrauterine growth restriction (IUGR), and congenital thrombophilia, after constant sound stimuli. *Materials and Methods:* Study was organized as multicentric prospective clinical trial under the supervision of Ministry of Health and Education of Republic of Serbia over four years from 2011-2014. The study included 60 patients in low-risk pregnancies, 31 patients with gestational hypertension, 17 patients with diabetes in pregnancy, four with IUGR, and nine patients with congenital thrombophilia. Ultrasound prenatal auditory screening was performed after the 27th week of gestation, following the protocol established in 1992. Defined sound stimulus was digitally generated sound intensity 90 dB, frequency range 1,500-4,500 Hz, and duration 0.2 seconds. *Result:* There is significant statistical difference between low-risk pregnancies and pregnancies with gestational hypertension, and insulin dependent diabetes mellitus. *Conclusion:* A small response interval was detected in pregnancies complicated with diabetes mellitus insulin dependent and gestational hypertension. The authors can conclude that these fetuses are in chronic hypoxia which results in their low reactivity to external stimulation.

Key words: Doppler changes in fetal MCA; External sound stimulation; Fetal well being.

Introduction

The auditory system in the human fetus and infant has its own developmental sequences. The anatomical or structural parts of the system develop early. The structural parts of the cochlea in the middle ear are well formed by 15 weeks' gestational age and are anatomically functional by 20 weeks' gestation. The somaesthetic (touch), kinesthetic (movement), proprioceptive (position), vestibular (motion-head), and chemosensory (smell and touch) systems all are both structurally and functionally operative before 20 weeks' gestation. The auditory system follows those systems in the sequence of development. The auditory system becomes functional at around 25 to 29 weeks' gestational age when the ganglion cells of the spiral nucleus in the cochlea connect inner hair cells to the brain stem and temporal lobe of the cortex. The earliest evidence of an auditory evoked response is at 16 weeks' gestational age. The neural connections to the temporal lobe of the cortex are functional at around 28 to 30 weeks' gestational age. This begins the development of tonotopic columns in the auditory cortex. They are needed to receive, recognize, and react to language, music, and meaningful environmental sounds [1]. However, no consistent auditory brainstem responses (auditory evoked potentials) have been observed before 25–30 weeks. In both humans and other mammals, maternal emotion and stress affect the offspring's *physiology* (neurochemistry, endocrine function) and *psychology* (emotion, cognition). Against a background of steadily increasing blood concentrations of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and cortisol throughout the pregnancy, information about maternal stress can reach the fetus as a temporary reduction in blood flow, transfer of maternal hormones across the placenta, or release of placental CRH; CRH enters fetal circulation via the umbilical vein, whereas cortisol enters via the umbilical arteries. Prenatal exposure to glucocorticoids such as cortisol affects fetal development, produces hypertension and other medical and behavioural problems in later life, affects the development of internal organs including the ear, and plays a part in the etiology of schizophrenia [2].

The physical data of hearing includes: the speed of neural conduction in cochlear nerve which is 20 m/s, the length of cochlear nerve which is 2.6 cm, and the time of neural conduction of auditory stimuli which is 0.001 s

The aim of this study was to determine fetal response to constant sound stimulus, measuring the change of pulsatile index (PI) in fetal median cerebral artery (MCA), after 27th week of gestation in low-risk pregnancies, several times during 30 seconds. The idea was to determine the degree of change of fetal cerebral circulation in two periods of time: the time of peak change of PI and the time of normalization of fetal cerebral circulation. The second goal was to correlate these measurements with PI of MCA in high-risk pregnancies, in order to determine the influence of risk factors on fetal behaviour.

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Materials and Methods

This study was organized as multicentric prospective clinical trial under the supervision of Ministry of Health and Education of Republic of Serbia over four years from 2011-2014. It included Clinic for Gynecology and Obstetrics Clinical Center Serbia and Clinic for Gynecology and Obstetrics Narodni Front in Belgrade, as well as the Institute for Experimental Phonetics and Speech Pathology in Belgrade. Institute for Experimental Phonetics and Speech Pathology in Belgrade, developed basic part for experiment called MIMS-GENERATOR SOUND STIMULANT. Production: INKOMARK, Belgrade, Serbia. Patent No. P 2010/0519.

The generator provides a sound stimulus required for detection of fetal auditory response. The device is portable, battery powered, easily manipulating, and easy to handle. Generated sound parameters are invariant, which ensures rapid repetition of measurements. MIMS is applied by the defined procedures PSS (method Sovilj-purple). Technical characteristics of the device are intensity: L (dB) = 90dB at a distance of s = 50 mm perpendicular to the propagation of sound with frequency range between 1,500-4,500 hz and the effective duration of the stimulus 0.21 s. Assessment of fetal cortical circulation was made by ultrasound Doppler measurements with a 3.5-MHz probe at the beginning of median cerebral artery before and immediately after the sound stimuli proposed near the fetal head, at the distance of no more then 10 cm. The authors measured PI before (PI1) and after the stimuli (PI2).

The study included 60 patients with low-risk pregnancies, 31 patients with gestational hypertension, 17 patients with diabetes in pregnancy, four with IUGR, and nine patients with congenital thrombophilia. All results were statistically analyzed with Student *t*-test, with levels of significance of 0.05 and 0.01.

Ultrasound prenatal auditory screening was performed after the 27th week of gestation, following the Protocol established in 1992. (Ljubic, Sovilj) included the following procedures: creation of medical documentation by trained perinatologists, standard procedure for ultrasonic inspection, set the antiphons lice on pregnant women, to turn off the sound effect of stimulus auditory system through the mother, determination of fetal head position, positioning of fetal MCA, reading the basic values of Doppler parameters PI., generation of defined digitized sound stimuli, and reading the peak values of Doppler parameters PI.

Defined sound stimulus was digitally generated sound intensity 90 dB, frequency range 1,500-4,500 Hz and duration 0.2 seconds, a speaker that produces it is placed horizontally at 5 cm distance in relation to the abdominal wall of pregnant women. Ear type EP-107 in the form of ear shells that cover the entire ear, placed and eliminate the influence of defined sound stimuli over auditory system of the mother to the fetal auditory response. Defined acoustic stimulus is presented only once in order to investigate changes in cerebral cortical circulation of the fetus, given that the repetition of the stimulus in the short period leading to fetal habituation to the same [3]. Other studies have confirmed that the fetus during the third trimester of pregnancy is clearly able to adapt to repeated stimuli applied to the mother's abdomen, as it also gives the response when the stimulus changes.

Results

At the very beginning the authors tested 30 fetuses from low-risk pregnancies and made several measurements in order to determine the precise time of maximal change of PI MCA, which was 1-3 seconds and the time of returning to prestimulation level, which was 14-16 seconds after the stimulation. Using these data we compared all risk groups to low risk group of fetuses. (Figure 1)

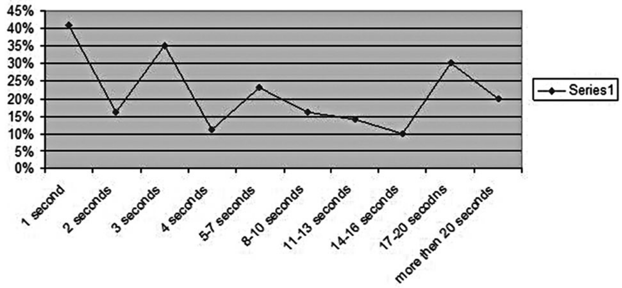

Figure 1. — PI changes in MCA after sound stimulation.

In the low risk group, median change of PI MCA in the first 3 seconds after the stimulation was 23.4%, and in after 14-16 seconds, it was 13.5%. In the group with gestational hypertension, median change of PI MCA in the first 3 seconds after the stimulation was 15%, and after it was 14-16 seconds 12%. In the group with insulin dependent diabetes, median change of PI MCA in the first 3 seconds after the stimulation was 6%, and after it was14-16 seconds 3.6%. In the group with gestational diabetes, median change of PI MCA in the first 3 seconds after the stimulation was 9%, and after 14-16 seconds it was 2.3%. In the group with congenital thrombophilia, median change of PI MCA in the first 3 seconds after the stimulation was 32 %, and after 14-16 seconds it was 15%.

There was significant statistical difference between low-risk pregnancies and pregnancies with gestational hypertension after the first 3 seconds (t1,2 3.5, $p > 0.01$). In healthy babies, change of PI MCA was 23.4 % and in gestational hypertension 15%, immediately after the stimulation. After 14-16 seconds change of PI MCA in the first group was 13.5 % and in the second group it was 12% (t 1,2 0.9, $p < 0.05$)

Correlation between the low-risk group and group with insulin dependent diabetes, showed significant difference after 3 seconds (t1,2 4, p>0.01), but no difference after 14-16 seconds (t1,2 0.7, $p < 0.05$). In fetuses whose mother had gestational diabetes, there were no statistical differences between changes of PI MCA in both intervals (t 1,2 0.05, t 1,2 0.6, $p < 0.05$). In healthy babies change of PI MCA was 23.4% and in insulin dependent diabetes 6%, immediately after the stimulation. After 14-16 seconds change of PI MCA in the first group was 13.5 % and in the second group it was 3.6% (t 1,2 0.9, $p < 0.05$). In healthy babies change of PI MCA was 23.4 % and in gestational diabetes 23%, immediately after the stimulation. After 14-16 seconds change of PI MCA in the first group was 13.5 % and

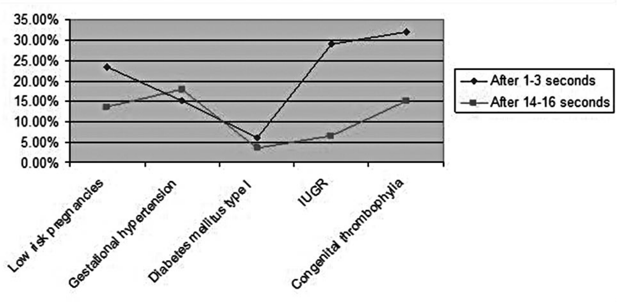

Figure 2. — Degree of change in PI MCA after audio stimulation.

Table 1. — *Degree of change in PI MCA after audio stimulation.*

Risks in pregnancy	After 1-3 seconds	After 14-16 seconds
Low risk pregnancies	23.4%	13.5%
Gestational hypertension	15%	18%
Diabetes mellitus type I	6%	3.6%
IUGR	29%	6.5%
Congenital thrombophilia	32%	15%

in the second group it was 9% (t 1,2 0.9, $p < 0.05$)

In the pregnancies with thrombophilia, no statistical difference was noted (t 1,2 0.4, t 1,2 1.7, $p < 0.05$). In healthy babies, change of PI MCA was 23.4% and in maternal thrombophilia it was 32%, immediately after the stimulation. After 14-16 seconds change of PI MCA in the first group it was 13.5% and in the second group it was 15%. (t 1,2 0.9, $p < 0.05$) (Figure 2, Table 1)

Discussion

Sovilj *et al.* [3] demonstrated fetal response to external auditory stimulus by changes in PI of MCA after the 28th week of gestation. The acoustic stimulus was 80-90 dB of intensity and 1,500-3,000 Hz in frequency. After five times repeated sound, fetus became used to it and had no changes in cerebral circulation [3].

Scibetta *et al.* [4] studied fetal auditory response during labour and detected the influence of peripartal distress on decrease of it. Luz *et al.* [5] attempted to implement this test to detect fetal hypoxia and fetal distress during delivery [5]. Kisilevsky *et al.* [6] studied complete physical activation or relaxation of fetuses after different sound stimuli.

Conclusion

Analysis of fetal response to auditory stimuli showed completely different patterns of fetal behaviour in different types of high risk pregnancies. Especially small response interval was detected in pregnancies complicated with insulin dependent diabetes mellitus and gestational hypertension. We can conclude that these fetuses are exposed to chronic hypoxia, which results in their low reactivity to external stimulation. After this phase of our study we can suggest that this test can be useful not only as hearing screening test, originally designed, but as an assessment test of fetal well being.

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