EVALUATION OF BLOOD FLOW IN THE MEDIAL CEREBRAL ARTERY IN FETUSES WITH HYPOPLASTIC LEFT HEART SYNDROME

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ABSTRACT — In the present study, we have attempted to systematize the possibility of Doppler sonography as a non-invasive diagnostic tool for monitoring the development of the central nervous system in the fetus with congenital heart disease. The detailed analysis of fetal hemodynamic changes in fetuses with hypoplastic left heart syndromes at different gestation stages was performed. The dynamic study of intrafetal hemodynamics was clearly demonstrated to help professionals to organize a more thorough prenatal care the fetuses of which have congenital heart diseases with obstructive lesions of the main arteries, and to predict the initial manifestations of developing the central nervous system pathologies, as well as to choose the optimal method of treatment to reduce complications in the postnatal period. Comprehensive assessment of the intrafetal hemodynamics in fetuses with congenital heart disease allows clearly identifying the stages of a pathological condition in the central nervous system and the degree of their severity.

KEYWORDS — congenital heart disease, dopplerometry, hypoplastic left heart syndrome, fetus, the medial cerebral artery.

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INTRODUCTION

Hypoplastic left heart syndrom includes a group of cardiac pathologies characterized by underdevelopment (hypoplasia) of the left heart cavities, atresia and/or stenosis of the aortic and/or mitral valves, and aortic hypoplasia.

Reliable diagnostic criteria of hypoplastic left heart syndrome are:

— Deviation from the norm of all linear parameters of the fetal heart at all gestation stages;

— A significant reduction in linear indices of the left heart combined with compensatory increase in similar parameters of the right heart;

— Predominant (atypical) hypertrophy of the left ventricle myocardium over the right ventricle at all gestation stages;

— Diameter of the patent ductus arteriosus is 1.5–2 times more than the norm during pregnancy, especially after the 30th week of gestation.

— Great variability of blood flow nature and its velocity parameters, and a significant difference from the standard values for all studied gestational subgroups in all cases of hypoplastic left heart syndrome.

— In pulsed Doppler blood flow mode in mitral valve stenosis, single-phase flow is recorded, it is high-velocity in the case of a moderate narrowing of the valve ring, and low-velocity in apparent stenosis.

— Retrograde filling of the ascending aorta through a patent ductus arteriosus is recorded in atresia of the mitral valve and aortic valve in color Doppler mapping.

Peculiarities of hemodynamics of the hypoplastic left heart syndrome before birth are such that the right ventricle provides blood flow in the descending aorta through the pulmonary artery and patent ductus arteriosus and retrogradely in the aortic arch, the ascending part and in the coronary vessels.

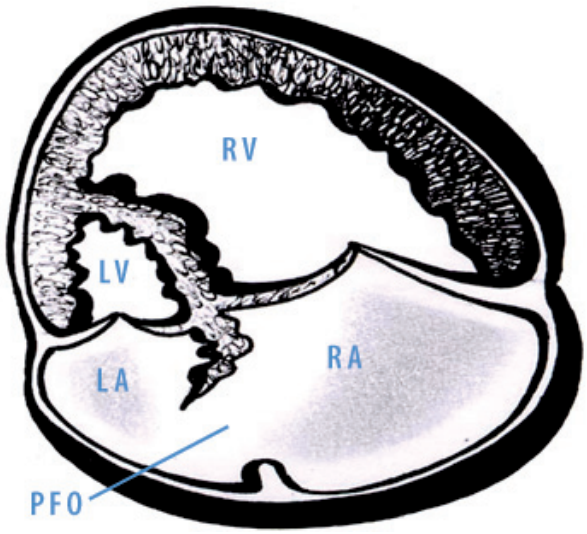

Fig. 1a. *Scheme of the 4-chamber heart section: RA — the right atrium, LA — the left atrium, RV — the right ventricle, LV— the left ventricle, PFO — patent foramen ovale. The LV cavity is dramatically reduced compared to the RV cavity, being compensatory dilated, PFO diameter is increased*

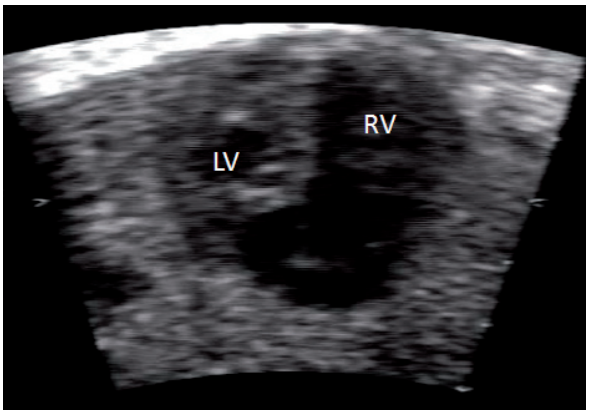

Fig. 1b. *23 gestation weeks. HLHS. Scan is in gray scale mode Projection of four chambers of the heart. Hypoplastic left heart syndrome. The left ventricle (LV) is dramatically hypoplastic, has a characteristic spherical shape (borders are shown in dotted lines). The cardiac apex is formed by the myocardium of the right ventricle (RV) - indicated by the arrow*

According to popular opinion, the expressed overload of the right heart, reducing blood flow in the aorta and coronary arteries leads to the development of tissue hypoxia, decreased myocardial contractility, and congestive heart failure only after the child's birth. [1]

However, neonatologists face problems on the part of the central nervous system development from the first week of life of children with congenital heart disease against functioning fetal communications [2–8].

So, according to Mahle WT data, the third of 138 examined school-aged children with various congenital heart diseases and operated in early childhood visits correctional educational institutions, the intake of various drugs was prescribed to 64% of patients to support the central nervous system work, and 18% of children demonstrated mental retardation; all this indicates the high percentage of patients with congenital heart diseases with signs of mental retardation [9]. Pathological phenomena on the part of the central nervous system development are determined in 50% of children with congenital heart disease before the heart defect correction [10–12] and persisted after the 1st and 2nd stages of surgical treatment. But the most dangerous is that patients undergo the great risk even in the preoperative period. This is confirmed by numerous reports of our foreign colleagues studying the influence of congenital heart diseases on the developing brain of fetus and newborn [13–18].

Priority of the nervous tissue in regulating all kinds of the organism vital activity depends directly on the features of its development and blood supply [19]. Several theories about the etiology of intrauterine growth retardation of the central nervous system in fetuses with congenital heart disease were proposed. As a result, scientists have unanimously concluded that the probable factor influencing this is the change in the circulation resulting from certain structural cardiac abnormalities, and which, in turn, may affect fetal growth and its brain development [20, 21 , 22, 23–24].

In the pathogenesis of impaired fetal hemodynamics, the leading place belongs to chronic intrauterine hypoxia, which may be caused by malformations [25]. At the same time, the degree of disorder of the central nervous system development has not yet been sufficiently studied.

Nervous tissue is more sensitive to oxygen deficiency, and the change of its blood supply nature primarily affects the development of the brain [25].

Thus, studying the state of the fetal brain in congenital heart diseases should be extended, and the assessment of the functional state of the nervous system in patients with congenital heart diseases should become standard practice.

The objectives of perinatologist should include not only the identification of cardiac abnormality in fetus, but also the determination of patients' risk group for developing the central nervous system pathology.

Under hypoxic conditions, compensatory-adaptive mechanism for protecting the fetal brain (*brain sparing*) the effect of which is aimed at strengthening the blood supply and maintaining the necessary level of brain oxygenation is activated. Decrease in sympathetic innervation of the vascular wall leading to an expansion of the lumen of cerebral vessels is the basis of this mechanism; arteriovenous anastomoses not fully functioning under physiological conditions and capillary network open, redistribution of blood flow aimed at ensuring a vital organ occurs. As a result, a reduction in brain vascular resistance occurs [8, 25]. According to summarized data from the world literature the method of antenatal diagnostics of fetal hemodynamics — Doppler sonography may shed light on the study of this problem [19]. In this regard, the aim of our work was the Doppler sonography study of the blood flow in the medial cerebral artery in fetuses with the presence of one of more complex heart defects — hypoplastic left heart syndrome

MATERIALS AND METHODS

The data of Doppler examination of blood flow in the medial cerebral artery of 24 fetuses with hypoplastic left heart syndrome are in the basis of this work. The control group consisted of 120 healthy fetuses. All patients in the group of congenital heart disease with obstructive lesions of fetal main arteries underwent a comprehensive study including:

— Assessment of the obstetric and gynecological history and extragenital pathology;
— The aimed comprehensive fetal Doppler echocardiography with the use of B-mode scanning and Doppler flow mapping techniques;
— Complete obstetrical ultrasound examination including fetometry as well as aimed examination of fetal anatomy;
— Doppler examination of fetoplacental and intrafetal blood flow.

To clarify the etiological factors of the development of intrafetal hemodynamic disorders, to identify intrafetal hypoxia and exclude fetal genotypic abnormalities, as well as to exclude the presence of maternal burdened gynecological and obstetric history, additional examinations were performed in pregnant women of this group:

— Cardiotocography;
— Immunologic examination
— Genetic testing of the fetus
— Clinical and laboratory examination of pregnant woman (to exclude somatic pathology).

Resulting from the data obtained, cases with gestational age of pregnancy being less than 30 weeks, cases of concomitant cardiac pathology in a fetus with intrauterine growth retardation, echographic signs of intrauterine infection of the fetus, chromosomal abnormalities, cardiographic and echographic signs of intrauterine hypoxia, congenital cerebral brain defects, in addition, the cases with the presence of maternal hypertension, anemia, urogenital infections, cardiovascular, respiratory or endocrine systems diseases were excluded from the study.

The age of pregnant patients did not exceed 35 years, the average one was 27,6 ± 5,4 years.

The standard values of Doppler indices of intrafetal circulation at different gestation stages (gestational standards) including the registration of the spectrum profiles of blood flow in the medial cerebral artery proposed by the staff of the Department of ultrasound diagnostics of RMAPO were used for comparative analysis. To assess the state of blood circulation, angular independent indices were used. Resistance index (RI) is calculated by the formula (SD)/S, and systolic-diastolic ratio (SDR) with the calculation formula - S/D, where S is a maximal systolic velocity, and D is an end-diastolic velocity.

In order to monitor changes of intrafetal hemodynamics, dynamic Doppler examination of intrafetal blood flow on the 30–32, 32–35, 35–39 gestation weeks as well as fetal echocardiography carried out on methodological advanced algorithm developed at the Perinatal Cardiology Center of SCCVS named after AN Bakulev of RAMS was performed in all women to exclude cases of changes in the initially diagnosis of CHD.

All cases of fetal congenital heart diseases that are included in this study were followed throughout the third trimester of pregnancy. The diagnosis was verified postnatally, intraoperatively during autopsy. This series of observations was carried out on the apparatus GE VOLUSON 730 Pro with the use of duplex sensor 3.5-5 MHz. When scanning in Doppler modes of the study, regulation of the Doppler angle «Dopplerangle rotate» was used to obtain the optimal insonation angle, and frequency filter of 50 Hz was applied.

STUDY RESULTS AND DISCUSSION

At the initial stage of the study the analysis of specific measurements of fetal hemodynamics during uncomplicated pregnancy was performed. The study of fetuses without hypoxia, signs of intrauterine growth retardation and without congenital heart diseases was

necessary for further comparative analysis of quantitative parameters characterizing the fetal hemodynamics with various cardiac abnormalities, and identification of more important indicators in the diagnostic and prognostic aspects.

For this purpose, fetal echocardiography and study of intrafetal blood flow velocity curves were carried out in the dynamics in 30 women with physiological pregnancy on the 30–32, 32–35 and 35–39 gestation weeks.

Table 1 shows the total number of observations of Doppler sonography parameters in the medial cerebral artery at each gestational period in norm.

SUMMARY

Table. 1. *Indices of fetal Dopplerometry in the medial cerebral artery estimated in the group of norms (N = 120)*

Parameter Age	Values	Medial cerebral artery	
		SDR	RI
30–32 weeks	middle	4,89 ± 0,91	0,80 ± 0,04
	min - max	3,6–6,9	0,73–0,87
33–35 weeks	middle	5,06 ± 0,9	0,80 ± 0,03
	min - max	3,9–7,0	0,74–0,85
36–39 weeks	middle	5,89 ± 1,21	0,82 ± 0,04
	min - max	3,5–7,4	0,71–0,87

Analysis of velocity curves in the middle cerebral artery of the fetus in norm showed:

— The increase in the diastolic component of blood flow in the fetal middle cerebral artery was determined during the third trimester of pregnancy

— The indices of vascular resistance in the fetal medial cerebral artery increased in direct proportion to the gestation age until the middle of the third trimester of pregnancy and remained constant to the end of the third trimester (it should be noted that in the very late stages of pregnancy, 38-39 weeks, we have seen a slight decrease in peripheral resistance indices, but given that the latter group includes a wide range of studied periods, this feature is not so obvious).

— There was no registration of zero and negative values of end-diastolic blood flow in the fetal medial cerebral artery. Our data obtained do not contradict the data obtained by researchers previously [25].

This is explained by decrease in the partial oxygen pressure in the fetal blood leading to a compensatory increase of blood flow in the brain vessels resulting from increasing volume blood flow and decreasing perfusion capabilities of the placenta during these periods [25].

Given that our data of Doppler indices in the fetal medial cerebral artery fit into the norm, the study of blood flow in the descending aorta and the CM (ВП) did not make sense.

At the second stage, we performed dynamic study of blood flow in the fetal medial cerebral artery in fetuses with hypoplastic left heart syndrome. While analyzing our own data, we found that fetuses with hypoplastic left heart syndrome on the 30–32, 32–35 gestation weeks have no deviations in the numerical values of RI and SDR below standard indicators in the middle cerebral artery, there were no zero and negative values of end-diastolic blood flow, as well as the signs of circulatory centralization.

However, at the age of 35–39 weeks reliable anomaly in peripheral resistance indices was found in the medial cerebral artery, while the blood flow nature in the aorta did not show increase in the numerical values of RI and SDR above the norm, there was no registration of zero and negative values of end-diastolic blood flow, as well. The study of blood flow in the ductus venosus also did not reveal velocity reduction into the late diastole phase below the normative values; zero and negative parameters were not detected respectively. It is possible that abnormalities in the oxygen transport to the fetal brain were caused by oxygen deficiency arising due to the fetus hypoplastic left heart syndrome. We have concluded that in the presence of this heart pathology in the fetus, deviations in brain development can be expected taking into account the changes in hemodynamic parameters in the medial cerebral artery caused by the cerebral [9, 25].

Thus, timely fetal monitoring and carrying out standard maintenance microcirculatory therapy (in particular, the use of drugs improving blood rheology and oxygen transport to the tissues) prior to delivery can improve the child's condition at birth and reduce the risk of functional disorders of the central nervous system.

Today, there are a large number of neuroimaging. The brain assessment is performed using US (neurosonography) and by magnetic resonance tomography. Preoperative neurosonography may reveal abnormalities in 15–59% of patients with congenital heart disease [3]. Magnetic resonance imaging also shows a high level of detection of preoperative brain abnormalities. Using these methods, it is possible to determine whether this deviation is of acquired nature or congenital.

The results of our study show that the evaluation of fetal hemodynamics using Doppler sonography

Table 2. *Dopplerometry indices of the fetal medial cerebral artery, the aorta and ductus venosus evaluated in the group of fetuses with hypoplastic left heart syndrome (N = 24)*

Age / Parameter		30–32 weeks	33–35 weeks	36–39 weeks	P
MCA	SDR	5,04 ± 1,39	5,18 ± 1,78	2,4 ± 0,49	p < 0,05
	RI	0,77 ± 0,04	0,78 ± 0,05	0,59 ± 0,08	p < 0,05
Aorta	SDR	5,72 ± 0,85	5,84 ± 0,57	5,73 ± 0,84	NS
	RI	0,82 ± 0,02	0,83 ± 0,02	0,82 ± 0,04	NS
DV	S/E	1,15 ± 0,04	1,14 ± 0,04	1,13 ± 0,03	NS
	S/A	1,99 ± 0,24	1,93 ± 0,18	1,97 ± 0,15	NS

NS – no reliable statistical differences in parameters values.

should be carried out targeting in the presence of hypoplastic left heart syndrome in fetus. Performing at the age of 35–39 gestation weeks is more appropriate and informative, while the method is not enough reliable in earlier periods.

CONCLUSIONS

1. Changes of intrafetal blood flow in the medial cerebral artery are characteristic of fetuses with hypoplastic left heart syndrome, which is a diagnostic criterion in predicting the development of neurological abnormalities after birth in this group of patients.
2. In the presence of fetal hypoplastic left heart syndrome, evaluation of intrafetal blood flow should be a standard diagnostics method in predicting the occurrence of neurological abnormalities
3. The change of intrafetal hemodynamics according to Dopplerometry is a risk factor for neurologic abnormalities in fetuses with hypoplastic left heart syndrome.

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The article is devoted to attempts to systematize the possibility of Doppler sonography as a non-invasive diagnostic tool for monitoring the development of the central nervous system in the fetus with congenital heart disease. The research was conducted in a *careful* and *objective* way and can be recommended for publishing in the medical Journal *Archiv Euromedica*.

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