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Monitoring of the intrauterine state of the fetus. Question history. New possibilities of phonocardiography

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ABSTRACT

The problem of decreasing perinatal mortality is one of the pressing problems in modern obstetrics. Unfortunately, current methods of monitoring the intrauterine state of the fetus that are at the disposal of an obstetrician – gynecologist (cardiotocography, Doppler velocimetry) do not guarantee fetal wellbeing in the near-term outlook, and the number of tests is limited due to safety concerns. Consequently, there is ongoing search for alternative methods of obtaining information about the intrauterine state of the fetus (phonocardiography, electrocardiography). Using IT and mathematical data analysis has considerably enlarged the phonocardiography potential, including implementation of remote monitoring of the fetal health state.

A Tomsk-based company Diagnostika + LCC developed software and hardware appliance FetalCare aimed at 24-hour monitoring of the intrauterine state of the fetus based on audio data on the fetal cardiovascular system. Cardiointervalograms (CIG) obtained by phonocardiography allow to estimate the state of the fetus based on standard assessment criteria: basal heart rate, heart rate variability, presence of accelerations and decelerations, short-term variation (STV), and long-term variation (LTV). The developed appliance is non-invasive, relatively cheap, portable, and safe both for the mother and the fetus.

Keywords: perinatal mortality, phonocardiography, cardiotocography, remote monitoring of the intrauterine state of the fetus

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Мониторирование внутриутробного состояния плода. История вопроса. Новые возможности фонокардиографии

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РЕЗЮМЕ

Снижение перинатальной смертности – одна из ключевых проблем современного акушерства. К сожалению, имеющиеся в арсенале у акушеров-гинекологов методы наблюдения за состоянием плода (кардиотокография, допплерометрия) не дают гарантии его благополучного состояния в ближайшей перспективе, а количество проводимых исследований ограничено из соображений безопасности, так как до сих пор не определено влияние ультразвука на развивающийся плод. В связи с этим продолжается изучение альтернативных (не связанных с ультразвуковым излучением) методов получения информации о состоянии плода – фонокардиографии, электрокардиографии. Использование цифровых технологий и математических методов анализа данных существенно расширило возможности фонокардиографии, в том числе реализацию идеи дистанционного мониторирования состояния плода.

В компании ООО «Диагностика +» (г. Томск) разработан программно-аппаратный комплекс FetalCare, предназначенный для круглосуточного мониторирования состояния плода на основе аудиоданных деятельности его сердечно-сосудистой системы. Полученные путем фонокардиографии кардиоинтервалограммы позволяют судить о состоянии плода на основании стандартных критериев оценки: базального ритма, вариабельности, наличия акцелераций и децелераций, STV (short-term variation), LTV (long-termvariation). Созданный программно-аппаратный комплекс неинвазивный, сравнительно недорогой, портативный, безопасный в применении для матери и плода.

Ключевые слова: перинатальная смертность, фонокардиография, кардиотокография, дистанционное мониторирование состояния плода

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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INTRODUCTION

Search for methods for decreasing perinatal mortality and morbidity remains one of the pressing problems in modern obstetrics. Improvement of perinatal care has led to a decrease in perinatal mortality, but fetal mortality and neonatal morbidity are still high.

The highest neonatal mortality rates (2019) are registered in the countries of Africa (up to 40.2‰), West and South Asia (up to 40.39‰), the lowest ones are in Japan (0.86‰), Europe (from 1.81‰

in Slovenia), Australia (2.36‰) and New Zealand (2.64‰), Canada (3.18‰), and the USA (3.53‰). As of 2019, leaders in the infant mortality ranking are Iceland with 1.6 (per 1,000 births), Slovenia – 1.7, and Finland and Japan – 1.9; the Russian Federation ranks 53rd (6.5) [1].

In 2018 in the Russian Federation, 11,659 (7.23‰) cases of perinatal mortality (per 1,000 live births and stillbirths) were registered, 8,894 of them are stillbirths (5.51‰). In 2019, the rate decreased to 7.10‰ (including 5.44‰ of stillbirths). In 2020, perinatal mortality increased insignificantly to 7.25‰ (including 5.67‰ of stillbirths). In 2021, perinatal mortality was 7.32 ‰ (including 5.77 ‰ of stillbirths). In the Tomsk Region in 2018, perinatal mortality was 5.66‰ (5.07‰ of stillbirths), in 2019 – 7.4 ‰ (6.22 ‰ of stillbirths), in 2020 – 7.5 ‰ (6.8 ‰ of stillbirths), in 2021 – 5.76‰ (5.24 ‰ of stillbirths). Over 4 months of 2022, given a decile in the birth rate (2,981 children in 2021, 2,752 – in 2022), perinatal mortality and stillbirth rates aggravated in contrast to 2021: perinatal mortality was 6.1‰, stillbirth – 5.4 ‰ [2–4].

The most common causes of antepartum fetal death are intrauterine hypoxia (43%), intrauterine infection (20%), diabetic fetopathy (17%), multifetal pregnancy (15%), and fetal congenital anomalies (5%). With an increase in gestation, the risk of stillbirth decreases: 60.3% at 22–37 weeks, 34.8% in 37–40 weeks, and 4.9% at 40 weeks and more [5].

Many Russian and foreign studies are devoted to sudden intrauterine fetal death of unspecified genesis. Attempts to explain it with thrombophilia, placental insufficiency, and developmental defects fail in 50% of cases [6–8]. Moreover, in this case even the risk-based approach is ineffective – 50% of sudden fetal deaths are registered within the group of multiparous women with a low perinatal risk [9, 10]. Given that, it is necessary to develop methods and tools for continuous monitoring of the intrauterine state of the fetus and search for causes and pathogenetic mechanisms of antepartum fetal death to provide emergency care in the presence of decompensation markers [9, 11–13].

Currently applied cardiotocography (CTG) and Doppler velocimetry are well-studied, informative, and evidence-based methods, but they are performed only in a medical institution, which is problematic during annual seasonal epidemics or occasional pandemics [14], when it is necessary to minimize contacts of pregnant women. Implementation of telemedicine technologies may resolve this issue. Daily remote monitoring of the intrauterine state of the fetus, given risk factors for intrauterine growth restriction (IUGR) or a present IUGR, starting from 32 weeks of pregnancy, is a desirable algorithm allowing to minimize severe fetal distress or a risk of intrauterine death [13,16,17].

Review of the literature shows an ongoing interest in remote fetal monitoring. Abroad, the first tests with the use of remote fetal electrocardiography (ECG) date back to 1980, fetal phonocardiography and vector electrocardiography – to 2008, accelerometry – to 2011. In current Russian healthcare practice, there is no one common method of remote fetal monitoring, which is explained by high price of imported equipment, lack of Russian alternatives, and underdeveloped legal framework for telemedicine. Therefore, reconsidering the fetal monitoring strategy and developing new effective methods for intrauterine fetal hypoxia prediction remain relevant.

The aim of the study was to perform review of the literature on methods for monitoring the intrauterine state of the fetus in modern obstetrics.

CURRENT METHODS OF DIAGNOSIS AND STRATEGY FOR MONITORING THE INTRAUTERINE STATE OF THE FETUS

Currently there are several methods for the diagnosis of the fetal state available: heart rate auscultation with fetoscope, cardiography, Doppler ultrasound of the fetomaternal circulation, actography. Apart from actography, all other methods require visits to the hospital and assistance of medical specialists.

According to the clinical guidelines “Physiological Pregnancy”, established by the Ministry of Health of the Russian Federation in 2020, the scope of fetal monitoring includes an interview concerning fetal movement, gravidogram and fetal heart rate (HR) auscultation every visit after 20 weeks, and CTG starting from 33 weeks every 2 weeks. In case of abnormalities in the gravidogram (fundal height of less than 10 or more than 90‰), changes in fetal movement, tachycardia or bradycardia, additional ultrasound and CTG are required.

With pronounced fetal growth restriction with anticipated weight of less than 3‰ given no Doppler echocardiography anomalies or oligohydramnios, delivery is recommended at 36–38 weeks of pregnancy [15]. Prior to this term, indications for hospitalization to level 3 inpatient services are only inversion of Doppler echocardiography parameters, oligohydramnios or fetal anomalies registered with CTG.

The most significant markers of intrauterine hypoxia include fetal movement anomalies and pathological changes in CTG. Here a rather long period of outpatient monitoring starts, within which a CTG is recommended 1–2 times a week. The higher monitoring frequency, the more effective the algorithm, but this intensity might be excessive for many healthcare institutions. Monitoring becomes impossible during a seasonal increase in acute rhinovirus infections and flu, epidemics, pandemics, or if a woman lives far from a healthcare institution.

ACTOGRAPHY

Functional fetal development is reflected through changes in fetal movement patterns [17, 21–23]. Movements represent early neural activity, spontaneously generated by the central nervous system. The nature of movements is defined by fetal metabolic state and its neurological development. A decrease or changes in the nature of movement may be a sign of intrauterine fetal anomalies, while total absence of movement is a sign of fetal death.

Actography (a count of fetal movements by a woman herself) is an accessible, free, but subjective and insufficiently informative method of monitoring the intrauterine state of the fetus. A movement count and fetal HR auscultation were the main methods to evaluate the state of the fetus up to the middle of the XX century, when phonocardiography and electrocardiography appeared [18].

According to Cochrane Review group [19, 20], a daily fetal movement count and absence of movements were analyzed in 5 studies involving 71,458 women. It was proved (with low significance level) that daily actography has an insignificant effect or does not influence C-section frequency (1,076 women; relative risk (RR) 0.93, 95% confidence interval (CI) 0.60–1.44), the use of obstetrical forceps or vacuum extraction (1,076 women; RR 1.04, 95% CI 0.65–1.66). At the same time, the everyday fetal movement count decreases the level of anxiety in mothers-to-be (1,013 women; standardized MD 0.22, 95% CI from –0.35 to –0.10). Actograpy is proved to have little or no effect on the frequency of preterm delivery (1,076 births; RR 0.81, 95% CI 0.46–1.46). It was also mentioned that the fetal movement count increases the frequency of CTG to monitor the state of the fetus [20].

Since 2011, devices to monitor fetal movement (accelerometers) within 24 hours and remotely have been developed [13, 17]. Currently in Russia, a system of fetal movement registration is being developed, which consists of movement detectors (which register vibrations caused by fetal movement) and a recorder [17]. The result of the test is shown on the screen as a movement count regardless of movement amplitude.

CARDIOTOCOGRAPHY

The study of fetal cardiac function, in contrast to actography, has become a promising method due to higher information value. It is proved that with development of hypoxia, caused by endogenous and exogenous factors, cardiac function is the first to change [11, 22].

Cardiac function is an important indicator of the intrauterine state of the fetus, and it was the heart function that started systematic research of the functional state of the fetus. Cardiac performance is controlled by the central and peripheral nervous systems. Oxygenation anomalies in the nervous system lead to changes in the nature of impulses to the heart, and consequently, in the heart rate [11].

Study of the fetal heart rate dates back to 1818, when a Swiss scientist Francois Mayor suggested using auscultation of the fetal heart rate through a mother's anterior abdominal wall to define whether the fetus is dead or alive. The next step was heart rate auscultation with a stethoscope, suggested by J. Kargaradec. It was concluded for the first time that the intrauterine state of the fetus depends on its cardiac activity. In 1906, M. Kremer was the first to record fetal ECG through a mother's abdominal wall.

In 1950, the founder of electronic fetal heart rate (FHR) monitoring, Edward Hon (USA) declared a new principle of processing fetal ECG results recorded through a mother's anterior abdominal wall. The principle of such processing consisted in measuring each R-R-interval, then calculating instantaneous heart rate, and presenting it in form of a graph.

Cardiotocography (CTG), based on Doppler shift, was introduced in clinical practice in early 70s of the XX century and is still widely used. An electronic system in a heart rate monitor transforms changes in each R-R interval into instantaneous HR (bpm) [11]. Initially, parameters to visually evaluate fetal cardiac activity were developed; later, scores for CTG evaluation were suggested; among the most widely spread are the Ficher's scale (1976), the modified Kreb's scale, and the scale of International Federation of Gynecology and Obstetrics (1987). It is worth noting that the use of this method allowed to increase the accuracy of fetal state evaluation only to 73–76%. In 1970, G. Dawes and C. Redman declared the beginning of the development of software aimed at automatically analyzing CTG data, based on determination of short-term variation (STV) in real time. Using the method proposed by G. Dawes and C. Redman, the accuracy of evaluating the state of the fetus is 83.6% (E.R. Guzman et al., 1996), 72.8% (A.M. Vintzileos et al., 1993), and 67.8% (E.V. Poplavskaya, 2005) [24].

ULTRASOUND

Ultrasound fetometry accurately registers fetal growth restriction. Placenta description may reveal early preclinical stages of placental deficiency, but as an isolated marker, placentometry has rather low specificity. Evaluating the volume and quality of amniotic fluid is important in antenatal hypoxia diagnosis, as significant changes in amniotic fluid characteristics serve as an indirect sign of kidney perfusion and the state of fetal microcirculation [22, 27, 28].

Doppler ultrasound of the uterine artery, umbilical cord vessels, and intrafetal blood flow became a routine procedure in obstetrics. A combination of Doppler ultrasound and CTG allows to increase the efficiency of diagnosing the state of the fetus.

Absent or reversed diastolic blood flow is a sign of impairment in the fetal adaptive and compensatory response; it is manifested by centralization of the blood flow and development of disseminated intravascular blood coagulation with vasoconstriction of vessels in the gastrointestinal tract and kidneys, which leads to their heavy ischemic injuries. After birth, such injuries clinically manifest by necrotizing enterocolitis, oligoanuria, hematuria, proteinuria, intracranial hemorrhage, neurological complication, and respiratory distress syndrome (RDS) [22]. The interval between the moment of registering critical blood flow characteristics in the umbilical artery and fetal death varies from 0 to 71 days [22].

Currently, in critical circulatory anomalies, apart from measuring the umbilical artery pulsatility index, it is recommended to study blood flow in the middle cerebral artery and ductus venosus and determine the cerebro – placental ratio [15]. The frequency and volume of the tests to monitor the state of the fetus depend on the degree of blood flow anomalies. At the same time, the use of the methods based on the Doppler shift (ultrasound, ECG) is limited for safety reasons, as the impact of ultrasound on a developing fetus is yet to be defined [29, 30]. According to the ALARA (As Low As Reasonably Achievable) principle, the test must only be run when justified to ensure minimal impact in minimal time period to achieve an adequate result [27, 31]. Therefore, ongoing use of Doppler ultrasound for dynamic fetal monitoring is inappropriate.

PHONOCARDIOGRAPHY

At the end of the XIX century, fetal cardiac activity was first registered with the help of phonocardiography (PCG) (a method for evaluating cardiac activity and valvular apparatus based on recording and analyzing sounds appearing at heart beat). In 1891, E. Pestalozza demonstrated first phonograms at the X International Medical Congress in Berlin. In the middle of the 1950s in Russia, at the Research Institute of Obstetrics & Gynecology of the USSR Academy of Medical Sciences, under the supervision of N.L. Garmasheva, the first phonocardiograph was developed, allowing to simultaneously register fetal heart beat and uterine contractions [32]. The main parts of the phonocardiograph are microphone, transforming sound vibrations into electrical ones; frequency filters, combined with signal intensifiers; and a registering device. Using different types of microphones (rifle, stethoscope, logarithmic) and band-pass filters allows to identify significant acoustic phenomena and register sound vibrations in full as well as in a selected frequency band.

In the aerly 60s of the XX century, L.S. Persianinov et al. [33] studied a method of combined use of PCG and ECG to diagnose acute hypoxia during delivery and detect fetal heart beat anomalies. Accuracy evaluation of the method undertaken by V.N. Demidov and A.A. Aristov showed that in 80% of cases PCG may detect chronic fetal hypoxia (ECG and PCG register a reduced amplitude of QRS tone and voltage, a decrease of mechanical systole duration, and arrhythmia), and in 71% of cases, it may help to suspect umbilical cord pathology (nuchal cord, true knot, velamentous cord insertion) [34]. PCG has been used in a number of Russian institutions but did not gain popularity due to a lack of capacities for mathematical data processing to analyze the adequacy of cardiointervalograms and, consequently, a hardware – software complex for arranging a monitoring system.

In recent years, digital technologies have been developing quickly and methods for mathematical analysis have been introduced, which increases the capacities of PCG. Development of this method as an alternative to ultrasound cardiography is considered relevant [12, 13]. Today PCG is actively used in cardiology to diagnose heart failure, cardiac defect, and pulmonary hypertension. New approaches to PCG application in the diagnosis of ischemic heart disease are being discussed. There are data on projects devoted to the use of this method for screening cardiovascular diseases [35].

Such advantages as noninvasiveness, safety, and relatively unexpensive equipment provide the basis for successful PCG implementation in modern perinatal medicine.

Taking into consideration the research and use of PCG to register and interpret fetal heart sounds, a number of issues may arise. Pregnancy term, subcutaneous tissue thickness, fetal and placental position, and mother's breathing patterns may influence signal intensity and amplitude. More often than with CTG, a signal loss or a change in its amplitude is explained by changes in the position and type of the fetus and application force of the detector to the mother's anterior abdominal wall. A large number of sounds on the part of the mother (abdominal aorta, uterine artery pulsation, breathing movement, abdominal sounds) and on the part of the fetus (fetal movement, breathing movement) create difficulties in signal filtration. The specifics of fetal blood circulation (patent foramen ovale, an arterial duct between main the pulmonary artery and the aortic arch, the absence of pulmonary circulation) change the PCG pattern [11, 28].

Thus, the main task of PCG adaptation to obstetrics is development of algorithms of external noise-cancelling and construction of an adequate cardiointervalogram, which allows to make conclusions about the intrauterine state of the fetus.

In Russia, there are successful phonography-based developments. For example, Diagnostika + LLC (Tomsk) has developed a software and hardware appliance FetalCare aimed at 24-hour fetal monitoring [36–39]. After detecting audio data, their primary processing takes place aimed at increasing sound quality. The result of PCG primary processing goes through an algorithm for detecting sounds similar to heart sounds, which generates an intensified audio signal and segmentation results of potential heart tones in PCG. This algorithm differs from other existing ones by its increased detection accuracy in the context of an amplitude change. To increase its reliability, external algorithms are in place, they classify the results by heart tone segmentation. At the end of the study, a graph of potential R-R intervals is processed by the algorithm for constructing an cardiointervalogram. The results of the study are presented as a report in PDF (Portable Document Format) [36–39]. Currently, on the basis of this equipment, software aimed at medical and technical support of a doctor and a pregnant woman is being developed. A doctor's workspace may exist as a separate software or become an element of a medical institution IT system. A telemedicine module based on artificial intelligence will allow to differentiate between technical and medical issues in the course of testing, producing an emergency signal in case of critical parameters and recommendations for frequently asked questions.

INTERPRETATION OF DATA RECEIVED IN PCG. CARDIOINTERVALOGRAM

The main component of heart rate evaluation of a fetus, a baby, or an adult is an interval between two heart beats. A cardiointervalogram allows to receive an integral estimate of cardioregulation with a minimal number of tested parameters: basal heart rate, heart rate variability, instantaneous frequency of oscillatory activity, accelerations and decelerations. It is not important which method is used for rhythm detection, as in PCG, like in CTG, standard parameters are used, therefore, for PNG we use standardized scales elaborated for CTG.

The following standard integral indices are analyzed. *Basal heart rate* is a parameter of interaction between parasympathetic and sympathetic nervous systems (sympathetic system is dominant at early pregnancy terms, thus fetal HR is higher, after reaching a certain level of parasympathetic maturity, the balance is achieved and the average HR decreases).

Heart rate variability (irregularity in the heartbeat) is the result of an interaction between parasympathetic and sympathetic divisions of the autonomic nervous system. The difference in the cardiac interval duration is on average 20–30 msec (or 2–3 bpm). HR anomalies, occurring from beat to beat and having specific direction and amplitude, appear on CTG in the form of HR oscillations. Basal HR variability is characterized by short-term and long-term oscillations.

Instantaneous oscillations (STV) reflect frequency differences, calculated on average every 1/16 of a minute. STV is controlled by the parasympathetic nervous system, measured in msec, and is a sensitive indicator of fetal tissue oxygenation. STV is only evaluated and interpreted with computer processing of the record. STV predictive value is being discussed and was proved, for example, in a cohort study of 28, 000 emergency childbirths in Great Britain [25].

Opposite results were received in the original prospective TRUFFLE study, which evaluated whether low STV index in combination with Doppler pulsatility index in the ductus venosus at early stages of IUGR may increase 2-year survival rate among infants without neurological anomalies in contrast to computer-assisted CTG only counting STV. The result of the research was a clinical recommendation not to conduct preterm delivery given low STV until circulation in the ductus venosus becomes normal, as such an algorithm did not improve prognosis [26].

Long-term oscillations (long-term variation, LTV) are cyclic variations in basal HR with a frequency of 3–5 cycles per minute with an amplitude from 5 to 20 bpm on average, which depend on the state of the fetus and are controlled by the sympathetic nervous system. Changes in LTV are characteristic of fetal oxygenation and its compensatory responses to stress.

STV and LTV change with a decrease in oxygen level in the blood. Given hypoxemia development, first, HR variability increases (since in oxygen deficiency, suprarenal cortex is activated, blood pressure rises, and a response to baroreceptor signals is generated). Then with hypoxemia aggravation in combination with acidemia, HR variability decreases due to functional CNS depression. STV reacts to hypoxia earlier than LTV.

CONCLUSION

Currently in obstetrics, there is no one best optimal method for constant monitoring of the intrauterine state of the fetus. In one of the conclusions of the TRUFFLE study, everyday standard CTG was proven inefficient in the high-risk group of antepartum fetal death. Monitoring the intrauterine state of the fetus by phonocardiography may become that missing link that will allow to decrease perinatal mortality. It is beyond argument that phonocardiography is more than just a cardiointervalogram. It is yet to prove its diagnostic efficacy at different degrees of fetal abnormalities. The efforts will be justified if a combination of acoustic and mathematical analysis allows to increase the capabilities of predictive perinatal medicine.

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