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Review Article

Intrauterine Hypoxia Caused by Uterine Contractility in Birth, Which Should not be Forgotten. An Update

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Abstract

Intrauterine fetal hypoxia, one of the unique physiological phenomena that accompanies the birth of each child during physiological delivery, is a consequence of placental ischemia, which occurs due to periodic short-term squeezing of intrauterine blood vessels by myometrium during its strong muscular contraction. The main danger of intrauterine hypoxia is that it is hypoxic damage to brain cells that is the biological cause of death of all fetuses. The main difficulty in diagnosing intrauterine hypoxia and its danger to the fetus is that the mother does not consciously feel it, and not only the continuity of oxygen delivery to the fetus is important for the health and life of the fetus, but also the fetal resistance to hypoxia and its consistency with the degree of hypoxia and its duration. This review summarizes recent advances in the diagnosis of fetal intrauterine hypoxia, assessment of fetal resistance to hypoxia, and new clinical strategies based on these findings.

Keywords: pregnancy; birth; fetus; resistance to hypoxia; diagnostics

Introduction

Fetal hypoxia remains one of the leading causes of perinatal morbidity and mortality, because, on the one hand, there is no generally accepted (standard) generally available and reliable method for timely diagnosis of intrauterine hypoxia, and, on the other hand, there is no method to assess fetal resistance to hypoxia [1,2]. One of the most severe consequences of low oxygen content in fetal blood is the development of hypoxic damage to the cells of the brain, initially reversible, and if the process is delayed, irreversible [3]. Depending on the localization and size of the focus of irreversible hypoxic damage to fetal brain cells, perinatal brain lesions develop, leading to a number of persistent neurological disorders in the newborn in the future (from minor cerebral disorders and cerebral palsy to decortication and fetal death) [1-4].

It is known that one of the most important adaptive responses of the fetus to hypoxia is redistribution of blood flow to the fetal brain, known as the "brain-saving effect" [1,5,6]. However, it has been found that this phenomenon cannot prevent the development of perinatal brain lesions in cases of severe or prolonged hypoxia. Therefore, even the ultrasound method of assessing the degree of redistribution of fetal blood flow in favor of the fetal brain, which allows detection and quantification using the Doppler cerebral/umbilical ratio, does not guarantee the safety of the fetal brain during hypoxia [5,6]. In addition, this method is not applicable without ultrasound equipment and without qualified specialists in the field of obstetric sonography [7]. Therefore, given the consequences of delayed diagnosis of fetal intrauterine hypoxia, the onset of fetal hypoxic brain damage of irreversible nature and the great importance of urgent real-time assessment of fetal resistance to hypoxia and fetal adaptation reserves by pregnant women, new studies aimed at improving the availability, timeliness, efficiency and accuracy of fetal hypoxia diagnosis and fetal resistance to hypoxic brain damage are important. This becomes especially relevant due to the special requirements imposed today by the introduction of telemedicine and artificial intelligence for diagnosis and treatment [8].

Voluntary apnea in a pregnant woman as a way to simulate hypoxia

It is known that fetal hypoxia can occur due to various pathological conditions of the mother, placenta and fetus, which can manifest in different ways and have different outcomes [4]. In this regard, it was proposed to divide hypoxic states of pregnancy into pre-placental (an example of such hypoxia may be highland hypoxia), uteroplacental (an example of such hypoxia may be placental insufficiency) and post-placental hypoxia (an example of such hypoxia may be pathology of the fetal cardiovascular system) [9]. It was also suggested to consider high-altitude hypoxia as an example of a true hypoxic pathology of the fetus, since fetal hypoxia, which develops only high in the mountains, occurs solely due to a decrease in the oxygen content in the inhaled air, and not due to any other reasons [4]. However, the use of high-altitude hypoxia to simulate fetal hypoxia is very

difficult and dangerous, so it is not available to most researchers and pregnant women. Therefore, a more accessible and safer model of preplacental hypoxia is required to study intrauterine hypoxia.

At the same time, to diagnose cardiovascular insufficiency in adult men and women at the beginning of the 20th century, the Russian researcher Vladimir Stange proposed to use an original test for resistance of people to acute hypoxia [10]. To assess the resistance of adults to acute hypoxia he proposed to measure the maximum possible duration of voluntary breath-holding (apnea) against the background of deep breathing. Today this test is known as the Stange test [11]. This functional test has been used in medicine for more than 100 years, and during this period of time has shown high informative value in assessing the resistance of healthy and sick adults to acute hypoxia. Today there is no doubt that the measurement of the maximum possible duration of respiratory arrest in a pregnant woman can provide information about her body's resistance to hypoxia. Moreover, the use of voluntary apnea in a pregnant woman makes it possible to simulate hypoxia not only in the body of the pregnant woman, but also in the body of her fetus. Moreover, modeling acute fetal hypoxia using voluntary apnea of a pregnant woman is much safer, easier, more affordable and less expensive than using high altitude hypoxia.

However, the classic Stange test has advantages as well as disadvantages. One of the most important disadvantages of the classical Stange test is that the test is not designed to assess fetal resistance to intrauterine hypoxia. Moreover, it has been shown that measuring the maximum possible duration of voluntary apnea in a pregnant woman using the classical Stange test does not exclude in some cases an excessively long duration of apnea, in which fetal hypoxia may cause hypoxic damage to the fetal brain. The fact is that in some cases the fetal resistance to hypoxia may be much lower than that of its mother [12].

However, the idea of using voluntary apnea in a pregnant woman to assess the resistance of her fetus to hypoxia was very attractive from the beginning, because apnea can easily be used as a standard obstetric model of individual fetal hypoxia in both clinical and home settings [13]. But for the successful practical application of voluntary breath-holding in a pregnant woman to diagnose the resistance of her fetus to hypoxia, a modification of the classic Stange test was required. First, it was necessary to ensure complete safety of the Stange test for the fetus. Second, it was necessary to supplement the well-known Stange test with a method for reliable real-time monitoring of fetal resistance to hypoxia. Today, we can already conclude that these tasks have been successfully accomplished.

Modified obstetrical Stange test, pregnancy prognosis and childbirth choice strategy

It is known that from the beginning of the 2nd half of pregnancy the fetal brain oxygen demand increases progressively [2,4]. At the same time, mechanisms of fetal adaptation to hypoxia begin to form and test, since short-term and mild periods of intrauterine hypoxia are inevitable both during pregnancy and during physiological delivery. The most frequent and prolonged periods of intrauterine fetal hypoxia develop during natural childbirth. Moreover, the duration of each successive period of intrauterine hypoxia gradually increases as the uterine contractions intensify [2]. This is associated with periods of development of placental ischemia, which occurs due to the fact that at the end of labor develops the strongest muscle contractions of the myometrium, which inevitably squeezes the intrauterine vessels. It has been shown that normally the fetus is ready for these periods of ischemia and can easily withstand them while in an immobile ("serene") state [12,13]. Therefore, normally, its mother also "doesn't notice" the fetus' changing "behavior" inside the uterus during accidental hypoxia, potentially safe for her fetus. However, in some cases, the fetus may exhaust its reserves of adaptation to hypoxia, so hypoxia begins to threaten the health and life of the fetus from the first seconds.

It has been reported that in such cases, fetal behavior inside the uterus resembles the behavior of aquarium fish inside a hermetically sealed container when the oxygen supply is cut off [12-14]. In this regard, the prognostic value of the results obtained by sonographic monitoring of fetal motor activity during voluntary breath-holding by pregnant women in the second half of pregnancy was investigated. It was reported that the studies were performed with simultaneous monitoring of ultrasound echogenicity of fetal fingertip soft tissues. The results of the studies confirmed the previously revealed dependence of the motor activity of fetuses and fish, as well as the radial properties of fetal fingertips and fish fins, on the oxygen availability of these living biological objects and on the availability of their adaptation reserves to hypoxia. At the same time, it was proved possible to assess the resistance of fetuses floating inside the uterus and fish floating in a sealed closed vessel to acute hypoxia. Moreover, it has been possible to develop methods of ultrasonic assessment of fetal resistance to hypoxia, which have been proposed for use in pregnancy and natural childbirth.

One part of these inventions was based on measuring the duration of fetal immobility from the onset of voluntary apnea in a pregnant woman (RU Patent No. 2432118, 10/27/2011; RU Patent No. 2511084, 04/10/2014; RU Patent No. 2529377, 09/27/2014). At the same time, fetal immobility more than 30 seconds after the onset of maternal apnea was proposed to be regarded as an indicator of good fetal resistance to hypoxia, and the appearance of fetal chest breathing movements in less than 10 seconds after the onset of apnea was proposed to be regarded as an indicator of poor fetal resistance to hypoxia. Therefore, good fetal resistance to hypoxia is an indication for natural childbirth, and poor fetal resistance to hypoxia is a contraindication. Moreover, if fetal resistance to hypoxia is poor, an additional, more thorough examination of the fetus and/or an emergency C-section is required.

It has been reported that another invention was based on the results obtained by recording the dynamics of ultrasound echogenicity of fetal fingertips (RU Patent No. 2441592, 10.02.2012). The point is that ultrasound echogenicity of soft tissues of adult and fetal fingertips reflects the content of oxyhemoglobin in their blood and can be used to diagnose hypoxia [12-14]. In particular, it has been shown that decreased echogenicity of the subcutaneous fatty tissue of fetal fingertip pads occurs in severe fetal hypoxia that threatens the viability of fetal cortical cells. Therefore, if ultrasound echogenicity be decreased and remained between uterine contractions during natural delivery, immediate maternal hyperoxygenation and/or immediate delivery by Cesarean section were recommended.

Thus, it has been shown that the classical Stange test is not suitable for diagnosing intrauterine hypoxia and assessing fetal resistance to it. At the same time, sonographic monitoring of fetal motor activity during voluntary breath-holding by a pregnant woman has been reported to assess fetal resistance to hypoxia. It has been shown that an indicator of the magnitude of fetal adaptation reserves to hypoxia is the maximum duration of fetal immobility from the onset of maternal apnea.

It is this index of the modified Stange test (obstetric Stange test) that has been proposed for the prognosis of pregnancy, natural childbirth, and for the choice of Cesarean section.

Diagnostic role of fetal motor activity during voluntary apnea of a pregnant woman

There is no doubt that from the second half of pregnancy there is an increase in fetal oxygen requirements and the likelihood of hypoxia, the excessive duration of which can cause various diseases and even fetal death [1,12]. At the same time, the onset of periods of fetal hypoxia is almost inevitable during physiological delivery, as during physiological delivery the uterus squeezes the intrauterine blood vessels and causes repeated consecutive periods of placental ischemia. The longest periods of placental ischemia and fetal hypoxia occur at the end of physiological labor, because in this period of labor the uterus contracts most strongly and for a long period [2[. However, the duration of each individual period of uterine contractions does not exceed 60 seconds [15]. In addition, the uterus is not able to fully constrict its blood vessels throughout this period, because the magnitude of myometrial muscle tone increases gradually each time, not in a flash, and after reaching the maximum value, uterine tone gradually decreases [2-4]. On this point we can say that the dynamics of uterine contractions are synoidal [15]. Therefore, during physiological labor, the longest period of

natural fetal ischemia caused by uterine contractile activity hardly reaches 30 seconds. That is why, normally, during physiological labor, a period of placental ischemia and fetal hypoxia occurs only in the middle of each uterine contraction and is absent in the intervals between them.

Currently, there is no generally accepted methodology for accessible and timely assessment of fetal resistance to the periods of hypoxia that await the fetus at the end of physiological delivery. There are also no reliable generally accepted criteria for choosing Cesarean section as an alternative to vaginal delivery in life-threatening fetal cases. At the same time, the increased risk of fetal hypoxic brain damage during physiological delivery is not disputed by anyone. Moreover, when the fetus's adaptive reserves to hypoxia are exhausted, Cesarean section is the way to save the fetus immediately [16,17].

As mentioned above, the main danger to the fetus is not so much hypoxia as the lack of reserves to adapt to it. The fact is that if the fetus has good resistance to the periods of hypoxia to which it will be exposed during vaginal delivery, the fetus will easily withstand these tests and maintain its health. However, fetal readiness for the upcoming periods of hypoxia during vaginal delivery is still not assessed by obstetricians. This problem has not been solved because there is no functional test for fetal resistance to hypoxia in the standard of obstetric care. Therefore, it is hoped that the development of new functional tests, available to pregnant women for self-assessment at home in real time, may improve the prognosis of pregnancy and vaginal delivery and give us indicators for the choice of the type of delivery [18].

It is hoped that one of the first such tests will become a modified test of the bar [18]. It is reported that the mother can hold her breath, note the time and wait for the montut, skin flod products, what to chat "from the mud, feet or head on the mud, that the announcement of the depletion of the fleet's adaptation reserves to hypoxia. Having received such a "belastia signal" from the photo, the mother therefore, the mother can easily determine the duration of the period between the beginning of apnea and the moment when she receives the "signal of disaster" from her fetus [19].

It has been shown that normally the fetus does not make a distress call during apnea for 30 seconds or more. In this case, the prognosis of childbirth is favorable. If the fetus gives a distress signal immediately after the onset of apnea, birth through the natural birth canal is contraindicated, as the fetus may drown in the amniotic fluid, or the newborn may develop asphyxia, encephalopathy, or pneumonia. In this case, the prognosis for childbirth may improve due to a planned caesarean section.

Conclusion

The prospects of using the modified Stange test, which gives new gynecological criteria for assessing fetal resistance to hypoxia and choosing a Cesarean section, are shown. It is expected that in the future, clinical strategies for assessing pregnancy, preparing pregnant women for childbirth, as well as choosing the date, time of day and types of childrirth, aimed at preserving fetal health, will improve the course of pregnancy in all women, increase the health indicators of the newborn and fully preserve the mental abilities of the infant for its successful intellectual development in the future.

Understanding the diagnostic role of the modified Stange test for a highly accurate assessment of fetal resistance to hypoxia, to physiological childbirth and for choosing the type of delivery in real time can lead to the development of new obstetric devices and technologies for self-use by pregnant women, especially in combination with telemedicine capabilities.

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Conflict of Interest

The authors declare that they have no conflict of interests.

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