INFANTILE CEREBRAL PALSY DEVELOPMENT FACTORS
(LITERATURE REVIEW)

Abstract. The term Infantile Cerebral Palsy refers to complex of chronic neurological disorders that occur during perinatal period because of brain damage. Brain damage can occur in both ante-, intra- and postnatal periods. There are variety of reasons and it is impossible to specify the main one. Damage often occurs before birth, antenatal, during the first 6 months of pregnancy. There are at least three reasons for this: Periventricular leukomalacia (PVL). PVL is a type of lesion that affects alba due to lack of oxygen in the uterus. Abnormal brain development. The lesion may be due to mutations in genes responsible for brain development, some infections, such as toxoplasmosis, parasitic infection, herpes and herpes-like viruses and head trauma. There may be intracranial haemorrhage, when the foetus has a stroke. Haemorrhage may stop blood flow into the vital tissue of the brain, which may cause tissue injury or necrosis. Blood may thicken and damage surrounding tissue. According to various data, intrapartum lesions, such as birth asphyxia or birth trauma, account for up to 42%. In the postnatal period, brain lesion factors with development of cerebral palsy are usually considered infectious, less traumatic ones, but some works mention the hereditary component. Nevertheless, to date, the etiology of this disease has not been fully studied and it is not clear which pathogenic factors and what conditions lead to cerebral palsy. Therefore, we can state only the multi-etiolo of cerebral palsy and need for greater attention to the study of both biological and environmental factors that have an impact on foetus and new-born.

Keywords: cerebral palsy, antenatal, intrapartum, postnatal period, periventricular leukomalacia, cerebral accident, hereditary factor.

The term "cerebral palsy" unites a group of different clinical manifestations of syndromes that arise as a result of underdevelopment of the brain and its damage at various stages of ontogenesis and are characterized by the inability to maintain a normal posture and perform arbitrary movements [1]. The definition of cerebral palsy excludes progressive hereditary diseases of the nervous system, including various metabolic defects, lesions of the spinal cord and peripheral nerves [2]. Cerebral palsy is the most common cause of disability in children, affecting approximately two out of every thousand live births. The term "cerebral palsy" refers to a complex of chronic neurological disorders that occur in the perinatal period due to brain damage [3]. At present, it is clear that the term "cerebral palsy" does not reflect the diversity and essence of the neurological disorders present in this disease, but it is widely used in the world literature, since another term that comprehensively characterizes these pathological conditions has not been proposed to date. The merging of a number of neurological symptomomplexes in nosological group allows to adequately plan the organizational actions directed on early diagnostics and treatment of cerebral palsy on the basis of high medical and social importance of the problem [4].

Population-epidemiological studies show that in industrialized countries, the frequency of cerebral palsy is 2-2.5 cases per 1000 of population [2-4]. So, in the United States, cerebral palsy affects about 764 000 [5]. Data on the prevalence of cerebral palsy change with the development of medical science. Some authors [6] note in recent years the tendency to reduce the incidence of cerebral palsy by improving obstetric techniques, prevention and treatment. Others, on the contrary, believe that for a number of years the frequency of cerebral palsy in industrialized countries remains stable [7, 8], which is probably due to
the defeat of the nervous system mainly not during childbirth, but in the prenatal period. However, the majority of authors claim that the disease began to meet much more often [9-12] and explain this reduced mortality among preterm and newborn infants with low body weight who have risk of developing cerebral palsy is highly significant. In the Republic of Kazakhstan there is no clear account of children with cerebral palsy, not clarified the reasons specific to the region. There are many different opinions about the etiology of cerebral palsy, and the disease is considered as polyetiologically. Analysis of the causes leading to cerebral palsy showed that in most cases it is not possible to identify one of them, as often there is a combination of several adverse factors in both pregnancy and childbirth [2]. However, there is a popular opinion that the causes of cerebral palsy often lie in the intra-natal period, that is, associated with birth trauma, but the literature and scientific data say the opposite. The ratio of prenatal and perinatal factors of brain damage in cerebral palsy, according to various authors, varies: prenatal forms of cerebral palsy vary from 35 to 60%, intranatal - from 27 to 54%, postnatal-from 6 to 25% [2, 13, 14]. According to a number of authors [14-16], in 80% of observations the brain damage causing cerebral palsy occurs in the period of fetal development, and subsequently intrauterine pathology is aggravated by intrauterine. However, in every third case, the cause of cerebral palsy cannot be determined [17-19].

Most often, the damage occurs before birth, that is, antenatal, during the first 6 months of pregnancy. There are at least three reasons for this.

1. Periventricular leukomalacia (PVL) PVL - it is a type of damage that affects the white matter of the brain due to lack of oxygen in the uterus. This can happen if the mother has an infection during pregnancy, such as rubella or measles, low blood pressure, premature birth, or if she is taking a drug.

2. Abnormal development of the brain. The impaired development of the brain can affect how the brain communicates with the muscles of the body and other functions. During the first 6 months of pregnancy, the brain of the embryo or fetus is particularly vulnerable. Damage may be due to mutations in the genes responsible for brain development, some infections such as toxoplasmosis, parasitic infection, herpes and herpes-like viruses, and head injury.

3. Intracranial hemorrhage. Sometimes intracranial brain hemorrhage occurs when the fetus has a stroke. Bleeding in the brain can stop the flow of blood to vital brain tissue, and this tissue is either damaged or dies. Spilled blood can thicken and damage the surrounding tissue.

Several factors can cause a stroke in the fetus during pregnancy:
- A blood clot in the placenta that blocks blood flow
- Violation of blood clotting in the fetus
- Disorders of delivery of arterial blood to the fetal brain
- Untreated pre-eclampsia in the mother
- Inflammatory processes of the placenta (chorioamnionitis)
- Inflammatory diseases of the female genital organs

During childbirth, the risk increases due to the following factors:
- An emergency C-section
- Prolonged second stage of labor
- Use of vacuum extraction during childbirth
- Fetal or neonatal heart abnormalities
- Umbilical cord disorders

Anything that increases the risk of preterm birth or low birth weight also increases the risk of cerebral palsy [20].

More than 400 factors affecting the course of normal intrauterine development are described, the cause of cerebral pathology in 70-80% of cases is the effect of a complex of harmful factors on the fetal brain [3]. Intrauterine factors include acute or chronic extragenital diseases of the mother, primarily hypertension, heart disease, anemia, obesity, diabetes and other [1, 3, 11], occurring in cerebral palsy in 40% of cases [8]. Other "maternal" factors of perinatal risk are taking medications during pregnancy (10%) [7], occupational hazards (1-2%) [19, 21], parental alcoholism (4%) [11, 19], stress, psychological discomfort (2-6%) [7, 19], physical injuries during pregnancy (1-3, 88%) [7, 19]. In recent years, great importance in the etiology of cerebral palsy is given to the effect on the fetus of various infectious agents, especially viral origin [3, 7, 15, 16, 22]. According to Potasmanet al. [26], in 22% of patients with cerebral palsy (in the control group - in 9%) antibodies to Toxoplasma gondii were found in the blood serum.
A certain role in the occurrence of cerebral palsy is given to violations of the normal course of pregnancy at various stages. There are uterine bleeding, disorders of placental circulation, placental presentation or abruption [3]. Similar complications of pregnancy occurred in 2-13% of cases [17, 19, 24]. According to the study of A. Spinoillo [28], 17.5% of the surviving children born in women whose pregnancy was complicated by premature placental abruption were diagnosed with intraventricular hemorrhage, and 11.1% - cerebral palsy. According to some authors, immunological incompatibility of mother and fetus (ABO-and RH-incompatibility) was the cause of cerebral palsy in 2.0-8.7% of cases [7, 14, 19].

Most of these adverse factors of the prenatal period leads to intrauterine fetal hypoxia and disruption of utero-placental blood circulation. Oxygen deficiency inhibits the synthesis of nucleic acids and proteins, which leads to structural disorders of embryonic development. The development of the embryo in hypoxia may be the main cause of deformities and pathology of fetal development [14].

According to a number of authors, multiple pregnancy has a history in 4% of persons suffering from cerebral palsy [11]. The incidence in situations with multiple pregnancy is 6-7 times higher than in normal pregnancy and is 7.1-8.8 per 1000 newborns [26]. The frequency of cerebral palsy in triplets is 28 per 1,000 live births, and in twins 7.3 per 1,000 live births [27]. In multiple pregnancies, the risk of cerebral palsy for low-weight infants is the same as in low-birth-weight infants born as a result of pregnancy with one fetus, and vice versa, for children with normal body weight from twins, the incidence of cerebral palsy is higher than in children with normal body weight born during normal pregnancy (4.2 per 1000 live births) [28].

Treatment of infertility using reproductive technologies (ART). Most of the increased risk is due to preterm birth or multiple pregnancies, or both; both preterm birth and multiple births are increasing among children born with ART [29].

The intranatal risk factors for cerebral palsy include various complications in childbirth, the frequency of which exceeds 40.2% [7, 11, 19]; these are weakness of contractile activity of the uterus during childbirth (23.6%), rapid labor (4%), caesarean section (11.36%), prolonged labor (24%), a long anhydrous period (5%), breech presentation of the fetus (5-6.25%), a long period of standing of the head in the birth canal (5%), instrumental obstetrics (5-14%). It should be borne in mind that in the presence of disorders of fetal development of the child, childbirth very often has a severe and prolonged course. Thus, conditions are created for the occurrence of mechanical head injury and asphyxia, which are essentially secondary factors that cause additional disorder of the primary affected brain [5, 18].

Childbirth in pelvic presentation of the fetus leads to asphyxia and birth trauma 3 times more often than conventional labor [4], and in 1% of cases leads to cerebral palsy [30]. Cerebral palsy is also correlated with low fetal body weight. Studies have shown that 12.1% of children with low birth weight continue to develop cerebral palsy [30, 32]. Its frequency is 36.7 times higher in children with a body weight of 500 to 1499 g and 11.3 times in children with a body weight of 1500 to 2499 g than in children with a body weight of more than 2500 g [31].

H. Scheider [7] believes that only 10% of full-term newborns may have developed cerebral palsy due to birth asphyxia. Cerebral palsy can be predicted only in severe childbirth with asphyxia leading to tissue damage to the brain, in the presence of clinical symptoms detected from the first days of life. However, even in the presence of severe labor asphyxia, the causal relationship with the subsequently developed psychomotor deficiency is not absolutely provable, since brain damage can occur before the birth itself and cause labor asphyxia.

A significant place in the genesis of cerebral palsy is intracranial birth trauma-local damage to the fetus during childbirth as a result of mechanical influences (compression of the brain, crushing and necrosis of the brain substance, tissue tears, bleeding in the membranes and brain substance, violations of dynamic blood circulation of the brain), which can disrupt the further development of the brain and lead to many cerebral symptoms [18]. However, it should be borne in mind that birth trauma often occurs against the background of a previous defect in the development of the fetus, with pathological, and sometimes even physiological childbirth [22]. According to various authors, the incidence of birth trauma in cerebral palsy has decreased over the past few decades from 21.6% [33] to 4-5% [14, 19], what is associated with improved obstetric care.

In the postnatal period, the factors of brain damage with the development of cerebral palsy are usually considered infectious, less traumatic [18, 19, 20]. Some works mention the hereditary component in
their etiology [10, 35]. Genealogical research in the families of patients with dyskinetic (hyperkinetic) form of cerebral palsy, made N. A. Fletcher [12, 13] revealed the presence of relatives of patients with a certain proportion of affected parents and sibs. The author draws attention to the fact that in most patients the disease progressed in adulthood, which suggests the genetic heterogeneity of the disease with autosomal recessive and dominant types of inheritance. It does not exclude the existence of X-linked form, and the late age of the parents in most sporadic cases of the disease suggests dominant gene mutations. The literature describes cases when the clinical manifestations of some hereditary diseases was conducted in the form of the syndrome cerebral palsy: this is the chromosomal aberrations of the type of patau syndrome and partial trisomy of the 18th pair of chromosomes [17], X-linked chromosomal hydrocephalus [32], DORA-dependent dystonia [35].

R. Curatolo [11] studied the combination of cerebral palsy with epilepsy and mental disorders. In the genealogical history of patients with cerebral palsy were surprisingly frequent cases of epilepsy among relatives of the first degree of kinship, which, according to the author, indicates the important role of genetic factors in the development of cerebral palsy.

Of interest is the fact that in cerebral palsy there is a defeat mainly of males [6]. Cerebral palsy in boys occurs 1.3 more often and has a more severe course than in girls [14]. According to N. A. Fletcher [12], three-quarters of cases of moderate and severe tetraplegia in cerebral palsy occur among males and tend to have more severe motor disorders than in women.

Specialists in Pediatrics and neurology from the University of Bergen (Norway) during the first of its kind such a large-scale study revealed a significant genetic component in the complex of causes underlying the development of cerebral palsy. So, if there is a child with cerebral palsy in the family, the risk of having another child with such a violation increases nine times [35].

Thus, the analysis of the literature data on the risk factors of cerebral palsy indicates their diversity. However, to date, the etiology of this disease has not been fully studied and there is no clarity on what pathogenic factors and under what conditions lead to the development of cerebral palsy. Therefore, we can now talk only about some pathogenetic mechanisms of cerebral palsy, as well as the great importance of studying both biological and environmental factors that have an impact on the body of the fetus and newborn.

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БАЛЫЛАР ЦЕРЕБРАЛЬДІ САЛАУРУНЫҢ ДАМУ ФАКТОРЛАРЫ
(ӘДЕБІЕТКЕ ШОЛУ)

Анатомия. Балылар церебральді салауры термині міддінің зықкандандығы салдаратан перинаталды кезеде пайда болуына әсер етеді. Бұл міддінің зықкандануы қуралынағы және антенаталды және постнаталды кезендерде де пайда болуы мүмкін. Себебері салдану болғандықтан сіз бастысыңыңың ықтау мүмкін емес. Закым едетте тұрғының туралы, яның антенаталды кезенде, жүктеліктін алғашқы 6 айының ішінде пайда болады. Бұған кемінде уш сәбеб бар. Перивентрикулярды дәйемалазия (PVL), PVL – жатырғы отептің жетіпсіз болуы міддің ак тәтіна есеретін закым тұры. Міддің жалпы нормадан ауытып дамуы. Бұл закым міддін дамуында жауапты генін мүмкіндігінақ, оқошталмаз, паратезит қорғақ, герпес, герпес төрізді вирустар және бас жаракаты сияқты инфекцияларға байланысты болуы мүмкін. Бас сүйік ішке қана құйылу, ұрықтың нысульты. Місқа қана құйылу міддін өмірлік маңызды білімге қамысқан бұрынғы тәкітті және қана байқылған тікіз закымдама және мемлекетті әлдем. Алака қана қозғалуы, қана жағындада тікі закымдық мүмкін. Тұрлі мәліметтерге сөйкес, тұңғызған аспириция немесе тұу жаракаты сөзінө перинаталды закымдар 42% құрайды. Балалының церебральді сал ауруының дамуына экзелетен босақұдан кейінгі факторларға құқырдап аурулар және сирек жаракат себеп болуы мүмкін, алайда кейін сүйкістерде олардың этиологиясында туғыз куәлуулықтың компонент бар екені айтылған. Дегенмен, елі күнге дейін осы аурулар этиологиясы төлік жәрдәмен сәбіз БЦСА-ға қандай қозғалысқа және қандай жақындар экзелетінің анық емес. Сондықтан, біз БЦСА этиологиясы бірнеше екенін және ұрықтың
жем жана тұған балалының ағысқына есер ететін биологиялық және экологиялық факторларды зерттеуе үлкен қөмөк болу қажеттілігін алға береді.

Түйін сөзлер: ұрысқұлдық, антенаталдық, интраталдық, пострнаталды қезен, перивентрикулярлы дейінмада, ұрысқұлдық нисүлті, тұқымкүлдіші шекті.

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ФАКТОРЫ РАЗВИТИЯ ДЕТСКОГО ЦЕРЕБРАЛЬНОГО ПАРАЛИЧА
(ОБЗОР ЛИТЕРАТУРЫ)

Аннотация. Термин "детский церебральный паралич" (ДЦП) объединяет группу различных по клиническим проявлениям синдромов, которые возникают в результате нарушения мозга и его повреждения на различных этапах онтогенеза и характеризуются неспособностью сохранять нормальную позу и выполнять произвольные движения [1]. Определение ДЦП исключает прогрессирующие наследственные заболевания нервной системы, в том числе различные метаболические дефекты, поражения спинного мозга и периферических нервов [2]. ДЦП является наиболее распространенной причиной инвалидности у детей, затрагивая приблизительно двух из каждой тысячи рожденных живыми младенцев. Под термином «ДЦП» понимают комплекс хронических неврологических нарушений, возникающих в перинатальный период вследствие поражения головного мозга [3]. В настоящее время ясно, что термин "церебральный паралич" не отражает многообразие и сущности, имеющих при этом заболевания неврологических нарушений, однако его широко используют в мировой литературе, поскольку другого термина, всесторонне характеризующего эти патологические состояния, до настоящего времени не предложено. Объединение целого ряда неврологических симптомокомплексов в нозологическую группу позволяет адекватно планировать организационные мероприятия, направленные на раннюю диагностику и лечение ДЦП, исходя из высокой как медицинской, так и социальной значимости проблемы [4].

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