

Neuroendocrine Mechanisms of Pain in Newborn Children

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Annotation.From the first days of their lives, newborns experience primary pain due to neonatal screening, primary treatment and blood collection for laboratory analysis. As a result of untreated analgesia, the risk of developing neurological consequences is high and prevention is necessary.

For a long time, painful reactions in newborns did not attach importance. All newborns are faced with painful procedures soon after birth, and often even in utero. Newborns are sensitive to pain, but they cannot signal about it, based on anatomical and physiological characteristics and a set of pathological processes.

The pain perception system begins to develop in early pregnancy (starting from 6-9 weeks of gestation) and is fully formed by 21-23 weeks of intrauterine development. All anatomical structures necessary for the pain impulses are ready at the time of delivery: the nerve fibers are sufficiently myelinated already in the second trimester of pregnancy and are completely myelinated by the 30-37th week of intrauterine development. Afferent pain tracts are present even in newborns with a minimum gestational age: by the 8-14th week, most neuropeptides, transmitters of pain, are determined, by the 20th, nociceptors are developed, and in the cerebral cortex there is a normal number of neurons - 10 billion or functional changes. Even premature babies are able to experience pain and react to it with hypertension, tachycardia, an increase in intracranial pressure, and a pronounced neuroendocrine reaction. Moreover, newborns have a higher pain threshold than older ones. Simons et al. proved that each newborn undergoes an average of 14 painful procedures daily and 39.7% of them do not receive any analgesia. The problem of pain prevention in the neonatal period stands at the intersection of medicine, philosophy, ethics, deontology of morality. This is why the dissemination and improvement of strategies to prevent neonatal pain needs to be supported not only from an evidence-based perspective, but also from a humanitarian perspective. The International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience with actual or possible tissue damage, or a condition that is verbally described as consistent with such damage. Newborns who have spent a long time in the intensive care unit have different pain thresholds and other characteristics of pain sensitivity compared to healthy newborns. Long-term neurological consequences include changes in neuropsychic development and social behavior, later development of attention and learning ability. Repeated pain in a child can cause the development of intraventricular hemorrhage, ischemia and periventricular leukomalacia, leads to the development of DIC syndrome, metabolic acidosis, and forms a state of constant stress, or hyperalgesia. Such conclusions are prompted by the opinion about insufficient myelination of nerve fibers and the maturity of nociceptors, as well as the system of neurotransmitters, high concentrations of endorphins, and increased BBB permeability.

Key words: hypothalamic-pituitary-adrenal system, intraventricular hemorrhage, ischemia and periventricular leukomalacia.

The hypothalamic-pituitary-adrenal system has been functioning since the 2nd trimester of pregnancy. Up to 30 weeks gestational age, the level of fetal cortisol is low (5-10 mg/ml), rising to 20 mg/ml by 36 weeks and continuing to increase to 45 mg/ml before childbirth, and the peak (up to 200 mg/ml) occurs in the first hours after birth. Premature maturation of the placenta and its weight, initiation and the process of childbirth itself, as well as the process of childbirth itself, as well as intrauterine infections also affect the level of steroids in the umbilical cord blood. Serotonin and gamma-aminobutyric acid are already active intrauterinely and play a role even with early pain modulation. Prolonged prenatal development interferes with neurological development and may affect pain response after childbirth. Immaturity and concomitant inhibitory activity of GABA neurons. Babies born at a gestational age <32 weeks undergo multiple painful procedures every day, especially during the first 2 weeks of life. Unfortunately, many of these painful procedures do not provide pain relief. Given the numerous possibilities and methods of analgesia, the absence or insufficient relief of pain cannot be justified from a clinical point of view and is regarded as unethical. Clinical studies show that neonatal pain cannot be consciously remembered, but multiple painful events have immediate and long-term negative consequences. Excessive activity in the developing CNS caused by pain alters and damages normal synaptic development and is encoded as structural or functional changes. Assessment of the intensity of pain in newborns is a complex and challenging task due to the limited ability of such a child to express pain and stress, which is associated with their physiological and biological immaturity.

Purpose of work. To pathogenetically substantiate early neonatal pain in newborns and prevent the consequences of pain syndrome, develop an algorithm for the management of newborns. For the first time, neonatal pain of various origins, the consequences of uncontrolled pain, as well as the risk of developing neurological consequences are studied. To substantiate pain in response to stress, hormonal and metabolic changes are studied for timely adequate analgesia.

Material and research methods. The collection of material was carried out in the neonatal department of the SamMI clinic, in the neonatal pathology department of the children's multidisciplinary complex.

The object of our study was newborns from 0 to 7 days with severe pain syndrome in the amount of 60 newborns (boys 27-45% and girls 33-55%). In stage I, we studied the history of the course of labor and clinical neurological examination; determined pain markers, conducted anthropometry, neurosonography.

Results and Discussions. Based on follow-up material, the neurological consequences and manifestations of intact pain in the early neonatal period were studied, pain markers related to the group of steroid hormones and the dynamics of the concentration of cortisol in the blood of newborns were studied using the COMGORT and CRIES scales. From the first days of birth, the parameters of the activity of the cardiovascular system (heart rate, blood pressure), saturation of arterial blood hemoglobin with oxygen, and endocrine metabolic parameters were determined to identify newborns in need of analgesia. The children of the main group were divided into 3 groups:

1 group of children 27 - 45% of the cause of neonatal pain is - aggressive obstetric tactics in childbirth (mechanical extrusion of the fetus, obstetric forceps, vacuum extraction, stimulated labor, rough extraction during cesarean section, etc.); - birth injuries of the central nervous system, cervical spine, bone fractures, hematomas, and other birth injuries; - intracranial hemorrhage.

Group 2 consisted of 23 children - 38, 33% children with congenital hydrocephalus; - congenital malformations (gastroschisis, ventral and spinal hernias); - purulent-inflammatory diseases of newborns.

Group 3 consisted of 10 children - 16, 66% of whom received resuscitation aids (intubation, artificial ventilation of the lungs, vascular catheterization, etc.); - surgical operations and interventions; - painful procedures (frequent examinations of the medical staff, injections, punctures and catheterization of blood vessels, drainage of the pleural cavity, pericardium and joint capsule, intubation and suction of the contents of the trachea, taking blood from the finger, heel and vein, changing the plaster, bandages).

Pain reactions of newborns are divided into behavioral, physiological, neuroendocrine and metabolic.

Behavioral reactions in 18 newborns (30%) lack of sociability, contact with the examiner - indifference and / or flinching, tremors of the limbs and chin when touched; - refusal to eat, regurgitation, vomiting; - screams, groans, more or less prolonged unemotional, irritated, monotonous cry, painful cry; - painful crying, painful grimaces - hypertonicity of the limbs and hands clenched into fists, a spontaneous Moro reflex, opisto- and hypotonicity of the limbs and lethargy; - lack of spontaneous physical activity or local immobilization.

Metabolic reactions - in 24 newborns (40%), changes in the frequency and mechanics of respiration (usually tachycardia and tachypnea, but apnea attacks are also possible); - changes in the frequency and rhythm of heart contractions; - changes in the increase in blood pressure; - decrease in PO₂ and increase in PCO₂ in the blood; - a decrease in the saturation of blood and tissues; - unstable body temperature; - tension of the large fontanelle; - flatulence; - sweating of the palms; - pallor or spotting of the skin; - dilated pupils.

Neuroendocrine - in 18 - 30%, a change in the level of cortisol in plasma, urine and saliva and a decrease in the secretion of insulin and thyroid hormone; an increase in plasma renin activity; hyperglycemia; metabolic acidosis due to increased levels of lactate, pyruvate, ketone bodies; catabolic orientation of metabolism, negative nitrogen metabolism and the absence of weight gain.

Having studied the endocrine - immune indicators of pain in newborns, depending on the severity of the clinical condition, we determined the features of behavioral reactions and changes in some indicators of homeostasis in newborns in response to pain due to traumatic childbirth.

Currently, there are several scales for determining pain, based on the behavioral reactions of the newborn. The COMGORT scale determines the following parameters: newborn activity, agitation, breathing amount, physical activity, heart rate, blood pressure, muscle tone, facial expression. CRIES - Crying, Requires Oxygen, Increased Vital Signs, Expression, Sleep; The assessment according to these scales, we carried out after 30 minutes from the moment of birth, and at 24.48, 72 hours.

Conclusion: Thus, the system of pain perception is formed in newborns. During painful procedures, early and long-term neurological consequences can occur. Currently, there is no

single algorithm for the treatment and diagnosis of pain syndrome. After assessing pain using special COMGORT and CRIES scales, it will be possible to determine the conduct of nopharmacological or pharmacological analgesia, as well as monitoring vital signs, taking into account neuroendocrine features.

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