MINISTRY OF HEALTH OF UKRAINE

I. HORBACHEVSKY TERNOPIL NATIONAL MEDICAL UNIVERSITY OF THE MINISTRY OF HEALTH OF UKRAINE

Manuscript copyright
UDC: 616.8-009.7-036.11-053.2

Dina Aiurzanaeva

Master's Thesis

TREATMENT OF ACUTE PAIN IN NEWBORNS, CHILDREN AND ADOLESCENTS

Master of Science in Nursing

The Scientific Supervisor of the Thesis:
Lyudmyla Mazur, PhD
Associated Professor
Department of Higher Nursing Education, Patients` Care and Clinical Immunology
I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine

Ternopil – 2022

ABSTRACT

STUDY OBJECTIVES

1. To explore the basic concepts of etiology and pathogenesis of acute pain in children of various age, as well as the stages of development and diagnostic criteria of the disease.
2. To validate medical and organizational technologies of nursing care for pediatric patients with acute pain and to conduct an assessment of performed care-related activities.
3. To provide an assessment of the problems arising when providing care for pediatric patients with acute pain, to assess the level of interactions between healthcare personnel and relatives of patients the pathology.

THE OBJECT OF THE STUDY

Organization of nursing care for newborns, children and adolescents with acute pain.

THE SUBJECT OF THE STUDY

The factors that define the quality of nursing care for newborns, children and adolescents with acute pain.

METHODS OF STUDY

- Sociological method,
- Statistical method

CONCLUSIONS

This study has explored the basic concepts of etiology and pathogenesis the acute pain in children of various age and determined the specifics of health status and, as well as the stages of development and diagnostic criteria of the disease. The research has determined the socio-hygienic and medico-psychological aspects of lifestyles in pediatric patients with acute pain and their family members. The study has validated medical and organizational technologies of nursing care for pediatric patients with acute pain.

Pain is a physiological phenomenon that informs us about harmful effects that damage or pose a potential danger to the body. Thus, pain is both a warning and a defense system [1].

Currently, the definition of pain given by the International Association for the Study of Pain (Merskey, Bogduk, 1994) is considered the most popular: “Pain is an unpleasant sensation and emotional experience that occurs in connection with the actual or potential threat of tissue damage or is depicted in terms of such damage.” Such a definition does not evaluate the nature and origin of the painful stimulus, but equally indicates both its affective connotations and conscious interpretation.

Pain is an unpleasant subjective sensation that, depending on its location and strength, has a different emotional coloring, signaling damage or a threat to the existence of the body and mobilizing its defense systems aimed at consciously avoiding the action of a harmful factor and the formation of nonspecific reactions that ensure this avoidance [10].].

The first scientific concepts of the physiology of pain appeared in the first decades of the 19th century. It was a century of breakthroughs in the study of the mechanisms of pain, allowing scientists not only to better understand pain, but sometimes alleviate it.

In the 20th century, advances in immunohistochemistry, neuropharmacology, and neurophysiology made it possible to make truly great discoveries in the anatomy, physiology, and pathophysiology of pain. Over the past 20 years, there has been a marked increase in interest in the fundamental mechanisms of pain. Findings from these studies have found application in the clinic and a number of applied programs in various fields of medicine. The identification of receptors and processes involved in the generation and transmission of pain has led to the application of new tools and techniques that provide new and increasingly effective approaches to pain control. These include the use of pre-analgesia with opioids or non-narcotic (non-steroidal anti-

inflammatory) drugs, alpha-2-adrenergic agonists and local anesthetics, patient-controlled analgesia in the postoperative period or administration of opioids through a patient-controlled device, pain modulation with biogenic amines such as endogenous opioid peptides, the use of intrathecal administration of drugs for patient-controlled epidural analgesia, epidural stimulation of the spinal cord [24].

New technologies and new tools have made it possible to manage pain more effectively. The use of such methods has led to patient satisfaction and improved clinical outcomes. Our ancestors were forced to believe moralists (and doctors) who convinced them of the necessity and usefulness of pain and forbade the use of such unnatural means as anesthetics during childbirth. Doctors today, when performing diagnostic procedures or surgeries, cannot allow their patients to suffer “for their own well-being”. The state of pain is a decisive basis for the appointment of effective treatment, which is a consequence of a deep conviction in the significant negative impact of pain on quality of life [25].

The meaning of pain. Pain can have a signal and pathogenic value.

The signal value of pain. The sensation of pain is caused by a variety of agents, but they are united by a common property - a real or potential danger of damaging the body. In this regard, the pain signal ensures the mobilization of the body to protect against a pathogenic agent and the protective restriction of the function of the organ affected by pain.

The mobilization of the body to protect against a pathogenic agent is also important. For example, activation of phagocytosis and cell proliferation, changes in the central and peripheral circulation, etc., are also important. A protective behavioral reaction to pain is also important, aimed either at “avoiding” the action of a damaging factor (for example, pulling back a hand), or at its elimination (extraction from the skin foreign body).

Pathogenic value of pain. Pain is often the cause and / or component of the pathogenesis of various diseases and disease states (for example, pain as a result of an injury can cause shock and potentiate its development; pain during inflammation of the nerve trunks causes dysfunction of tissues and organs, the development of general reactions of the body: an increase or decrease in arterial pressure, dysfunction of the heart, kidneys) [1].

Acute pain is defined as pain of short duration with an easily identifiable cause. Acute pain is a warning to the body about the current danger of organic damage or disease. Often persistent and sharp pain is also accompanied by aching pain. Acute pain is usually concentrated in a certain area before it somehow spreads wider. This type of pain usually responds well to management [10].

Acute pain is a sensory reaction followed by the inclusion of emotional-motivational vegetative and other factors in violation of the integrity of the body. The development of acute pain is associated, as a rule, with well-defined painful irritations of superficial or deep tissues, skeletal muscles and internal organs, and dysfunction of smooth muscles. The duration of acute pain is determined by the recovery time of damaged tissues and (or) impaired smooth muscle function. The main afferent "highway" of acute pain is the lateral or neospinothalamic system.

Acute pain is divided into superficial, deep, visceral and reflected.

Superficial pain arising from damage to the skin, superficial subcutaneous tissues, mucous membranes, is felt as local, sharp, stabbing, burning, throbbing, piercing.

Deep pain occurs when the pain receptors of muscles, tendons, ligaments, joints and bones are irritated. It has a aching, pressing character, is localized less clearly than superficial.

Visceral pain occurs when internal organs and tissues are damaged and can be of a diverse nature. Often they are tied to some somatic region, but, as a rule, they are poorly defined topographically. Characteristic of visceral pain is the launch of autonomic and somatic reflexes, causing general and local autonomic symptoms, hyperalgesia and muscle spasms.

Reflected pains are pain sensations in certain peripheral areas (Ged-Zakharyin zones), in pathological processes, in deeply located tissues or internal organs. In this case, local hyperalgesia, hyperesthesia, muscle tension, local autonomic reactions may occur. The mechanism of referred pain has not been fully elucidated. There are several hypotheses. According to one of them, pathological impulses from the internal organs, entering the posterior horn of the spinal cord, excite the conductors of pain sensitivity of the corresponding dermatomes, where the pain spreads. In accordance with another hypothesis, afferentation from visceral tissues on the way to the spinal cord switches to the cutaneous branch and antidromically causes an increase in the sensitivity of skin pain receptors, which implements the phenomena of hyperalgesia and hyperesthesia in the corresponding zone. The third option suggests that two branches depart from the cell of the spinal ganglion: one - to the internal organ, the other - to the skin. Therefore, visceral pain afferentation can be mistakenly perceived as irritation of the nociceptors of the corresponding skin dermatomes [10].

Chronic pain is pain that has "broke away" from the underlying disease and acquired a "supra-organ" character. The International Association for the Study of Pain defines chronic pain as "...pain that continues beyond the normal healing period." There are various approaches to assessing the duration of chronic pain. According to experts from the International Association for the Study of Pain, the most appropriate period is 3 months. However, the main difference between chronic pain and acute pain is not the time factor, but qualitatively different neurophysiological, psychophysiological and

clinical relationships. In recent years, chronic pain has begun to acquire the status of not only a syndrome, but also a separate nosology. Its formation depends more on a complex of psychological factors than on the nature and intensity of peripheral nociceptive effects. A variant of chronic pain is psychogenic pain, where a peripheral factor may be absent or play the role of a “triggering” or predisposition mechanism, thus determining the choice of a “painful” organ (headache, cardialgia, abdominalgia, etc.) [25].

In contrast to acute, the dominant mechanisms for the formation and perception of chronic pain are cerebral systems, among which, undoubtedly, the integrative non-specific systems of the brain play a leading role. The clinical manifestations of chronic pain and its psychophysiological correlates are largely determined by the psychological characteristics of the individual, his personality, the influence of emotional, cognitive, social and cultural factors.

Pain is the most striking sign of illness and a traumatic factor for a child. Despite this, it is often underestimated, in pediatrics, pain relief has only recently become part of the treatment. In 1968, Swafford and Allen stated that children rarely needed narcotic analgesics. Most often, the child says that he does not feel well, he is uncomfortable or requires the presence of his parents, but cannot explain that he is in pain. In reviews of past years, data have been published, according to which pain relief in children, starting from infancy, is far from perfect. Checks in the 1970s and 1980s showed that the likelihood of postoperative analgesia in children, including infants, is less than the corresponding figure in adults. During this period, some newborns were operated on under minimal anesthesia, although this practice was criticized [16].

Almost 20 years later, in 1987, it was found that the density of pain receptors in children and adults is the same. Their connection with the central nervous system exists already at the 30th week of development, pain impulses are transmitted along unmyelinated or

incompletely myelinated nerve fibers. This confirms that the anatomical and physiological basis for pain perception exists from the moment of birth [19].

Wider research into the neurophysiology of pain and the consequences of inadequate therapy (eg delayed recovery or behavioral changes) has led to the development of new methods of pain relief. At the same time, it was necessary to create pediatric “pain centers” and new protocols for pain management and monitoring [24].

Studies conducted in the last 15 years show that newborns, infants and children of subsequent age groups can be safely administered with analgesia and anesthesia if age-related corrections in methods and doses are observed [1].

In the treatment of acute pain syndrome in children, the main focus is on drug treatment of pain, but it should be remembered that several non-pharmacological methods, including hypnosis and specific cognitive behavioral approaches, have shown good efficacy in children. If the hospital environment is rearranged so that it is no longer frightening for the child, then, naturally, the anxiety and fear, which, in themselves, can aggravate the pain, will be weakened. However, the presence of non-pharmacological approaches should not be a reason for not choosing analgesics [8].

Assessing the severity of the pain syndrome in a child is not easy, but it is an extremely important task, since treatment tactics depend on it. The perception of pain and the reaction to it, depending on age, is different. The gold standard for assessing pain in adults is the Visual Analogue Scale, which can be used in children as young as 5–6 years of age. For this purpose, children aged 3–5 years can be offered a modified scale, where the numbers are replaced by drawings in the form of facial expressions of emotions, or the so-called ladder of pain, along which the child must answer how many steps the toy could climb if it had it hurts just as much as the baby [6].

In addition to emotional pain, it also causes a number of pathophysiological and behavioral reactions that can be used to objectively assess the severity of the pain syndrome [8] .

Children of different age groups express their pain differently than adults. So, the body of babies can intensely tense up, stretch out, while arching, and a grimace of pain is observed on the face (eyebrows are lowered and tilted towards each other, eyes are closed, the mouth is open in the shape of a square). The child cries loudly and inconsolably, presses his knees to his chest, is hypersensitive or irritable. It should be noted that crying is the most nonspecific symptom and can be considered a manifestation of a reaction to pain only when other, most common causes (hunger, thirst, anxiety, desire to attract the attention of parents) are excluded [19] .

Older kids express verbal aggression, move away from communication and games, physically resist, repelling a painful stimulus after its application, and spare the area of the body that causes suffering. Thus, in children over the age of 3 years, the assessment of the pain syndrome is greatly facilitated, since at this age the child can quite clearly express and identify pain using special rating scales (for example, the Faces Pain Rating Scale), and also clearly show the place where it hurts. , on your body or in a picture [25].

However, it should be remembered that children suffering from pain do not always present active complaints. The reason for this may be: fear of a doctor or illness, resentment or irritation with parents or others, fear of injections or drugs, as well as the fact that they can be admitted to the hospital, fears of additional examinations. In this regard, physicians are advised to make the most of the information obtained from interviewing parents, testing on scales, and assessing physiological and behavioral responses [6].

Preschoolers can already describe the intensity of pain, cling to their parents, demanding additional emotional support (kisses, hugs), realize that they can benefit from their condition, and in some cases perceive pain as punishment.

School-age children use objective characteristics and comparative adjectives to describe pain, may complain of nightmares, and also clench their fists, clench their teeth, frown, close their eyes, tighten the muscles of the body, spare the sore spot, and also behave like younger children .

Older children consciously localize and verbalize pain, their behavior is unstable and can change (irritability, whims, rudeness). Appetite and sleep can be disturbed at any age [10].

In the interpretation and assessment of pain in newborns and infants, as well as in children with psychomotor retardation and impaired communication functions, the use of specially designed scales that allow a complex assessment of the behavioral and physiological reactions of the child: the Neonatal / Infant Pain Scale (NIPS) is of great help for children under 1 year old, the FLACC scale for children from 1 to 3–4 years old, etc. Additional help can be provided by using the bedside pain assessment scale, as well as using the parental scale, according to which the child's pain sensations are graded as no pain, mild pain, moderate and severe [6].

Pain perception and pain memory in children. Pain is one of the earliest psychophysical functions that form and is associated with the most "ancient" brain structures. By 30 weeks of fetal development, all pathways for conducting and perceiving pain have already been formed. Since that time, the child perceives pain, and its intensity is often even greater than in adults. However, the subjective nature of pain makes it difficult to measure. This is especially true for those who find it difficult to express their pain in words. As a result, according to the researchers, until the early 80s of the twentieth

century, the treatment of pain in newborns was rarely carried out adequately, because. it was assumed that because of the immature nervous system, babies are practically unfamiliar with pain. The work of Anand et al. showed that preterm infants after surgery with conventional minimal anesthesia had stronger reactions (increased concentrations of catecholamines, glucagon, corticosteroids), they had more postoperative complications, and mortality was higher compared to the group of newborns who received full anesthesia. McCrath and Unruh have shown that the immaturity of newborns is not about their ability to experience pain, but about the exclusivity of their inability to signal it to adults [1].

The evidence currently available allows professionals to strongly demand the provision of pain relief to children of all ages, if only because all human beings are entitled to adequate assistance in controlling pain, whether they can report it or not [25].

It should also be taken into account that the general perception of treatment and illness by an adult patient and a child is different. An adult is able to evaluate the benefits of medical procedures and medical manipulations and positively perceive the situation of treatment, medical staff, despite the pain and discomfort experienced [5] .

The child's thinking (until approximately the initial adolescence) is concrete, visual, more fragmented. Thus, a large randomized study showed that children of almost all ages consider needles and procedures associated with their use to be the most frightening and painful component of a visit to the doctor [8].

Due to the lack of semantic regulation, emotions and sensations play an important role in assessing the situation and adapting to it. Therefore, curative and preventive medical procedures associated with painful sensations, or diseases accompanied by pain, are often associated in children with punishment and violence. Children often feel guilty for their own poor health, regarding it as a manifestation of their own "badness" [6].

Even children who are not yet able to speak remember very well all the details of painful procedures and events. When the procedure is repeated, they have an increase in the “stress” reaction already at the time of skin treatment before the procedure. Negative experience can increase the pain response from time to time, like a snowball, determining the child's further response to painful stimuli [6] .

Memory causes the body to avoid those situations that, due to the experience of pain, have acquired the meaning of "dangerous" in the child's life. If this pain is the result of medical manipulation, treatment, or illness, then such avoidance is called "medical post-traumatic stress disorder syndrome." A well-known manifestation of this disorder is “needlephobia”, which is familiar to many adults.

Influence of different factors on the perception of pain in children. Pain is an individual response of each organism, which develops under the influence of, among other things, emotional, social, cultural, and environmental factors. The pain response is due to the influence of constant and changing factors over time (environment, situation). The constant variables traditionally include gender, the temperament of the child, and the age period. It is known that girls give a greater pain response than boys, small children compared to older children, children with less developed thinking, more capricious (uncontrollable) children, children with reduced general adaptation, more sensitive and more emotional children, with more a vivid and figurative description of pain, as well as with an internal locus of control (the tendency to ascribe responsibility for ongoing events, to respond to difficult situations with a sense of guilt) [19] .

It is noted that intraethnic differences in individual responses to pain stimuli are much wider than interethnic ones [10].

Variables that change over time include everything related to the medical situation in which the child is located and to his immediate environment at the moment. Significantly increases the pain response in children, the tendency of others and the child himself to regard the situation of illness or medical intervention as a catastrophe; anxiety, desire to benefit from the situation, fear of health professionals and procedures, hectic and noisy environment, lack of positive motivation (for example, explaining to the child that the painful procedure is done to overcome or prevent illness), absence of parents or their anxiety, inability to the parent to “contain”, restrain the child’s feelings and calm him down. In the same child, during the same procedure, under the influence of negative external factors (such as serious anxiety of the child, absence of parents, anxiety of parents), pain sensations can significantly increase [6].

Influence of pain on the further development of the child. Despite the fact that pain has a signaling function, indicating a malfunction, damage in the body, mobilizing the body's reserve forces to ensure the reaction of flight and defense, often its "positive" meaning is extremely exaggerated. Pain calls for help, treatment [19].

From a psychological point of view, to endure pain is not only useless, but also harmful. Pain impairs the quality of life (perception of the possibilities and fullness of life) in children of different ages and with various diseases and in cases of various medical procedures. Thus, in adolescents with arthritis, a high level of pain led to a decrease in such indicators of quality of life as physical, emotional and social functioning. In children with chronic abdominal pain of non-organic origin, as well as in children with gastroisophagitis or inflammatory bowel disease accompanied by pain, there is a decrease in the quality of life in all respects compared to healthy peers [25].

Pain has pronounced negative effects: both short-term and delayed in time. Some authors, depending on the severity of the reaction and the duration of the consequences in response to medical situations and diseases accompanied by various pains, divide

acute stress disorder (OST) (acute stress disorder) and post-traumatic stress disorder (PTSD) (posttraumatic stress disorder). The first (OST) are characterized mainly by dissociation, avoidance behavior, anxiety and excitability, obsessive repetition of the experience, the symptoms last from 2 days to 4 weeks and gradually fade away. The second (PTSD) is also characterized by repetition of the experience, avoidance behavior, high excitability, but the symptoms last at least one month [6].

According to the ICD-10 and DSM-IV, post-traumatic stress disorder is classified as an anxiety disorder. Depending on age, the ability to cope with traumatic pain experience, the characteristics of medical situations, the reactions of children may be different.

Infants and young children show signs of regressive behavior, whimpering, enuresis, loss of new skills, loss of speech, difficulty falling asleep or nocturnal awakenings [1].

Preschool children tend to reproduce their experiences in games, along with this, difficulty falling asleep and nightmares, decreased speech activity, increased separation anxiety (when parting with loved ones), as well as fears, such as fear of the dark, may also appear.

Children of primary school age demonstrate nightmares, fixation on a traumatic event, obsessive repetitions, various psychosomatic reactions, overexcitation, inadequate emotional reactions, fears, avoidant behavior, aggressive attacks [19].

In adulthood, there may be a desire for greater independence - early sexual relations, the desire to leave the house - or, conversely, an age-inappropriate increase in dependence. It is also possible deviant behavior, the use of psychoactive substances. Adolescents are more likely than younger children to develop feelings of guilt and intrusive memories.

At any age, a child, faced with experiences of pain, often loses interest in ordinary activities, his self-esteem decreases, and the prospect of the future is often lost. Such experiences can upset relationships with relatives and friends, especially if pain is associated with vital procedures or a serious illness, as well as violence [19].

In turn, the consequences of PTSD can lead to a violation of the child's adaptation to school, habitual life and environment.

Different types of traumatic situations associated with pain experience in children were compared: type I traumatic situations associated with sudden events (fire, accidents with injuries, various medical procedures) and type II situations associated with long-term exposure to an unpleasant event (cancer, organ transplant).). Both cases were characterized by avoiding behavior in children, increased anxiety, and repetition of situations. Children with type I trauma were more likely to have a complete detailed memorization of the situation, the development of premonitions, a violation of the perception of reality, while children with type II trauma showed greater denial of the situation, dissociation, lack of feelings or problems. In response to medical procedures, both type I responses (if the procedures are associated with dangerous interventions) and type II responses (if the procedures are more painful are repeated many times, and the treatment itself is prolonged and aggressive) can develop [19] .

Various psychological consequences of pain experience in children are analyzed depending on the experience, the context of various diseases. The pain experience associated with burns is more likely to provoke nightmares, enuresis, and phobias in children within a year or even more after the accident. The pain experience associated with injuries and car accidents leads to the fact that children are less able to differentiate fear, whether it is associated with the accident itself or with painful procedures during treatment. Replaying traumatic situations, reproducing the situation in dreams, and avoiding behavior were noted [26] .

In response to surgery, accompanied by pain, more than 80% of children and their families experience acute stress. Such trauma provokes fears, depression, generalized anxiety. Every fifth child develops post-traumatic stress disorder, lasting more than 4 months and manifesting itself in everyday life [6].

In many ways, this stress is provoked by the level of pain experience during illness and treatment. More severe early stress (acute stress response) in children and parents can help prevent children from developing post-traumatic stress disorder.

Particular attention is paid to the effect of pain in children with cancer. The increase in symptoms of PTSD, in comparison with other diseases, is associated with the duration of treatment, painful manipulations and intensity of treatment. Especially in young children, the association of PTSD with subjective measures of treatment increased.

Data from the US-based Center for Pediatric Traumatic Stress in Philadelphia also confirm that the experience of pain in children can have significant negative short-term and long-term psychological and social consequences. Among the psychological consequences in adult life are: chronic pain disorder, anxiety, various phobias, hypochondriacal personality development, panic attacks. Among the social ones are reactions of avoiding and avoiding behavior from new and unfamiliar situations, which significantly reduce the level of social adaptation [8].

Significant social and emotional problems in the case of pain in childhood are experienced not only by children, but also by their parents.

Some chronic and acute diseases of children, accompanied by pain, unfortunately, end in death. In such cases, the fact that the child experienced less pain and suffering before

death may be of decisive importance for the family in rehabilitation and coping with the loss of the child [26].

Reducing pain experiences reduces the severity of medical stress in children and their families.

Thus, it becomes obvious that the problem of pain in pediatrics currently occupies a special place. Childhood experiences can make a person more or less susceptible to pain. Lack of analgesia, pain management can have serious negative consequences for the development of a harmonious and well-adapted personality, as well as for the establishment of doctor-patient partnerships in adulthood.

THE RELEVANCE OF RESEARCH

1. Currently, the medical community recognizes the seriousness of the problem of treating pain in newborns, infants, preschool children, other age groups who are treated in intensive care units, surgical hospitals, underwent surgery. At the same time, the right of the child to receive effective and safe analgesic therapy is emphasized.
2. The problem of treating pain in children, especially newborns, is not only related to medicine, it stands at the intersection of medicine, philosophy, ethics, deontology and morality. Therefore, the dissemination and improvement of a strategy aimed at the effective treatment of pain in children must be supported not only on the basis of evidence-based data, but also on humanitarian grounds.
3. Thus, the relevance of this work can be defined as the need to find optimal, affordable and effective methods for diagnosing and treating pain in children, which would provide maximum pain relief in a child and have minimal side effects.

PURPOSE OF THE STUDY

Optimization of measures aimed at identifying and treating pain syndrome in children of different age groups

RESEARCH TASKS

1. Determine ways to assess the severity of acute pain in children of different age groups
2. Determine the general aspects of the pharmacology of different periods of childhood.
3. Outline the basic principles of pain control in children, pharmacological and non-pharmacological methods of its relief.

Features of assessing the strength of acute pain in children of different age groups

For children aged 8 years and older, the same visual analog scales for assessing the severity of pain as for adults can be used - this scale is applied to the ruler, which should be placed horizontally.

For children from 3 to 8 years old, when self-assessing the strength of pain, you can use either mimic scales (the faces in photographs or drawings are lined up in a row in which the facial expressions of distress gradually increase) or scales with color analogy (rulers with increasing brightness of red, indicating the strength of pain) . A high degree of similarity was reported in terms of pain intensity obtained using the scale of photographic portraits and the scale of color analogy in children aged 3 to 7 years after surgery.

The use of the Child Behavior Observation Scales is the main method for assessing pain in newborns, infants and children aged 1 to 4 years, as well as in children with developmental disabilities. In such scales, pain is assessed by facial expression, motor responses from the limbs and trunk, verbal responses, or a combination of behavioral and autonomic changes. In some of these methods, the term "distress" reflects not only pain, but also fear and anxiety [19].

During surgery and in intensive care settings, it is useful to document physiological responses to pain, although these responses may be nonspecific. For example, tachycardia can be caused not only by pain, but also by hypovolemia or hypoxemia. Therefore, it is difficult to assess the severity of pain in newborns, infants and children aged 1 to 4 years, as well as in children with significant developmental disabilities. If the clinical picture does not allow for definite conclusions, one should resort to the use of measures that level out stress, which include the creation of comfort, nutrition and analgesia, while the effect can be used to judge the cause of distress [25].

General aspects of pharmacology of different periods of childhood

As the organism develops, changes in pharmacokinetics and pharmacodynamics occur. Trends in the development of some physiological parameters in different age periods are summarized in Table. 1. Many of these trends are determined by the fact that different hepatic systems responsible for the metabolism of different drugs mature at different rates [19].

Table 1.

Physiological features of different ages related to the action of painkillers.

Physiological system	**Features of different ages**	**Clinical Significance**

Various environments of the body	Newborns: relatively little fat and muscle; quite a lot of water; increased volume of distribution for water-soluble drugs	Increased duration of action of some water-soluble drugs; increasing the interval between doses
Plasma protein binding	Neonates: decreased concentrations of albumin and alpha-1-acid glycoprotein	An increased concentration in the unbound form of those drugs that are characterized by high protein binding - an increased likelihood of overdose and toxic effects
Liver enzyme systems that metabolize drugs	Newborns and infants: immaturity of hepatic enzymes - subtypes of cytochrome P-450 and glucuronyl transferases. In children 2-6 years old - increased liver mass	Neonates and infants: reduced metabolic clearance, reduced infusion rate and increased intervals between doses required
Renal filtration and excretion of drugs and their metabolites	Neonates and infants: reduced glomerular filtration rate	Neonates and infants: accumulation of drugs or active metabolites excreted by the kidneys - reduced infusion rate and increased intervals between doses are required

Metabolic rate, oxygen consumption and respiratory function	Newborns and infants: increased oxygen consumption; increased ratio of oxygen consumption to functional residual capacity; few type 2 diaphragm fibers (resistant to fatigue); reduced airway caliber; increased resistance to breathing; reduced control of the muscles of the pharynx and tongue; reduced rigidity of the larynx and upper trachea; reduced ventilation response to oxygen and CO2; functional residual capacity close to alveolar closure volume	Newborns and infants: breath holding and apnea quickly lead to hypoxemia; the effect of inhalation anesthetics comes on faster and stops faster; increased risk of atelectasis and respiratory failure if illness or surgery places additional stress on the respiratory system; increased risk of hypoventilation, as weakness of ventilation reflexes and weakness of responses to opioids and sedatives are manifested together

* It is understood that the physiological parameters in children are characterized here relative to the parameters of the physiological functions of adults (per unit weight) and are designated, for example, as "low" or "high". Doses (per kg of body weight) or infusion rates (mg/kg/hour) in children are compared with those in adults and are also referred to as "reduced" or "increased".

In newborns, there is a rather low clearance (per unit body weight) of many drugs, compared with children of subsequent age groups and adults, and the main reason for this difference is the incomplete maturity of the hepatic enzyme systems at birth [1].

Conversely, compared with adults, children aged 2-6 years have greater clearance (normalized by weight) of many drugs. The higher productivity of cytochrome P-450 metabolism in these children, compared with adults, is mainly due to the greater mass of the liver per kilogram of body weight in children, and not to the greater catalytic ability of the enzyme itself.

Increased clearance rates in children 2-6 years of age, compared with adults, may mean that children should have a shortened interval between doses of the drug. For example, a slow-release formulation of morphine given twice daily for adults should be given three times daily for children [19].

Genetic variability in metabolism between individuals can increase or decrease the analgesic effects of drugs. For example, the genetically determined absence of the 2D6 subtype of cytochrome P-450 (namely, this subtype converts codeine to morphine) can lead to the ineffectiveness of codeine as an analgesic.

In the first weeks of life, renal blood flow, glomerular filtration and tubular secretion increase, and at the age of 8-12 months these indicators reach the level observed in adults. The clearance of drugs through the kidneys can be especially low in preterm infants immediately after birth [1].

With age, the structure of the body changes. The proportion of body weight to water is greater in newborns than in children of subsequent age groups. In newborns, a larger proportion of body weight is made up of tissues with a high level of perfusion, including

the brain, heart and other internal organs, and a relatively small proportion is represented by muscles and fatty tissue.

In newborns, the concentration of plasma proteins that bind to drugs is quite low. With regard to drugs with high protein binding, low plasma protein concentrations in neonates can lead to an increase in the fraction of free (unbound) drug, and, consequently, to an increase in both the beneficial effect and toxicity of the drug [1].

Age-related changes in lipid content in the brain and drug binding to proteins can affect the distribution of drugs throughout the body, in particular, on the indicators of drug content in the cerebrospinal fluid and in the brain relative to blood concentration, which does not depend on changes in the permeability of the blood-brain barrier. The penetration of a drug into the central nervous system is determined not only by passive diffusion, but also by the work of specific carrier substances, which can either prevent the substance from passing through or ensure its entry into the brain. These carriers include P-glycoproteins.

Most medicines come in forms intended for use in adults, and dosages or dilutions in pediatric practice can be misleading. Common miscalculations in pediatric dosages include confusion between milligrams and micrograms, misunderstanding decimals, mistaking a daily dose for a single dose (e.g., a dose of 100 mg per kilogram per day is prescribed, divided into doses given at 6-hour intervals, and instead every 6 hours give a dose of 100 mg per kilogram).

Postoperative pain

In children, as in adults, various interventions are performed using local and/or regional anesthesia, which uses a wide range of drugs, including opioids, non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol [5].

Basic principles

1. Postoperative pain is a complication of surgery (like infection or fluid and electrolyte imbalance), it should be eliminated and prevented. Prevention of the appearance of postoperative pain should be part of the modern theory and practice of postoperative treatment.
2. When conducting antianginal therapy, attention should be paid to the level of pain and their characteristics. It is necessary to assess the level of pain and, on the basis of this, create special scales and tables so that medical personnel can use them as a tonometer or thermometer when assisting a patient.
3. A protocol to prevent the development of postoperative pain should be used in every department of pediatric surgery. Prevention of pain should be carried out before the start of the operation. Such activities include an explanatory conversation with parents and the child, adequate anesthesia during surgery, the appointment of antianginal therapy in the postoperative period, the identification of possible side effects, as well as monitoring the patient (pain may occur).
4. In order for analgesia to be effective, it must be well planned. Painkillers should be given before the pain appears or becomes unbearable. This explains the appointment of small doses of analgesics (paracetamol) to surgical patients, even in cases where they do not require anesthesia.
5. Medical treatment of pain by necessity is not effective enough, it is not preventive and should not be used as standard. When conducting rational postoperative analgesia, drugs should be administered at certain hours and by infusion, with insufficient effectiveness of therapy, it is advisable to additionally prescribe certain drugs.
6. Prescribing a large number of drugs has its advantages: their combination allows you to achieve a synergistic effect, reduce the doses of some drugs and thereby reduce the risk of side effects.

7. In children, it is preferable to administer drugs orally, rectally, intravenously, or epidurally (if it is not possible to install intravenous catheters). Intramuscular administration of drugs is undesirable, since this is a painful manipulation that children are afraid of [7].

Preoperative period. Parents and the child should be familiar with the proposed pain relief plan, and be sure that the pain will be identified and neutralized in time. Prevention of postoperative pain begins with premedication.

In the operating room. During surgery, anesthesia methods should be chosen that provide adequate analgesia during surgery and in the postoperative period, such as local and / or regional, and general anesthesia (using opioids).

If it is not possible to perform regional anesthesia, the wound should be infiltrated with long-acting local anesthetics before or after surgery (bupivacaine + adrenaline). This technique is very simple and convenient for some surgical procedures, such as pyloromyotomy. Wound infiltration with bupivacaine does not require subsequent administration of analgesics in the postoperative period.

The child should be brought back to the ward without feeling pain. He needs to carry out adequate and autonomous therapy, monitoring, and sedation in accordance with the type of surgery, age, and severity of the condition [16].

In the intensive care unit. Considering the age of the patient and the intensity of pain, it is necessary to develop special schemes for its monitoring, prevention, and treatment. Operations are divided depending on the intensity of postoperative pain (mild, moderate intensity, acute), and according to these groups, treatment regimens are drawn up. They should be simple without a lot of drugs, given their side effects [5].

The appearance of pain, sedation, and the occurrence of side effects of drugs should be recorded at regular intervals depending on the type of operation and analgesia performed. With the help of special scales of pain intensity and sedation, the minimum

pain value should be determined individually for each patient, and according to the scheme, the drug prescribed for this case should be administered. The effectiveness of additional injections should be determined by assessing the intensity of pain. Parents and even medical staff are sometimes against the use of opioids in children. Pain intensity, sedation, and vital signs should be monitored when using them.

Studies have shown that children under three months of age are just as susceptible to depressive effects as older patients. There is no evidence that opioid-induced respiratory depression is more common in children than in adults. When administering opioids, naloxone should always be on hand [18].

Opioids in the treatment of acute pain syndrome

Opioids are indicated for postoperative pain, sickle cell pain, and cancer pain. As with adults, the risk of addiction (compulsive drug-seeking behavior) is very low in children who receive opioids for pain relief. In the past 15 years, the use of opioids in children from infancy has been extensively studied [12] .

Pharmacokinetics of opioids in neonates
infants and children over 1 year of age

The clearance of some opioids, per unit weight, is low in newborns and in the first 2-6 months of life reaches the same levels as in adulthood. The half-life of morphine when analyzed by age group was: 9 hours in preterm infants, 6.5 hours in full-term infants and 2 hours in children of subsequent age groups.

The active metabolites of morphine are excreted by the kidneys and may accumulate in neonates as their renal function has not yet matured. Prolongation of the clearance time of morphine metabolites in neonates may enhance the effects of morphine, such as

analgesia, respiratory depression, and, rarely, convulsions. In newborns after abdominal surgery, fentanyl clearance may be impaired [1].

Opioid pharmacodynamics and clinical outcomes in neonates, infants and children of subsequent age groups.

At birth, the child has not yet fully formed reflex reactions to airway obstruction, hypercapnia and hypoxemia, these reflexes gradually develop during the first 2-3 months of life of both premature and full-term newborns. Newborns and infants with chronic lung disease have impaired ventilation reflexes, which may increase their risk of opioid respiratory suppression.

Descriptions of individual clinical cases and studies of groups of patients who have not been intubated indicate a higher incidence of respiratory suppression with the use of opioids among newborns compared with children over 6 months of age. However, morphine infusions in intubated neonates in the postoperative period result in low pain scores (according to behavioral scales) and high hemodynamic stability [12]

In infants aged 3-6 months, the analgesic effects of morphine and fentanyl are the same, and respiratory suppression is not greater, compared with the corresponding effects in adults with the same plasma concentrations of morphine and fentanyl.

Continuous infusion of opioids in the postoperative period is widely used in children from the age of 6 months, while, as a rule, there is good efficacy and safety, which, however, is associated with a significant incidence of peripheral side effects. Starting doses for continued infusions of morphine range from 0.01 mg/kg/hour in children younger than 6 months to 0.025-0.04 mg/kg/hour in children over 1 year of age. In neonates, opioid infusion rates per unit body weight should be lower and subsequent

doses (also calculated by body weight) should be lower and/or administered at longer intervals than in children of the following age groups.

Neonates receiving opioids should be electronically monitored, preferably with pulse oximetry, and should be observed in settings that allow prompt intervention to treat respiratory problems, as respiratory rate monitoring alone may not indicate upcoming apnea. Studies have not clearly established whether morphine or fentanyl is the preferred opioid for use in neonates and infants [1].

The clinical usefulness of hydromorphone, as experience shows, is the same as that of morphine; it is about 5 times stronger than morphine in children. Fentanyl provides a rapidly developing and short analgesia; it is used for short painful procedures. If fentanyl is administered repeatedly or as continuous infusions, it appears to be a long-acting drug. Accelerated administration of fentanyl can lead to chest wall stiffness, which in some cases is reduced by the administration of naloxone; in other cases, it is necessary to resort to neuromuscular blockade and artificial ventilation under high pressure.

There are new forms of fentanyl that may be useful for certain groups of patients. Oral fentanyl with transmucosal absorption provides fast onset and short analgesia, which is required for short painful procedures in children who are in the hospital, in the absence of access to the vein. Oral transmucosal administration of fentanyl is effective because it avoids the first metabolic cascade of this substance in the liver, which processes a significant part of this drug after its absorption in the small intestine [12].

Transdermal fentanyl provides a persistent analgesic effect in some patients, such as children with severe cancer pain. When administered transdermally, fentanyl has a slow onset of action, absorption variability, and is contraindicated for the primary treatment of pain if opioids have not been used previously. Oral or intravenous methadone has such a very useful quality as a long-lasting effect. However, due to its slow and variable

clearance, it requires careful monitoring and titration to prevent delayed sedation. Methadone elixir is useful as a long-acting opioid in patients unable to swallow sustained-release opioid tablets whole.

In addition to the respiratory side effects, nausea, ileus, pruritus, and urinary retention are common side effects of opioids in children from infancy, which can cause additional distress to the child. Many side effects of opioids can be alleviated by drugs that counteract specific effects (such drugs include antiemetics to relieve nausea and vomiting, antihistamines (used for itching), and laxatives for constipation) [18] .

Paracetamol, aspirin, and non-steroidal anti-inflammatory drugs in the treatment of acute pain in children

In pediatrics, the use of aspirin began to decline in the 1970s, after reports that it was associated with the development of Reye's hepatogenic encephalopathy. Aspirin remains in practice as a drug effective in rheumatological disorders, as well as a drug that inhibits platelet adhesion. Dosing recommendations for aspirin, paracetamol, and non-steroidal anti-inflammatory drugs (NSAIDs) are summarized in Table 1. 2.

Table 2.

Recommendations for oral doses of commonly used non-opioid analgesics.

A drug	Dose for a patient weighing <60 kg, mg/kg	Dose for a patient weighing >60 kg, mg	Intervals, h	Maximum daily dose for patients weighing <60 kg, mg/kg	Maximum daily dose for patients weighing >60 kg, mg

Paracetamol	10-15	650-1000	4	100*	4000
Ibuprofen	6-10	400-600#	6	40#^	2400#
Naproxen	5-6#	250-375#	12	24#^	1000#
Aspirin I	10-15#§	650-1000#	4	80#^§	3600#

 The maximum daily dose of paracetamol for infants and newborns is currently the subject of controversy. Preliminary recommendations are that the daily dose should not exceed 75 mg/kg for infants, 60 mg/kg for full-term and preterm infants whose gestational age at birth was greater than 32 weeks, and 40 mg/kg for preterm infants whose gestational age at birth was 28-32 weeks. The risk of hepatotoxicity may be increased by any of the following factors: fever, dehydration, liver pathology, difficulty with ingestion [2]

 In children, starting from infancy, aspirin can provoke the development of Reye's syndrome. If other analgesics are available, aspirin should only be used when its anti-platelet and anti-inflammatory effects are required; this drug is not recommended as a routine analgesic or antipyretic in neonates and children of subsequent age groups. Recommendations for the dosage of aspirin in neonates have not been developed.

Paracetamol (acetaminophen) has replaced aspirin as the most used antipyretic and mild analgesic in children. Plasma concentrations effective for fever control and for analgesia are 10-20 μg/ml. A dose of 10–15 mg/kg given every 4 hours is recommended [4]. Rectal administration is characterized by delayed and variable absorption, with a single dose of 35-45 mg/kg usually achieving therapeutic plasma concentrations with prolonged clearance. Subsequent rectal doses should be less (eg 20 mg/kg) and the interval between doses should be at least 6-8 hours, i.e. longer than oral administration. Single rectal doses of 20 mg/kg provide non-toxic plasma concentrations in preterm infants [2].

The daily total dose of paracetamol for oral or rectal use should not exceed 100 mg/kg per day in children over 1 year of age, 75 mg/kg in infants, 60 mg/kg in newborns, including preterm infants born after 32 weeks, and 40 mg /kg for premature infants whose gestational age was 28-32 weeks. An adequate dosing regimen for a preterm infant whose gestational age is 30 weeks is 20 mg/kg every 12 hours. Exceeding the recommended doses led to liver failure in both infants and children of subsequent age groups [3].

NSAIDs are widely used in children. Systematic reviews have shown that in adults, different NSAIDs differ little from each other in analgesic effect, and the injection route of administration does not provide significant advantages over oral administration.

Pharmacokinetic studies of several NSAIDs in children have shown that, based on weight, clearance and volume of distribution are higher in children than in adults, and half-lives are the same.

Complications from the gastrointestinal tract and kidneys from short courses of ibuprofen or paracetamol in children are quite rare. Some studies comparing paracetamol with NSAIDs found no difference in pain relief, while other studies found better analgesia with NSAIDs. NSAIDs may increase the risk of bleeding after tonsillectomy. NSAIDs provide good postoperative analgesia, with children having less need for opioids than non-NSAID controls [21].

Among NSAIDs, ibuprofen deserves attention. Ibuprofen is a non-steroidal anti-inflammatory drug that was developed in 1962 by Boots Research Laboratories as an alternative to aspirin, the main NSAID available at the time. Ibuprofen was first registered in England in 1968 and is currently registered and used in more than 30 countries under the patented name Nurofen. In the 80s, in several countries, including

the USA and Great Britain, ibuprofen was introduced into pediatric practice, and is currently used, including in Russia, in children from 6 months of age. as an over-the-counter drug and from 3 months. on the recommendation of a doctor.

Ibuprofen is a white or almost white crystalline substance with a characteristic aroma, containing (4-isobutylphenyl) propionic acid (C13H18O2) (see figure). Ibuprofen is the active ingredient in Nurofen for Children, a white, sugar-free, orange-flavored oral suspension. 5 ml of suspension contains 100 mg of ibuprofen. The drug is prescribed at an average dose of 7.5 mg per 1 kg of body weight, fluctuations from 5 to 10 mg / kg are possible.

Ibuprofen is a propionic acid derivative with antipyretic, analgesic, and anti-inflammatory properties. The pharmacodynamics of ibuprofen is primarily due to the suppression of the biosynthesis of prostaglandins, which, along with thromboxanes and leukotrienes, are part of the group of oxygenation products of polyunsaturated long-chain fatty acids known as eicosanoids. In the formation of prostaglandins, arachidonate is first mobilized from membrane phospholipids by one or more lipases of the phospholipase A2 type, or together by phospholipase C and a diglyceride lipase. Arachidonic acid, catalyzed by cyclooxygenase (COX) enzymes, is then oxidized to form prostaglandin endoperoxide (PGG2), which is rapidly converted by the enzyme peroxidase to PGH2. Then prostaglandins, thromboxane and prostacyclin are formed from PGH2 in different ways [25] .

Prostaglandins are present in all cells of the body and activate nerve endings (pain receptors) to the effects of pain-initiating substances such as histamine, 5-hydroxytryptamine, and bradykinin. Prostaglandins are important mediators of inflammation and are involved in the pathogenesis of all signs of inflammation (ie pain, tenderness, swelling and heat). As a result of infection or inflammation, blood monocytes and tissue macrobacteriophages are activated with the formation of

interleukin-1, which through intermediate links (such as prostaglandin PGE2) in the hypothalamus contributes to an increase in body temperature [27].

When taken orally, ibuprofen is partially absorbed in the stomach and then completely absorbed in the small intestine. The time to reach maximum plasma concentration (Tmax) is approximately 1-2 hours after ingestion of ibuprofen tablets or ibuprofen pediatric suspension, although, according to some reports, in infants aged 6-18 months. there is a higher Tmax (3 hours). In human plasma, ibuprofen is 99% protein bound. The high degree of protein binding results in a relatively low volume of distribution (0.1 l/kg). Although ibuprofen actively binds to albumin, this does not affect drug interactions.

Ibuprofen is extensively metabolized in the liver, rapidly eliminated from plasma with a relatively short half-life (about 2 hours).

The rapid metabolism and excretion of ibuprofen account to some extent for the relatively low toxicity of ibuprofen compared to some other NSAIDs. In a study that included more than 84,000 children aged 6 months. up to 12 years, it has been shown that the risk of serious side effects with the use of ibuprofen is not higher than with paracetamol.

Ibuprofen causes a rapid and effective reduction in high body temperature. The pharmacodynamics of ibuprofen contributes to the physiological processes that are important during therapy. Ibuprofen has also been found to be more effective than paracetamol in reducing very high body temperature in children.

Effect of ibuprofen on pain. Prostaglandins mediate the pain response by activating the sensitivity of pain receptors to pain stimuli. Ibuprofen relieves pain by re-suppressing COX enzymes, which prevents the conversion of arachidonic acid to PGG2 and thus

suppresses the formation of prostaglandins in inflammation. This reduces the hyperalgesic effect of prostaglandins on pain receptors, reducing the inflammatory response and resulting tissue damage. Peripheral action is considered the main mechanism by which ibuprofen relieves pain, especially in clinical conditions associated with inflammation and tissue damage, which are accompanied by increased prostaglandin synthesis [27].

Less significant mechanisms that may contribute to the analgesic/anti-inflammatory effects of ibuprofen include direct suppression of (experimentally induced) migration of leukocytes to the area of inflammation and a direct central effect on the tissues of the central nervous system.

Various studies show that ibuprofen is an effective treatment for mild to moderate pain in children (eg, toothache, acute sore throat, migraine, and pain from tonsillitis or acute otitis media).

The effectiveness of ibuprofen in reducing ear pain is due to both its anti-inflammatory and analgesic effects. In a multicentre, double-blind, controlled trial in children, ibuprofen (at a dose of 10 mg/kg) was effective in reducing pain in otitis media. Ibuprofen was significantly more effective than placebo in reducing pain ($p<0.01$), while there were no significant differences between paracetamol and placebo.

Safety and tolerability of ibuprofen in children. Short-term treatment with ibuprofen for fever and pain is well tolerated in children over 6 months of age. up to 12 years old. Serious adverse events from the gastrointestinal tract are very rare.

The widespread use of ibuprofen from 1969 to the present has shown that it has a high safety margin and low overdose toxicity.

With an overdose of ibuprofen, toxicity appears more likely as an increase in its therapeutic effect or as a known side effect.

Overdose symptoms may include nausea, vomiting, abdominal pain, headache, hypotension, dizziness, drowsiness, nystagmus, blurred vision, tinnitus and, rarely, metabolic acidosis, renal failure, and loss of consciousness. Since there is no clear correlation between the doses taken and the clinical effect, patients are given symptomatic treatment, if necessary, supportive therapy. You can use activated charcoal within an hour after taking a high dose or gastric lavage.

Nurofen for children should be used with extreme caution in patients treated with antihypertensive drugs or diuretics, since ibuprofen may reduce their therapeutic effect.

Thus, Nurofen for children provides:
• rapid reduction of high body temperature during fever - only 15 minutes after its application;
• prolonged antipyretic effect, lasting up to 8 hours;
• decrease in body temperature during fever for a longer period of time than when taking a suspension of paracetamol;
• fast analgesic action;
• good tolerance in children.

Selective cyclooxygenase-2 (COX-2) inhibitors have been developed as drugs that retain the analgesic and anti-inflammatory effects of NSAIDs, but do not have the same risk of gastric irritation and bleeding. Additional large-scale studies are needed to evaluate the efficacy, cost-effectiveness, and risk-benefit ratio of this group of drugs [20].

Anesthesia under the control of the child

In controlled studies of children, starting from the age of 6 years, the safety and effectiveness of self-administered analgesia has been proven. The type of such analgesia should be selected individually. If a continuous infusion with a low basal rate is given, and the patient supplements it if necessary, this increases the level of patient satisfaction, but increases the risk of episodic hypoxemia at night. Basal infusions are often routinely given to children with cancer or sickle cell anemia. In patient-supervised treatment, a morphine bolus of 0.02 mg/kg is usually given first, followed by a shut-off interval of 7 minutes, and no dose exceeding 0.3 mg/kg in 4 hours is allowed. If a basal infusion is used , then it usually starts at 0.01-0.015 mg/kg/h [9].

Nurse-assisted “patient-managed pain management” is widely used in infants to avoid delays in analgesia for occasional pain. Many palliative care professionals allow parents of patients to press the "as desired" button ("parental-guided analgesia") if necessary. However, the use of this technique for the treatment of postoperative pain is controversial due to the risk of both overdosing and underdosing in opioid-naive individuals.

If there is an indication for patient-managed analgesia, then we recommend that parental education be planned, which should be combined with mandatory close supervision by nursing staff [17].

Local anesthetics

Currently, local anesthetics are widely used in children. They are quite acceptable in terms of safety, although their excessive concentration in plasma may cause convulsions and depression of cardiac activity. Amino amides (eg, lidocaine and marcaine) have narrower indications for the treatment of neonates and infants than for older children and adults. These drugs should be used with extreme caution in newborns and infants

because their metabolic clearance is slow in such children and, consequently, there is an accumulation of the drug during infusions, in addition, at this age, rather high concentrations of unbound anesthetic are noted due to the reduced content of alpha1 - glycoprotein in plasma, moreover, in children who are not yet able to talk about their complaints, it can be difficult to recognize the symptoms of impending toxic effects [15].

The maximum recommended doses of lidocaine in newborns are 4 mg/kg without epinephrine and 5 mg/kg with adrenaline, and in children older than 1 year, 5-7 mg/kg. The maximum recommended doses of Marcaine, with or without adrenaline, are 2 mg/kg in neonates and 2.5 mg/kg in children over one year of age.

Topical forms of anesthetics are useful for the pain relief of needle procedures. When suturing wounds, a combination of tetracaine with adrenaline (epinephrine) and cocaine, which is known by the abbreviation "SO", is widely used. Mixtures without the addition of cocaine have an equally pronounced effect. There are several drugs that provide analgesia to intact skin and are effective for pain relief in needle-stick procedures.

These include a cream containing both lidocaine and prilocaine (EMLA, AstraZeneka) and tetracaine gel (Ametop, Smith and Nephew. EMLA has been shown to be effective and safe in neonatal circumcision compared with placebo, although it and less effective than a circular blockade.

Regional anesthesia is widely used, it is distinguished by high efficiency and safety in children after anesthesia and surgery, with blockade of peripheral nerves and with epidural anesthesia. Epidural anesthesia is effective even in newborns (premature and term). Epidural anesthesia in newborns and infants requires physicians and nurses to have experience in this field, as well as careful observation, modification of techniques and careful selection of drugs [13].

Two new local anesthetics - ropivacaine (ropivacaine) and levobupivacaine (levobupivacaine) are attractive, since their overdose is accompanied by a lower risk of cardiotoxicity, compared with Novocain [13]. Clonidine is a good adjuvant to epidural local anesthesia, as it prolongs and intensifies anesthesia, and causes fewer side effects such as nausea, ileus, pruritus, urinary retention, and respiratory depression compared to opioids [14].

Children undergoing outpatient surgery often have high pain scores, partly due to parental concern about the administration of analgesics. Peripheral and segmental blockades give satisfactory analgesia, but its duration is usually less than 8 hours. In such situations, parents should be told to give the child repeated doses of analgesics whenever the pain begins to worsen [23].

Anesthesia in newborns and infants

Over the past 30 years, general anesthesia has become much safer for newborns and infants; the risk of cardiac arrest and death during anesthesia in infants has decreased over this period by more than 20 times. Even newborns in the most critical condition can endure anesthesia, which is necessary for long operations. Vegetative and hormonal-metabolic stress reactions in newborns are largely leveled by anesthesia using high doses of opioids, epidural administration of local anesthetics, and inhalation anesthesia agents [22].

Treatment of pain associated with cancer

Pain in children with cancer may be caused by tumor progression, the effects of treatment, or needle procedures, including bone marrow aspiration. In needle procedures, both pharmacological approaches (infiltration anesthesia, conscious

sedation, and general anesthesia) and non-pharmacological methods (hypnosis and cognitive-behavioral programs) can be effective. The optimal combination of pharmacological and non-pharmacological approaches should be determined individually.

In most children with advanced cancer, satisfactory pain relief can be achieved by titration of oral doses of opioids, with adequate management of side effects. If the patient is intolerant of oral administration, alternative routes of administration of opioids should be considered, including intravenous, extended-release subcutaneous, and transdermal routes.

A retrospective analysis of patient memories shows the need for better methods of dealing with pain and other common symptoms, especially weakness and sleep disturbances in children with terminal cancer. Methylphenidate is effective in counteracting opioid-induced sedation. Significant increases in initial opioid doses (eg, 100-fold or more) are sometimes required, especially in individuals whose primary solid tumors have metastasized to the spine or central nervous system.

In some of these patients, the pain is resistant to high doses of opioids, but even in them, pain can be eliminated while maintaining consciousness, using subarachnoid infusions of local anesthetics and opioids.

Cancer pain is best treated in a multidisciplinary setting that specializes in general support or palliative care and is not limited to pharmacological interventions [25].

Pain during medical procedures

Chronic diseases require long-term treatment and diagnostic and therapeutic procedures, which are often painful and invasive. Reducing the effect of the traumatic factor on the

child is the main component of treatment. Although the pain during these manipulations is short-lived, fear and anxiety increase it.

There are medical and non-medical methods for controlling the pain that occurs during manipulation. Treatment should be individualized for each child. The main task in eliminating pain is to assess the intensity of pain using special scales. The degree of sedation should also be determined, which indicates the effectiveness of pain control and makes it possible to identify side effects [6].

To eliminate pain during manipulations in pediatrics, the following should be followed:

1. Provide parents and the child with adequate information about the procedure and psycho-emotional assistance.
2. Provide adequate pain management and anxiety relief during the first procedure to eliminate the possibility of premature anxiety during subsequent manipulations.
3. Medical personnel should be aware of the possible reaction of the child and be familiar with the methods of treating acute pain.
4. The manipulation room should have the necessary equipment for monitoring and resuscitation in case of sedation.
5. The doctor performing the manipulation must be well prepared. Assess the child's behavior to provide effective pain management and anxiety. Create a favorable atmosphere.

Non-medical methods

Non-medical methods include psychological influences (attention switching, muscle relaxation and controlled imagination), which are successfully used in young children during certain procedures. The goal is to divert the attention of the child from manipulation as a traumatic factor According to Bowmer, games are the easiest way to

help children overcome fear during their stay in the hospital. It should be emphasized that non-medical methods of pain control are an addition to the main treatment. The method is selected individually. It is very important that the child himself chooses a method that will help him endure the painful procedure [8].

Non-pharmacological methods of relieving pain in a child also include: emotional support from the parents, including ensuring the possibility of their joint stay during illness or painful diagnostic procedures; physical methods, which include stroking, massage, vibration, motion sickness, local application of cold or heat, controlled deep calm breathing; cognitive methods such as distracting the child, reading books, drawing, singing, playing games, going to church, praying [11].

It is known that the use of 0.5–1 ml of a 30% glucose solution orally 1–2 minutes before a painful procedure (blood sampling, injections) along with a dummy relieves pain in newborns and infants up to 3 months of age. All the above methods are additional, widely used in foreign pediatric practice of anesthesia, but in no way replace drugs [19].

Psychotherapeutic methods of pain control in children. In some cases, these methods can be carried out by parents and medical staff (and sometimes by children themselves), specially trained in special techniques; in others, by experienced psychologists and psychotherapists. One of the groups of such methods is associated with the creation of a special environment in which medical manipulations with a child take place, accompanied by pain. Usually, step-by-step informing the little patient and the parent about what will happen during the procedure, what the child will see and hear is used. At the same time, it is recommended to avoid incomprehensible medical terms, highly disturbing and emotionally saturated words, and not to try to suggest that the procedure will be absolutely painless.

The use of jokes, clear commands, praise of the child, reading books describing the procedure, sincere and open communication have a positive influence at the time of the

procedures. Additional comfort for children can be created due to the appearance of the office, where procedures and manipulations are carried out, where toys or a nice blanket are placed, walls are painted and pictures are hung.

It is also useful to include the smallest patient in the procedure: the child can be offered, for example, to count the time until the end of certain stages of the procedure or to hold any medical instrument; it is important to give the child a sense of freedom, for example, by choosing one or another bandage, deciding which hand to take the analysis from, etc.

If the child is hospitalized and is being treated in the hospital, it is not recommended to carry out procedures in the ward, on his bed. It is better to use a special room for manipulations to keep the child feeling safe, at least in his room. It is also important to respect its boundaries, emphasized by the presence of a schedule of procedures and events, accompanied by rounds with a preliminary knock on the door of the ward where the child is.

Parents who stay with them reduce pain and distress in children, they can also learn from them what can be stressful for their child in the procedure and what can help to better cope with the situation. However, it is important not to ask the parents to hold the child, to instruct the parents not to threaten the child with additional injections, but on the contrary, to challenge them to behave in a way that helps to “hold back” the pain. To do this, various methods of distracting the child during the procedure are widely used in different ways, depending on the age of the child, his hobbies, and interests. Distracting conversations (about school, about hobbies) are always available [11].

For infants, bodily contact between the mother and the baby, such as pressing him to the mother's breast, is often used as a distraction during the procedure. Tactile distraction is also used with older children: with the help of pressure on some point of the body, stroking, patting.

Pain management is often done through controlling the child's breathing: the child may be asked to breathe rhythmically slowly and deeply during the procedure; blow bubbles, blow on imaginary candles; magically "drive away" pain by blowing to the side. Through suggestion and the use of guided imagination, the child is sometimes asked to "turn off" the pain using a "magic invisible" cream, imagining himself as a superhero on a special mission; remembering pleasant places and favorite activities. For many children, various rewards and prizes provide assistance in overcoming pain. It is useful to pre-play the expected procedure with the child. Modeling situations reduces the significance of the procedure, relieves anxiety (desensitization), and gives the child an understanding of what behavior others expect from him, and what behavior will be negatively evaluated. Additionally, various methods of muscle relaxation are used.

Among the recommendations for a similar containment of pain in children for medical personnel are the following: conduct activities in a calm and friendly atmosphere; be confident and avoid apologies, excuses, criticism; avoid talking with colleagues, parents, students (especially about the side effects of the procedure); try to avoid stressful influences (sharp sounds); do not play it safe during the procedures. Special trainings and seminars are organized for the staff for this purpose.

Cognitive (behavioral) psychotherapy can be used to combat PTSD. For the prevention and treatment of medical stress, it is proposed to provide information to children, parents of the patient about the disease, the causes of pain and painful procedures; early diagnosis of pain response; raising the level of awareness of the specialists themselves, including on the problems of experiencing pain in children and ensuring pain management.

Medical methods.

Medical treatment of pain that occurs during manipulation should include sedation and effective analgesia. The medical method includes local anesthesia, adequate (moderate) sedation, deep sedation, and general anesthesia. The latter should never be forgotten when using medical and non-medical methods.

In children, it is very difficult to determine the line between deep sedation and general anesthesia. Therefore, general anesthesia should be carried out directly in the ward in the presence of parents if they wish to be with the child during the manipulation. Adequate (moderate) sedation is carried out after the procedure. When performing a puncture of the red bone marrow, parents are asked if they want moderate or deep sedation. Local anesthesia and non-medical approaches are used for both venous catheterization and blood sampling [19].

Conclusions

Recently, new methods of pediatric anesthesia have appeared. It can be concluded that the use of many drugs and methods of their administration is the most correct choice in the treatment of acute pain. Mutual assistance of the medical staff and relatives of the child is necessary for effective pain control. This will eliminate acute pain in the most appropriate way for the child.

Knowing the principles governing drug dosing, effects, and interactions, clinicians should generally achieve effective relief of acute pain from infancy, while ensuring dosing has a sufficient margin of safety.

BIBLIOGRAPHY

1. Anand K.J., Phil D., Mickey P.R. Pain and its effects in neonate and fetus // N Engl J Med. – 1987. – Vol. 317. – P. 1321-1329.

2. Anderson J.B. What we don't know about paracetamol in children // Paediatr Anaesth. – 1998. – Vol. 8. – P. 451-460.
3. Anderson B., Kunagasundarum S., Woollard G. Analgesic efficacy of paracetamol in children using tonsillectomy as a pain model // Anaesth Intens Care. – 1996. – Vol. 24. – P. 669-673.
4. Anderson B.J., Pons G., Autret-Leca E., Alegaert K., Boccard E. Pediatric intravenous paracetamol (propacetamol) pharmacokinetics: a population analysis // Paediatr Anaesth. – 2005. – Vol. 15. – P. 282-292.
5. Astuto M., Disma N., Rizzo G., Messeri A. Developments in the treatment of postoperative pain in paediatrics // Minerva Anestesiol. – 2002. – Vol. 68. – P. 428-432.
6. Astuto M., Favara-Scacco C., Crimi E., Rizzo G., Di Cataldo A. Pain control during diagnostic and/or therapeutic procedures in children // Minerva Anestesiol. – 2002. – Vol. 68. – P. 695-703.
7. Bosenberg A., Thomas J., Lopez T., Lybeck A., Huizar K., Larsson L.E. The efficacy of caudal ropivacaine 1, 2 and 3 mg x 1(-1) for postoperative analgesia in children // Paediatr Anaesth. – 2002. – Vol. 12. – P. 53-88.
8. Bowmer N. Therapeutic play and the impact on anxiety in hospitalized children // Ky Nurse. – 2002. – Vol. 50. – P. 15.
9. De Negri P., Ivani G., Visconti C., De Vivo P. How to prolong postoperative analgesia after caudal anaesthesia with ropivacaine in children: S-ketamine versus clonidine // Paediatr Anaesth. – 2001. – Vol. 11. – P. 679-683.
10. European Commission Enterprise Directorate-General. Better Medicines for children: proposed regulatory actions on pediatric medicinal products. Consultation Document. Cancun, Mexico: 5-8 May 2002. Opening Plenary // Int J Pharm Med. – 2002. – Vol. 16. – P. 25-259.
11. Favaro-Scacco C., Smirne G., Schiliro G., Di Cataldo A. Art therapy as support for children with leucemia during painful procedures // Med Pediatr Oncol. – 2001. – Vol. 36. – P. 474.

12. Habre W., Wilson D., Johnson C.M. Extrapyramidal side-effects from droperidol mixed with morphine for patient-controlled analgesia in two children // Paediatr Anaesth. – 1999. – Vol. 9. – P. 362-364.
13. Hansen T.G., Ilett K.F., Lim S.I., Reid C., Hackett L.P., Bergesio R. Pharmacokinetics and clinical efficacy of long-term postoperative epidural ropivacaine infusion in children // Br J Anaesth. – 2000. – Vol. 85. – P. 347-353.
14. Ivani G., De Negri P., Conio A., Amati M., Reero S., Giannone S. et al. Ropivacaine-clonidine combination for caudal blockade in children // Acta Anaesth Scand. – 2000. – Vol. 44. – P. 446-449.
15. Ivani G., De Negri P., Conio A., Grossetti R., Vitale P., Vercellino C. et al. Comparison of racemic bupivacaine, ropivacaine, and levo-bupivacaine for pediatric caudal anesthesia: effects on postoperative analgesia and motor block // Reg Anesth Pain Med. – 2002. – Vol. 27. – P. 157-161.
16. Krechel S.W., Bildner J. CRIES: A new neonatal postoperative pain measurement score. Initial testing and reliability // Paediatr Anesth. – 1995. – Vol. 5. – P. 53-61.
17. Kerschbaum G., Altmeppen J., Funk W. Taeger K. Parent controlled analgesia in a 3 years-old boy after traumatic amputation // Anaesthesist. – 1998. – Vol. 47. – P. 238-242.
18. Kokinsky E., Thormberg E., Nilsson K., Larsson L.E. Postoperative nausea and vomiting in children using patient-controlled analgesia: the effect of prophylactic intravenous dixyrazine // Acta Anaesthesiol Scand. – 1999. – Vol. 43. – P. 191-195.
19. Mitchell P. Understanding a young child's pain // Lancet. – 1999. – Vol. 354. – P. 1708.
20. Moores M.A., Wandless J.G., Fell D. Paediatric postoperative analgesia. A comparison of rectal diclofenac with caudal bupivacaine after inguinal herniotomy // Anaesthesia. – 1990. – Vol. 45. – P. 156-158.

21. Murat I., Baujard C., Foussat C., Guyot E., Petel H., Rod B. et al. Tolerance and analgesic efficacy of a new i.v. paracetamol solution in children after inguinal hernia repair // Paediatr Anaesth. – 2005. – Vol. 15. – P. 663-670.
22. Person J., Scheinin H., Hellstrom G., Bjorkam S., Gotharson E., Gustafsson L.L. Ketamine antagonises alfentanil-induced hypoventilation in healty male volunteers // Acta Anaesthesiol Scand. – 1999. – Vol. 43. – P. 744-752.
23. Sciard D., Matuszczak M., Gebhard R., Greger J., Al-Samsam T., Chelly J.E. Continuous posterior lumbar plexus block for acute postope-rative pain control in young children // Anesthesiology. – 2001. – Vol. 95. – P. 1521-1523.
24. Stevens B., Johnston C., Petryshen P., Taddio A. Premature infant pain profile: development and initial validation // Clin J Pain. – 1996. – Vol. 12. – P. 13-22.
25. Swafford I.L., Allen D. Pain relief in the pediatric patient // Med. Clin. North. Am. – 1968. – Vol. 52. – P. 131-136.
26. Tramer M.R., Walder B. Efficacy and adverse effect of prophylactic antiemetics during patient controlled analgesia the raphy: a quantitative systematic review // Anesth Analg. – 1999. – Vol. 88. – P. 1354-1361.
27. Watcha M.F., Ramirez-Ruiz M., White P.F., Jones M.B., Lagueruela R.G., Terkonda R.P. Perioperative effect of oral ketorolac and acetaminophen in children undergoing bilateral myringotomy // Can J Anaesth. – 1992. – Vol. 39. – P. 649-654.