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Review



Current concepts in the diagnosis and management of acute pain in children

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ABSTRACT

BACKGROUND: In children, injuries are the focus of attention both for the increasing incidence and necessity of pain management, and pain can indicate the severity of injuries or serious complications that worsens the treatment results. Despite the obvious problem, information available in the literature regarding the theoretical and practical aspects of acute pain in children is often contradictory and needs to be systematized.

AIM: To present current information about the epidemiology, physiology, diagnosis, and treatment of acute pain in children to pediatric orthopedic and trauma specialists.

MATERIALS AND METHODS: Selective analysis and narrative review of relevant studies analyzing the epidemiology, diagnosis, and management of acute pain in children were performed.

RESULTS: Although various pain assessment tools are available, the clinical assessment of acute pain in children remains challenging. The use of these tools depends on the child's age, cognitive and communication skills, and pain location. The term oligoanalgesia has been used to describe inadequate pain relief in the emergency department. Oligoanalgesia in children has negative physiological and psychological effects, sometimes with long-term consequences, and may negatively affect their future pain experiences. Parents often underestimate their child's pain level and have serious misunderstandings about how children express pain. The World Health Organization has developed recommendations for pain management in children. Ibuprofen and paracetamol are recommended as analgesics for mild-to-moderate pain in children aged >3 months. This choice considered extensive data on the effectiveness and safety.

CONCLUSIONS: Personalized management strategies utilizing biopsychosocial approach will ensure that children are treated comprehensively according to their unique pain status.

Keywords: trauma; pain; children; oligoanalgesia; analgesics.

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Научный обзор

Современные представления о диагностике и лечении острой боли у детей

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АННОТАЦИЯ

Обоснование. Несмотря на очевидность проблемы, на сегодняшний день информация, касающаяся широкого спектра теоретических и практических аспектов острой боли у детей, носит весьма разрозненный и нередко противоречивый характер и нуждается в систематизации.

Цель — представление широкой аудитории специалистов, сталкивающихся с острой болью у детей, и врачей — травматологов-ортопедов современной обобщенной информации об эпидемиологии, этиопатогенезе, диагностике и лечении острой боли у детей.

Материалы и методы. Для реализации поставленной цели изучена литература, опубликованная преимущественно за последние 15 лет и посвященная проблемам эпидемиологии, диагностики, лечения острой боли у детей, с последующим анализом основных положений и фактических данных.

Результаты. Клиническая оценка острой боли у детей может быть затруднена, хотя существует множество инструментов оценки болевого синдрома, использование которых зависит от возраста ребенка, когнитивных и коммуникативных навыков, а также локализации боли. Термин «олигоаналгезия» применен для описания недостаточного обезболивания в отделении неотложной помощи. Олигоаналгезия у детей сопряжена с отрицательными физиологическими и психологическими эффектами, иногда приводящими к долгосрочным последствиям, и может негативно повлиять на их будущие переживания боли. Родители часто недооценивают уровень боли ребенка и не знают, как дети выражают боль. Всемирная организация здравоохранения разработала рекомендации по купированию боли у детей, в том числе при ее персистирующем характере. В качестве анальгетиков при боли легкой и средней степеней тяжести у детей старше 3 мес. рекомендованы два препарата: ибупрофен и парацетамол. Данный выбор был сделан с учетом многочисленных данных по эффективности и безопасности этих средств в педиатрии.

Заключение. Персонализация стратегии ведения посредством биопсихосоциального подхода обеспечит комплексное лечение ребенка в соответствии с его уникальным болевым статусом.

Ключевые слова: травма; боль; дети; олигоаналгезия; обезболивающие препараты.

Как цитировать

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BACKGROUND

Pain is one of the most common reasons for patients visiting medical institutions [1, 2]. Despite the apparent certainty that pain is a common symptom of injuries and diseases, the practical issues of its diagnostics and treatment as an independent problem, including (and, as will be demonstrated below, to a greater extent) in pediatrics, are still not addressed. Pain can be an indication of the severity of the pathology and can lead to severe complications that worsen treatment outcomes. According to the World Health Organization, trauma is the third leading cause of death and disability in all age groups, with injury-related pain accounting for 80% of total complaints [3], although the results of the same study showed that the majority of patients, particularly children, were not receiving analgesics upon admission.

Traditionally, quantitative and qualitative pain management have been less employed (if at all) in pediatric practice than in similar situations in adults. This phenomenon is called oligoanalgesia [4]. Despite decades of research on this phenomenon, very few studies have discussed the issues of oligoanalgesia in the Russian medical literature. Documenting pain in children is also often neglected. Thus, in one of the largest studies published in the USA in 2006 and covering more than 24 thousand patients, only 44.5% of children with pain on admission to the emergency department were assessed for the severity of pain syndrome. Moreover, the pain scale used is associated with a higher probability of using analgesics [5]. Primary medical care for pediatric patients with injuries and trauma is often provided by doctors who are not specialists in traumatology and orthopaedics. However, pediatricians and emergency physicians tended to use analgesics less actively when treating children with acute pain. This phenomenon arises because of the limited opportunity to assess pain adequately in children, narrow range of available drugs, some traditional views on pain in children as an almost inevitable phenomenon accompanying treatment, lack of information about pain management in children, and lack of specialists and centers for the treatment of pediatric pain in most clinics [6].

Despite the certainty of the problem, current information concerning theoretical and practical aspects of the treatment of acute pain in children is not unified and often contradictory and must be systematized.

The study aimed to present modern generalized information about the epidemiology, etiopathogenesis, diagnostics, and treatment of acute pain in pediatric patients to a wide audience of specialists dealing with acute pain in children and orthopedic traumatologists.

MATERIALS AND METHODS

To achieve this aim, literature data published mainly over the last 15 years and focused on the epidemiological

problem, diagnostics, and treatment of acute pain in pediatric patients and actual data were analyzed. For subsequent analysis and synthesis of information, publications in highly rated international journals and studies with a high level of evidence were extracted. Considering data diversity, the results were analyzed and presented in a narrative review to present consistently the main facts presented in the literature.

RESULTS AND DISCUSSION

Acute pain in pediatric patients

Acute pain is defined as pain lasting up to 3 months [7] and is usually due to an illness, injury, or medical procedure [8]. Children often experience acute pain; however, in practice, acute pain tends to be underestimated and treated less intensively because of children's limited ability to identify and report effectively their complaints and adults and health professionals may perceive a child's pain as not serious enough to require interventions [9]. Pain is a subjective sensation that is unique to each person. Clinical assessment of acute pain in pediatric patients can be difficult. Although various pain assessment tools are available, their use depends on the child's age, cognitive and communication skills, and pain location. Currently, no convincing evidence confirms the superiority of some methods over others. When assessing the prevalence of acute pain in pediatric patients, data quality may be affected by various factors related to study methodology, such as sample size, age range, and ethical issues [10].

The World Health Organization (WHO) has declared adequate pain management a human right [11].

Researchers concluded that all sensory systems, including nociception, are functional and active in newborns; however, the cognitive processes required to make meaning and understand the nature of painful experiences remain undeveloped. Perceptual processes in newborns serve to organize a significant influx of information and provide a mechanism by which the earliest experiences are registered and gradually acquire significance [12].

Earlier studies have several erroneous assumptions, particularly the common belief that pediatric patients do not experience severe pain because incomplete myelination of nerve fibers delays the transmission of pain impulses, and these have hampered research into the assessment and effective treatment of pediatric pain [13].

Injury- and damage-related pain in pediatric patients and oligoanalgesia

According to E. Izsak et al., up to 64.1% of pediatric patients admitted in the emergency department report pain as their chief complaint [14]. However, in the same study, only

15% of these pediatric patients received sufficient and timely analgesia. Numerous studies have highlighted the obvious shortcomings in the treatment of acute pain in pediatric patients [15, 16]. The term oligoanalgesia was first used in 1989 by Wilson and Pendleton to describe inadequate pain relief in the emergency department for adult patients [17]. Several years later, oligoanalgesia in pediatric patients not only has immediate negative physiological and psychological effects but can also lead to long-term consequences and affect negatively the future experience of pain [18]. An association was found between early pain experiences and numerous negative behavioral and psychological consequences in later life [19]. Despite these long-established findings, pediatric pain is recognized, documented, and treated less frequently than in adult patients. Even when acute pain in pediatric patients is correctly assessed, pain relief is often insufficient [20, 21].

Aspects of diagnosing pediatric pain

Undiagnosed pain in children may negatively affect the child's future pain experiences in terms of behavioral, sensory, and affective responses [22]. Long-term consequences of suboptimal pain management include negative effects on the quality of life and school performance, decreased pain threshold, and increased pain sensitivity, and analgesics may become less effective [23]. Most pain types in pediatric patients can be described using the same classification as in adults. The most commonly used descriptive classifications are based on pain duration (acute or chronic pain) and its pathophysiology (nociceptive or neuropathic pain) [24]. A study reported a subjective element in children's reporting of pain and its intensity if pediatric patients do not want to bother their parents or are afraid of the prospect of visiting a medical facility [25].

Parents' attitude toward pediatric pain

Although a substantial proportion of pediatric patients are admitted to healthcare facilities with their parents or after parental referral, these often do not provide additional benefits in the medical assessment of the child's complaints. Literature and ideas on prehospital pain management are limited, and most scientific sources are devoted to the use of painkillers, primarily narcotic analgesics, in medical institutions. The treatment of acute pain in pediatric patients, unlike adults, does not receive the same degree of research interest; thus, studies presenting high level evidence are needed [26]. However, in recent years, the attitude toward pain management in pediatrics has changed. C. Conrad et al. studied current practice in prehospital analgesia and established that 54% of pediatric patients admitted to the emergency department with acute pain received analgesia before hospital admission, and this indicator has increased compared with similar earlier studies. This finding suggests

that the use of analgesia has increased over the past decades. Potentially, this is attributed to parents becoming more aware of the importance of prehospital pain relief in children. However, in 54.3% of cases of home pain relief, drug dosage did not correspond to the age or weight of the child. Upon hospital admission, specialists recorded the intensity of pain; however, only 74% of pediatric patients received painkillers. Thus, a substantial proportion of pediatric patients were in a state of oligoanalgesia. According to surveys, parents refused pain relief because "they did not think the child needed it." However, 75% of these parents reported that their child had a pain score of ≥ 4 (moderate to severe) on the visual analog scale (VAS) [27]. This indicates the current lack of understanding of the situation between parents who believe that the child does not need pain relief and the child feels pain. Parents often underestimate the level of pain in children and do not understand how pediatric patients express pain [28]. Another study concluded that parents' underestimation of the child's pain severity is a significant barrier to adequate pain management [29]. A substantial proportion of parents did not use painkillers because they believed that this would be an inappropriate action, that is, "they did not want to smooth out the true severity of the problem" (16.1%), "they believed that medications should be given in the hospital" (9.5%), or "they were afraid that it would be wrong or harmful" (8.5%). Collectively, 34.1% of the parents did not manage their child's pain because of these fears and concerns about the role of prehospital analgesia. This finding is confirmed by other studies; for example, in the work of R.L. Spedding et al., 28% of parents did not provide pain relief because they were afraid of causing harm [27, 30]. M.S. Maimon et al. identified "concerns that analgesics will mask signs and symptoms," which was a major barrier to prehospital analgesia [31].

Prehospital analgesia: advantages and disadvantages

Studies analyzing current pain management practices have suggested that difficulty assessing pain and limited choice of medications and routes of administration are major challenges in prescribing pain management in children. The traditions of medical education and clinical practice in a particular country/region/clinic are also important factors [32, 33]. However, most researchers cite a lack of high level evidence and the need for further research into prehospital pain management [26].

Several researchers have aimed to determine the causes of insufficient pain relief in pediatric patients at the prehospital stage. Obviously, in most cases, this was explained by the opinions of parents and their practical actions. Established sociodemographic factors were associated with a higher probability of parental use of prehospital analgesia. These included having siblings, an emergency department

visit within <48 h, and a VAS pain score of ≥ 5 . This may indicate that greater parental experience increases the probability of pain relief. Interestingly, the proportion of pediatric patients receiving pain relief did not increase linearly with the increase in pain intensity. A stepwise increase in the use of analgesics in pediatric patients with a pain score of up to 4 points (inclusive) and with a score of ≥ 5 points was noted, which identifies these indicators as delimiting parents' decisions about the use of analgesia. Some studies have demonstrated that younger pediatric patients received analgesia less frequently than older children [34], whereas others have found no association between the child's age and frequency of analgesia [27].

Diagnostics of pain syndrome and aspects of assessing pain intensity in pediatric patients

Pain assessment in children is a critical component of successful pediatric practice and has received much attention over the past decade. The International Association for the Study of Pain has developed a standard definition that "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage." Determining actual or potential tissue damage is important in the treatment of pediatric pain because objective assessment is difficult. In 2001, the American Academy of Pediatrics and the American Pain Society published a memorandum calling for humane and competent treatment of pain and suffering in all children and adolescents, focusing on an interdisciplinary approach that includes pharmacological, cognitive-behavioral, psychological, and physical treatment methods [8].

At present, various methods are available for assessing pediatric pain. In infants, cry, movement, facial expressions, and physiological changes are used as pain assessment methods [35, 36]. For children aged 3 years, behavioral scales that interpret the child's reactions are used. For preschoolers (aged 3–7 years), rating scales are used. For children aged >7 years, the VAS is used. As a rule, pediatric patients clearly verbally describe pain, and no noticeable differences were noted among age groups [37]. Despite this, no uniform tool for pain assessment in pediatrics has been established. Diagnostics and assessment of intensity and treatment of pain at the prehospital stage are suboptimal; thus, systemic measures are required to improve their quality [38]. In a large study of the National Emergency Services Information System database, pain was listed as the primary reason for hospital transport in nearly 30% of patients. However, the same study showed that pediatric patients received pain medications less frequently than adults [39]. A study reported undertreatment of pain in the prehospital setting, with only half of pediatric patients receiving pain medications before arrival at the emergency department, 54% of children were

given ibuprofen, 26% received paracetamol, and 8% received other medications [27].

Children's verbal descriptions of pain by providing information about the quality, severity, location, and duration of pain help facilitate diagnostics. Certain projective methods have been used as self-report methods, in which children's attitudes toward pain are inferred from their choice of colors, drawings, etc. [40]. However, how qualitative differences in children's reactions reflect quantitative differences in their perception of pain is unclear. Direct scaling methods (particularly VAS) provide the most flexible and comprehensive result of pain assessment in older children. However, factors such as cognitive level, previous pain experience, and age should always be considered when evaluating these methods. Thus, numerous indicators for pain assessment and various tools for determining its intensity in pediatric patients are available. However, gaps persist, and a specific objective measure of pediatric pain is still insufficient for universal clinical practice.

Approaches to the treatment of acute pain in pediatric patients

To ensure appropriate patient management, pain severity should be assessed at the prehospital stage, upon hospital arrival, and again throughout the inpatient or outpatient stay. An integrated approach based on the combined use of physical, psychological, and pharmacological methods may be more effective than either of these methods alone [41]. Even simple everyday techniques that help reduce fear caused by unfamiliar surroundings (a well-equipped pediatric ward that provides a child-friendly environment with bright walls, adapted lighting, cartoon pictures or wall displays, and familiar objects, books, and toys) can reduce pain sensation [42]; despite the apparent simplicity of these techniques, in practical activities, there is not always the opportunity and desire to implement them.

Interventions should be focused on the individual characteristics of the child, considering age and psycho-emotional development [43]. Because pediatric pain is a health problem of high significance in most countries and as part of routine practice, is often not recognized, ignored, and even denied, WHO experts have developed recommendations for pain management in pediatric patients. Two drugs (ibuprofen and paracetamol) are recommended as analgesic in pediatric patients aged >3 months. This choice was made based on data on the efficiency and safety of these drugs in pediatrics. In the first 3 months of life, only paracetamol can be used. Another important point of the recommendations concerned the optimal route of drug administration. In pediatrics, this refers to the oral administration of ibuprofen or paracetamol in an age-appropriate form (tablets, suspensions, etc.). In the case of individual intolerance, other

nonsteroidal anti-inflammatory drugs (NSAIDs, such as diclofenac, naproxen, or nimesulide) can be considered [44]. Although the Russian Federation generally supports the recommendations and decisions of the WHO, the prescription of drugs in Russia is regulated by national legislation, and taking into account the criteria for the safety of therapy, in the Russian Federation, the use of most NSAIDs are restricted in children [45]. The above-mentioned WHO recommendations also suggest the use of various drugs, including opioid analgesics, depending on the intensity of pain (mild, moderate, and severe); however, no clear guidance was provided on determining pain intensity, and the decision on which severity category to classify pain in a particular patient is proposed to be taken clinically, which makes the choice not entirely accurate and again forces us to return to the issue of assessing pediatric pain, as discussed earlier.

The use of metamizole sodium (Analgin) for pediatric pain is very controversial because of the controversial “reputation” of this drug. In Russia, metamizole sodium has been used for many decades; however, no high-quality clinical studies of its efficiency and safety in children have been conducted, as well as internationally recognized recommendations for its use [44, 46].

Thus, ibuprofen, as a representative of NSAIDs, and paracetamol have priority in the management of pediatric

pain [47]. Several studies have confirmed their efficiency. The analgesic effect of ibuprofen is not less than that of opioids for acute pain after bone fractures in pediatric patients [48]. In addition, NSAIDs not only have equal analgesic properties but also lead to better functional results and fewer side effects than opioid analgesics. Indicative data (Table 1) were presented by a blinded, randomized trial of 134 pediatric patients aged 5–17 years admitted to the pediatric emergency department with an uncomplicated limb fracture and receiving morphine (0.5 mg/kg) or ibuprofen (10 mg/kg) orally every 6 h if it is necessary within 24 h after discharge. Both drugs improved pain scores without significant differences in analgesic efficacy. However, in the same study (Table 2), opioid use was associated with a higher incidence of adverse events [49].

When administered intravenously, ketorolac has demonstrated efficacy comparable to opioids administered intravenously in reducing moderate to severe pain [50].

In world practice, extensive experience has been accumulated in the combined use of ibuprofen and paracetamol. This regimen for the treatment of pain syndrome is of particular interest because its efficiency indicators exceed those of the use of active substances in monotherapy. Having different points of action, they mutually enhance each other’s therapeutic effects. According to a 2016 review, this

Table 1. Results of a randomized trial of morphine versus ibuprofen given orally for pain relief after fractures in pediatric patients. Mean differences in pain scores before and after* between groups† [49]

Dose number	Oral morphine		Oral ibuprofen		Difference between groups (95% CI)	p‡
	Number of participants	Difference before and after, mean ± SD	Number of participants	Difference before and after, mean ± SD		
1	66	1.5 ± 1.2	68	1.3 ± 1.0	0.2 (–0.2–0.6)	0.3
2	55	1.3 ± 1.3	54	1.3 ± 0.9	0.0 (–0.4–0.4)	0.9
3	41	1.3 ± 1.4	48	1.4 ± 1.1	–0.1 (–0.7–0.4)	0.6
4	34	1.5 ± 1.4	36	1.1 ± 1.2	0.4 (–0.2–1.1)	0.2

Note. SD, standard deviation. *Determined using the revised Wong–Baker faces pain scale. †The number of participants who took a dose of each drug in the corresponding time interval. ‡Unpaired *t*-test.

Table 2. Results of a randomized trial of morphine versus ibuprofen taken orally for pain relief after fracture in pediatric patients. Adverse events in groups [49]

Adverse events*	Patient group, n (%)		p‡
	Morphine, n = 66	Ibuprofen, n = 68	
Total	37 (56.1)	21 (30.9)	<0.001
Nausea	18 (27.3)	4 (5.9)	<0.01
Vomiting	8 (12.1)	2 (2.9)	0.04
Drowsiness	23 (34.8)	14 (20.6)	0.07
Dizziness	8 (12.1)	6 (8.8)	0.5
Constipation	4 (6.1)	1 (1.5)	0.2
Other‡	8 (12.1)	3 (4.4)	0.1

*Some patients experienced >1 side effect. †Pearson χ^2 test. ‡Includes headache, abdominal pain, irritability, and hyperactivity.

combination was as effective as opioids in treating musculoskeletal pain. In the double-blind randomized study by A.K. Chang et al. (Fig. 1), no significant difference in the effectiveness of the combination of paracetamol and ibuprofen was found when compared with combinations of opiates and paracetamol in relieving severe pain [51].

The combination of paracetamol and ibuprofen turned out to be more effective than either drug alone because participants who took the combination drug after surgery less probably required additional emergency medications. In a previous study, information on adverse events indicated that they were comparable between all treatment groups [52].

One of the difficult issues when treating pediatric patients is the compliance of patients or their parents. Results of a retrospective analysis conducted in 2002–2012, based on a study of data from poison control centers, showed that nearly half of all drug use violations in pediatric patients aged <6 years belonged to the category of cold and pain relievers. In 43% of cases the dosage was not followed. Overall, the researchers concluded that parents made medication errors with children every 8 min [53]. Based on this, the risks of parental errors when prescribing pain therapy must be minimized. A fixed combination of ibuprofen and paracetamol in one drug in an anesthesia regimen in outpatient practice can reduce the risks of dosage violations and provide the necessary therapeutic effect when using the “hourly” regimen. In Russia, this combination is registered in the form of dispersible tablets, and its safety in pediatric patients aged 3–12 years was confirmed in a Russian study on the treatment of febrile conditions [54].

CONCLUSION

The results of a literature analysis, which included systematic reviews, original studies, descriptions of current practices, and recommendations, revealed that the issues of pain management in children are still not clarified for both diseases and injuries. Not every injury is accompanied by pain, just as not every pain indicates tissue damage and its severity. This leads to the need to reconsider some emergency care axioms regarding pain management because damage and pain should be assessed independently, and the treatment and management of pain should be an independent task. Moreover, a child's complaints of pain may not always be accompanied by tissue damage, as is clear from the accepted definition of pain. This dilemma forces us to turn to the biopsychosocial concept of pain as the basis for its understanding, assessment, and treatment [55].

Even the section of this article on diagnostics and assessment of pain intensity in pediatric patients, which does not pretend to be complete, demonstrates the lack of a unified approach and the low involvement of pediatric specialists, including orthopedic traumatologists, in documenting pediatric

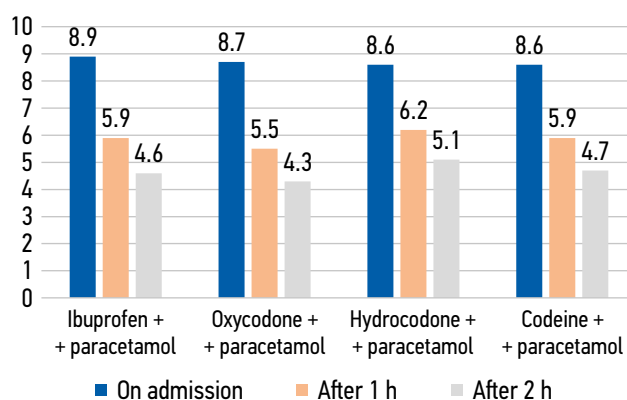


Figure. Results of a randomized clinical trial of the effect of single-dose opioid and nonopioid analgesics given orally on acute limb pain in the emergency department [51]. Pain scores according to the numerical rating scale and their reduction after 1 and 2 h of followup

pain. Pain diagnostics in the practice of both orthopedic traumatologists treating pediatric patients, as well as other specialists, is often empirical and limited to ascertaining whether the child has a complaint of pain. This may be due to the age of patients (particularly in preschool children), stereotypes of pain perception in children by parents and medical workers, and limited methods for assessing pain intensity in children. Within this publication, international sources were analyzed, primarily because of the limited number of studies of the corresponding design and level of evidence in the Russian literature. In addition, the differences should be emphasized when providing care to pediatric patients with injuries and diseases, including the musculoskeletal system, in the Russian Federation. Depending on the level of the medical institution and stage of medical care, it can be provided by orthopedic traumatologists (primarily in children's institutions), pediatric surgeons, ambulance and emergency doctors, anesthesiologists and resuscitators, and pediatricians. Moreover, regardless of the doctor's specialty, pain management during hospitalization and outpatient and inpatient medical care should remain a priority. The availability and practice of using painkillers in the Russian Federation also differ from those in other countries, which clearly follows from the literature analysis. In Russian medical literature, even the very concept of “oligoanalgesia” does not actually appear. In a search in the Russian segment of the Internet, including resources of eLibrary, Cyberleninka.ru, and several local libraries of medical periodicals, this term was not mentioned in general, particularly in relation to pediatric patients. This is a characteristic finding that partly testifies to the medical attitude of the professional community to this problem. Certainly, the excessive use of opioid analgesics and the subsequent “epidemic” of opioid addictions, primarily in the United States, force us to consider this problem more broadly. However, taking into account both the negative and positive experiences of international research and practice,

the most acceptable pain management algorithms in pediatric patients can be developed. Prehospital pain management in pediatric patients is very significant. The use of painkillers at home helps reduce the frequency of oligoanalgesia in children, including those with musculoskeletal injuries; however, there is the traditional opinion about the inappropriateness and even depravity of the practice of prehospital anesthesia in the professional community, based on the idea of the importance of pain assessments in diagnosing diseases and injuries contradict each other. The above-mentioned thesis about the inappropriateness of prehospital anesthesia was largely based on the limited resources of instrumental and laboratory studies in acute conditions in pediatric patients. Currently, most clinics providing specialized medical care to pediatric patients have employed modern research methods that enable them not to rely on a clinical assessment of the course of pain as the main diagnostic tool and thereby avoid oligoanalgesia at the examination stage. The practice of using drugs for pain relief in children is determined by regulatory documents, primarily instructions for the drugs. As indicated in the relevant section of this article, in the Russian

Federation, options for painkillers for pediatric patients are limited. The availability of an accessible combination drug expands the possibilities of pain relief in pediatric patients, including in the case of musculoskeletal diseases and injuries. Most studies reviewed devoted to solving local problems of diagnosing and treating pain; therefore, in this study, presenting a single consistent presentation and drawing general conclusions are quite challenging. This highlights the need for further research on this issue. In addition, personalization of the management strategy through a biopsychosocial approach (considering the trinity of physiological, emotional, and social factors that influence the occurrence of pain and its subjective perception) remains important in providing comprehensive treatment to the child in accordance with his/her pain status.

ADDITIONAL INFORMATION

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