

REVIEWS

PHARMACOLOGICAL APPROACHES FOR MANAGEMENT OF NEUROPATHIC PAIN IN CHILDREN

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ABSTRACT

INTRODUCTION: Neuropathic pain in children is a significant challenge to medical practice due to difficulties in diagnosis and limitations of pharmacological therapies.

AIM: The review aimed to summarize the current knowledge about the pharmacological treatment of neuropathic pain in children and adolescents.

MATERIALS AND METHODS: Scientific publications from the last 15 years, including clinical cases, results of clinical trials and systematic reviews, were included in the current article. Resources such as PubMed and UpToDate were used for the search. It was performed by using the keywords “neuropathic pain in children”, “pediatric therapy”, “topical treatments”, “pharmacological therapy”, and “personalized treatment”.

RESULTS: The review briefly describes the main causes of neuropathic pain in children, the specific clinical signs of that kind of pain, and the diagnostic approaches in the pediatric population. Attention is paid to scales used in clinical practice for assessing pain intensity. The emphasis is set on pharmacological treatment with a focus on current data on the efficacy of main drug groups used for alleviation of neuropathic pain in children: gabapentinoids, which remain the most commonly used drugs; some antidepressants, particularly suitable for children with accompanying mood disorders; opioid analgesics, especially those with additional mechanisms of action; and lidocaine applied topically or in the form of intravenous infusions. In addition, the prospect of personalized treatment based on pain phenotyping through quantitative sensory testing is discussed.

CONCLUSION: Management of neuropathic pain in children includes pharmacological and non-pharmacological methods. It requires an interdisciplinary and individualized approach and development of evidence-based therapeutic strategies.

Keywords: neuropathic pain, pediatrics, diagnosis, pharmacological therapy, personalized treatment

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INTRODUCTION

Neuropathic pain is a complex clinical problem that affects a significant portion of the pediatric population. Although the incidence of neuropathic pain among children is lower than in adults, its consequences can be extremely severe, including chronic pain, impaired quality of life, and difficulties in daily activities.



The diagnosis of neuropathic pain in children is challenging due to the lack of consistent biomarkers and the difficulty in interpreting symptoms, especially in younger children or those with cognitive impairment. Correctly distinguishing neuropathic from other types of pain is essential for determining the most appropriate therapeutic approaches.

AIM

The aim of the current article is to summarize the existing knowledge regarding neuropathic pain in children, focusing on pharmacological methods for its relief.

MATERIALS AND METHODS

This article is based on a detailed review of the current scientific literature related to the pharmacological treatment of neuropathic pain in pediatric practice. Publications from established medical sources—peer-reviewed scientific articles, clinical guidelines, and systematic reviews, available through resources such as PubMed, UpToDate, and specialized pediatric journals—were included in the analysis process. Searches were performed with keywords such as “neuropathic pain in children”, “pediatric therapy”, “topical treatments”, “pharmacological therapy”, and “personalized approaches”. Special attention was paid to clinical guidelines from the European Medicines Agency (EMA) and the US Food

and Drug Administration (FDA) to ensure the practical applicability of the data.

Publications from the last 15 years (2009–2024) were selected for the work in view of their topicality and relevance. Studies that address aspects such as diagnosis and treatment of neuropathic pain in children were included. Particular attention was paid to publications that provide an evidence base for therapeutic approaches. Each source was assessed for its scientific credibility, methodological quality, and relevance to practical application. The results were summarized, emphasizing the unique characteristics of the pediatric population and current guidelines for individualized pharmacological treatment.

RESULTS AND DISCUSSION

Definition and Distribution

Pain is defined by the International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”. It can be classified into three main categories: nociceptive, neuropathic, and nociplastic [1]. This distinction is crucial because correct determination of the type of pain facilitates the identification of the underlying cause and guides the appropriate therapeutic approach.

Neuropathic pain is a consequence of damage or disease affecting the somatosensory nervous sys-

Table 1. Causes of neuropathic pain in children (according to Einhorn et al., 2024)

Classification	Disease or Mechanism of Injury	Mechanism of Pain Mediation
Malignant	Compression from a tumor	Peripheral
	Invasion of the nervous system	Central
	Chemotherapy-induced	Peripheral
Metabolic	Fabry disease	Peripheral
Genetic	Erythromelalgia	Peripheral
	Charcot-Marie-Tooth disease	Peripheral
Traumatic	Postoperative pain	Peripheral
	Plexus avulsion	Peripheral and central
	Transection of a peripheral nerve	Peripheral
	Mechanical compression	Peripheral
Phantom-Limb	Associated with burns	Peripheral
	Amputation	Peripheral and central
Neurologic	Spinal cord injuries	Central
	Guillain-Barré disease	Peripheral
	Multiple sclerosis	Central

tem. It can occur as a result of compression, ischemia, infiltration, or metabolic disorders of the nerves. Table 1 presents the most common causes of neuropathic pain symptoms in children, summarized by Einhorn et al. (2024) [2].

The prevalence of neuropathic pain in children remains unclear due to the lack of extensive epidemiological data. Causes of neuropathic pain in adults, such as diabetic neuropathy, postherpetic neuralgia, trigeminal neuralgia, and cerebrovascular accidents, are rare or absent in pediatrics. However, pain is common in children and a somatic origin is found in only 10–30% of cases of unexplained pain [2].

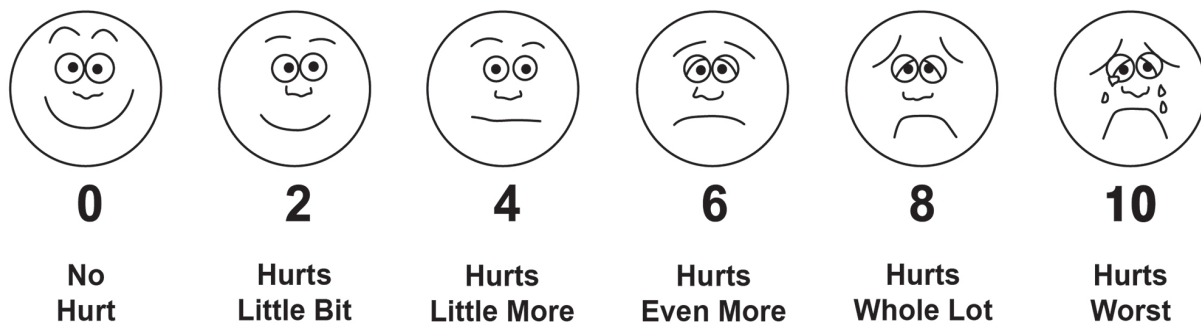
Clinical Symptoms

The clinical features of neuropathic pain are specific, which helps to distinguish it from other types of pain and predetermines the need for a different therapeutic approach. Patients with neuropathic pain often describe symptoms as ongoing spontaneous pain, characterized by sensations of burning, tingling, pressure, or throbbing. Sometimes episodes of

lus), persistent pain sensations after cessation of the stimulus, and referred pain sensations at unstimulated areas have also been described [3].

In children over 6 years of age, these symptoms can be reported and documented, but in younger children or those with cognitive impairments, diagnosis remains a challenge. Self-rating scales are commonly used to assess pain severity, with one of the most preferred being the Wong-Baker scale, which is applicable even to 3-year-old children (Fig. 1). The scale combines facial expressions, numbers, and words, which helps children to determine the intensity of pain as accurately as possible, by indicating the facial expression that best describes the way they feel [4]. Another frequently used scale for assessing the severity of pain in children is the FLACC scale (face, legs, activity, cry, consolability), presented in Table 2. Its advantage is that it is suitable for use in even younger children, including infants over 2 months of age, as well as in patients unable to express their pain [5].

Wong-Baker FACES® Pain Rating Scale



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Fig. 1. Wong-Baker Pain Rating Scale.

pain resembling electric shocks occur, which can exist alone or in combination with persistent pain. Neuropathic sensations often include dysesthesias and paresthesias, which can be spontaneous or provoked by external stimuli. Clinically, neuropathic pain can also manifest with symptoms such as allodynia (pain elicited by innocuous stimuli) or hyperalgesia (an intense painful response to a weak pain stimulus). Hyperpathia (intense pain response to repetitive stimu-

Diagnosis

The diagnosis of neuropathic pain is complex, as there is no specific biomarker, diagnostic finding or test to confirm it. Some disorders, such as Fabry disease in children, have a well-defined etiology, but in cases such as low back pain, which is characterized by a mixed nature of pain (a combination of nociceptive and neuropathic components), accurate diagno-

Table 2. FLACC pain assessment scale (after Merkel et al., 1997)

Categories	Scoring		
	0	1	2
F Face	Smiling or expressionless	Occasional grimaces, frowning, sad or worried expression, withdrawal, disinterest	Frequent to constant chin tremor, clenched jaw, tortured face—an expression of fear or panic
L Legs	Normal position or relaxed	Tense position, restlessness, periodic twitching	Kicking, legs drawn up, marked spasticity, constant tremor or twitching
A Activity	Calm body position, normal posture, easy movement	Body twisting, back and forth movement, tense body, agitation (e.g., head back and forth, aggression), shallow and ragged breathing, periodic sighs	Twisting or rigid body, extreme agitation, head banging, trembling, breath-holding, panting, or gasping of breath
C Cry	Lack of crying (when awake and during sleep)	Moans or whines, occasional complaints; periods of verbal outbursts or grunting	Constant crying, screaming or sobbing, frequent complaints, repeated outbursts, constant grunting
C Consolability	The child is calm and content	Reassured by touching, hugging, or talking	Difficult to comfort and console, pushing away caregiver, resisting attempts at soothing

sis is difficult. This necessitates the use of a hierarchical system for classifying neuropathic pain, based on three levels: possible, probable, and certain. The classification is based on the clinical history and anatomical distribution of the pain, objective sensory signs from the physical examination, and additional tests to confirm damage or disease of the nervous system. It is also necessary to rule out other possible types of pain as unlikely causes of the symptoms. This approach improves the accuracy of the diagnosis (Fig. 2) [2,3].

Pharmacological Therapy

Antiepileptics

Antiepileptic drugs, such as *gabapentin*, *pregabalin*, *carbamazepine*, and *valproic acid*, relieve chronic pain by blocking specific sodium and calcium channels in neurons. This action leads to the suppression of spontaneous electrical activity and normalization of the depolarization threshold of nociceptive cells, without disrupting normal nerve conduction. These drugs are particularly suitable for patients with neuropathic pain and comorbidities such

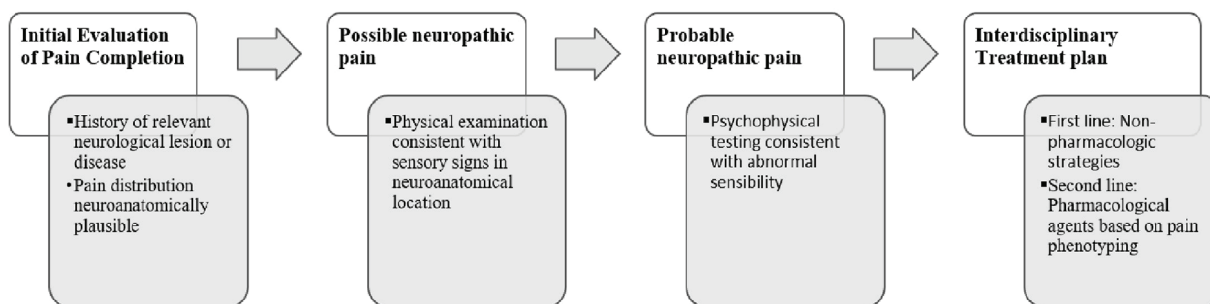


Fig. 2. System for diagnosing neuropathic pain in children and adolescents (after Einhorn et al., 2024).

as bipolar affective disorder, generalized anxiety disorder, and epilepsy. They are approved by FDA and EMA for treatment of specific pain conditions in adults, with *carbamazepine* being used in trigeminal neuralgia, *pregabalin* in fibromyalgia and neuropathic pain associated with diabetes and herpes zoster, and *gabapentin* in postherpetic neuralgia. Gabapentinoids have a relatively good safety profile and minimal risk of drug interactions, which is why they are preferred rather than other antiepileptic drugs. In any case, due to the renal elimination of the drugs, doses should be adjusted in patients with renal failure [6].

Despite the good efficacy of *gabapentin* and *pregabalin* for the relief of neuropathic pain in adults, their use in children has been approved by EMA and FDA only for treatment of epilepsy. However, they are often prescribed off-label for analgesia in pediatric patients with pain of various origins, including neuropathic pain. According to a study by Donado et al. (2021), this off-label use has increased in recent years and significantly exceeds their use as antiepileptic drugs in children [7]. However, data on their effectiveness as analgesics in children remain limited. Although publications have reported beneficial effects in various forms of neuropathic pain [8,9], there is a lack of large randomized clinical trials proving the benefit of their use. Moreover, a double-blind study in pediatric patients (n = 50) with malignant diseases and iatrogenic (*vincristine*-induced) neuropathic pain showed a lack of additional analgesic effect of *gabapentin* when used as an adjunct to an opioid analgesic [10]. Despite these conflicting results from clinical trials conducted to date, gabapentinoids remain the first choice for pharmacological treatment of neuropathic pain in pediatric patients [11,12].

The use of gabapentinoids is often associated with adverse effects such as sedation, dizziness, and weight gain. There is also evidence for possible behavioral effects, especially in adolescents, including aggressive behavior and increased suicidal ideation. In recent years, attention has also been drawn to the risk of abuse of gabapentinoids, associated with their potential to cause drug dependence [13]. Therefore, their use in children and adolescents requires a careful monitoring.

Antidepressants

Antidepressants are the other main pharmacological group with proven efficacy for relieving neuropathic pain in adult patients, with the doses used being lower than those required for treatment of depression, which determines better tolerability and safety. The most effective drugs are tricyclic antidepressants (TCAs) and serotonin and norepinephrine reuptake inhibitors (SNRIs). The mechanism of analgesic action is related to the inhibition of norepinephrine and serotonin reuptake, characteristic of both groups, which alters the neurochemical pathways associated with pain conduction.

An additional advantage of TCAs is that they have a beneficial effect on sleep disturbances, which often accompany pediatric pain, due to their sedative action. For treatment of neuropathic pain, TCAs are usually administered at bedtime, especially when medications with pronounced sedative effect such as *amitriptyline* are used [6]. Although the use of TCAs in neuropathic pain is well-studied in adults, data on their efficacy in children are almost nonexistent. There is also a lack of FDA and EMA approval for use as analgesics in this population. However, like gabapentinoids, they are used off-label and are included in standard recommendations for treatment of diseases associated with neuropathic pain, such as Fabry disease [14]. The effect of *amitriptyline* for treatment of non-malignant neuropathic pain in children was studied in a randomized clinical trial in which the drug was compared with *gabapentin*. The results showed similar efficacy and safety of the two drugs [15].

Duloxetine, belonging to the SNRIs group, is widely used to treat neuropathic pain (specifically diabetic neuropathy) and fibromyalgia in adults. A significant advantage of SNRIs over TCAs as drugs for neuropathic pain, is that doses that effectively control pain are also beneficial in anxiety. In addition, compared with TCAs, SNRIs have a more favorable side effect profile, leading to better patient compliance. Another important advantage of SNRIs is that, while TCAs typically stimulate appetite and lead to weight gain, *duloxetine* is often associated with weight loss, making it more suitable for use in overweight adolescents [6]. In the pediatric population, *duloxetine* was initially approved for use in generalized anxiety dis-

order and subsequently received FDA approval for alleviation of fibromyalgia (now classified as nociceptive pain) in adolescents aged 13–17 years [16]. The efficacy of *duloxetine* in the treatment of neuropathic pain in the pediatric population has been investigated in a few clinical trials in which the drug was administered as an antidepressant and anxiolytic in children with generalized anxiety or depressive disorder and concomitant neuropathic pain [17,18]. Efficacy remains controversial, and in many cases, treatment was discontinued due to adverse effects.

The use of TCAs is generally associated with an unfavorable safety profile—a narrow therapeutic window with a risk of cardiac arrhythmias and numerous adverse drug reactions related to their ability to block various postsynaptic receptors. In addition to sedation and changes in appetite, anticholinergic side effects such as dry mouth and constipation are also pronounced. The use of TCAs should be accompanied by careful monitoring of side effects, cardiac conduction and possible electrophysiological changes. In connection with the narrow therapeutic window of this pharmacological group, it is important to carry out individual monitoring of the clinical condition, with special attention paid to blood levels of the drug and cardiac function by ECG, especially when it is necessary to increase the dose. Serotonin and norepinephrine reuptake inhibitors are distinguished by a better safety profile, as side effects, usually gastrointestinal disorders, hyperhidrosis, dizziness and agitation, decrease during the course of treatment. Changes in blood pressure are possible, which requires regular monitoring. The risk of intoxication with this group is low and plasma concentration monitoring is not required, as with TCAs [6].

It should be noted that all antidepressants, both TCAs and SNRIs, administered to children and adolescents (usually for the treatment of major depressive disorder) increase the risk of suicidal ideation and behavior. It is recommended that all pediatric patients treated with these drugs be carefully monitored for worsening symptoms, suicidality, and unusual behavioral changes, especially in the initial stages of therapy or with dose changes. Although antidepressants have not been proven to induce suicidal ideation, close monitoring is mandatory to ensure the safety of treatment [6].

Opioids

Although opioids are the most potent analgesics for nociceptive pain, they demonstrate moderate efficacy in relieving neuropathic pain and are second- or third-line drugs for this indication. However, it should be noted that some members of the group have a more complex mechanism of action that is not limited to the activation of opioid receptors. These opioids are more effective in neuropathic pain and are often used in its complex therapy in adult patients. However, the management of neuropathic pain in children with opioids remains a challenge due to the lack of sufficient research, especially prospective randomized trials, and at this stage, there is insufficient data to support the routine use of opioids to affect neuropathic pain in the pediatric population.

Opioids with additional mechanisms of action that demonstrate higher efficacy in neuropathic pain (based on data in adult patients) are *tramadol*, *tapentadol*, and *methadone*.

Tramadol is an opioid with a relatively low affinity for opioid receptors, making it safer and better tolerated in long-term use than potent opioids. It has additional mechanisms of action, including inhibition of serotonin and norepinephrine reuptake, which determine its effectiveness in neuropathic pain. Although it is recommended as a second-line agent in the adult treatment guidelines, FDA restricts its use in children younger than 12 years of age, as well as in those between 12 and 18 years of age who are overweight or have concomitant respiratory disorders (obstructive sleep apnea or severe lung disease). The reason is the genetic polymorphism in the activity of CYP2D6, which metabolizes *tramadol*, leading to a high risk of respiratory depression in ultra-rapid metabolizers among these patients. In children over 12 years of age without the aforementioned concomitant diseases, the use of *tramadol* is not absolutely prohibited, but it is not recommended [19].

Tapentadol is another opioid with an additional mechanism of action similar to that of *tramadol*—inhibition of norepinephrine reuptake. It is considered safer than *tramadol* in children because it is not metabolized by CYP450 and has no active metabolites with analgesic activity. It is approved by EMA for treatment of acute postoperative pain in the pe-

diatric population, but efficacy data in neuropathic pain and chronic pain are currently lacking [20,21].

Methadone combines agonism at opioid receptors with antagonism at glutamatergic NMDA receptors and inhibition of serotonin and norepinephrine reuptake, making it suitable for complex pain. Its use in pediatric patients includes prevention and treatment of iatrogenic opioid dependence and management of cancer and postoperative pain, including those with a neuropathic component [11,12].

Due to the lack of sufficient studies and the risk of adverse effects, opioids are not recommended for routine use in pediatric neuropathic pain. They may be considered as a therapeutic option in cases of cancer-related pain or when other approaches have failed. When prescribing opioid therapy, a systematic approach is recommended: using the lowest effective dose and preferring short-acting preparations; documenting adherence to an opioid-sparing strategy and prior unsuccessful pharmacological and non-pharmacological therapy; clearly defining treatment goals and expected outcomes; carefully monitoring for abuse risk and comorbid conditions; and closely monitoring and managing any side effects [22].

Nonsteroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) have traditionally not been considered effective in the treatment of neuropathic pain, and this class of drugs is not included in standard recommendations for treatment of such conditions. Despite the lack of data on their effectiveness, they are the most preferred analgesics by patients, and it is estimated that about 35–40% of those suffering from neuropathic pain use NSAIDs. This widespread use could be explained by the easy availability of most of the drugs as over-the-counter medications, the comorbidity of the patients with a mixed mechanism of pain generation or a placebo effect [23]. However, due to the lack of adequate clinical studies, it cannot be ruled out that NSAIDs affect the neuropathic component of pain. Additional research and clinical trials are needed to provide a definitive answer on the presence or absence of an effect of this group of drugs in neuropathic pain.

Lidocaine

Local anesthetics block voltage-gated sodium channels and inhibit the generation and transmis-

sion of nerve impulses. When administered intravenously, *lidocaine* exhibits additional mechanisms of action by affecting other voltage- and ligand-gated ion channels, as well as G-protein-coupled receptors [24].

Lidocaine patches are often used to treat localized neuropathic pain in adults, and are characterized by very good tolerability and safety compared to systemic pharmacological therapy. Although these patches are not approved for pediatric use, studies on a limited number of patients have shown their effectiveness in children and adolescents. Topical application of *lidocaine* has been studied in children with sickle cell anemia and associated vaso-occlusive pain, with improvement in symptoms observed in more than half of the patients [25,26]. A prospective multicenter clinical study in pediatric patients with various forms of localized chronic peripheral and central neuropathic pain also confirmed the good efficacy of *lidocaine* patches and reported a reduction in pain intensity and improved functionality and sleep in almost 70% of patients. The *lidocaine* patch shows a very good tolerability and safety profile, with the only adverse effects observed being mild skin reactions in a few patients [27].

To treat neuropathic pain, *lidocaine* can be used not only locally in the form of patches, but also intravenously by infusion. The efficacy of *lidocaine* intravenous infusions in adults has been confirmed in several randomized clinical trials. Infusion *lidocaine* provides significant pain relief at the cost of relatively few side effects such as dizziness, nausea, and lethargy [28,29]. A study in children showed that intravenous *lidocaine* can be successfully used in chronic pain of various etiologies, including neuropathic or pain with mixed mechanism of generation. The intensity of pain decreased significantly during 80% of the infusions performed, with the best analgesic effect developing in patients who received at least 3 infusions. The observed adverse effects are relatively mild and dose-dependent and subside quickly after cessation of the infusion [30]. *Lidocaine* infusions have also been shown to be effective as adjuvant therapy in patients with pain due to vaso-occlusive crises in sickle cell anemia [31], as well as in cancer patients with neuropathic pain [32], treatment-refractory malignant pain [33] and drug-induced pain [34]. Limitations in the use of intravenous *lidocaine* in-

clude the need for intravenous access and close monitoring of plasma levels due to the narrow therapeutic window, as well as the lack of data on the dose-effect relationship of intravenous *lidocaine* in the pediatric population.

Pediatric Doses

Most of the currently used medicines have been developed for and are primarily prescribed to adults. Their therapeutic potential in the pediatric population can be investigated mainly in clinical practice, as clinical trials in children are limited by ethical considerations and concerns about the safety of the therapy. Dosage modulation in this group of patients is usually based on age and body weight, taking into account the risk of side effects, the specific features of the pediatric population, and other individual characteristics [35]. Medications used in the management of neuropathic pain in children are usually used in the following dosages:

Gabapentin [11]

- ◆ First-line drug for neuropathic pain
- ◆ Oral administration
- ◆ Single dose—3–5 mg/kg (maximum single dose 300 mg)
- ◆ First day—1 dose in the evening at bedtime; second day—1 dose 2 times a day, from the third day—1 dose 3 times a day (daily dose—10–15 mg/kg)
- ◆ If well tolerated, the dose is titrated to 30 mg/kg/day; after 2–4 weeks of administration, the dose is reduced to 10–20 mg/kg/day
- ◆ Common side effects include dizziness, drowsiness, fatigue, and headache.

Amitriptyline [11]

- ◆ Suitable for management of neuropathic pain in children over 6 years of age with concomitant depression
- ◆ Pain is affected by lower doses than those needed to treat depression
- ◆ Oral administration
- ◆ Daily dose—0.35–0.4 mg/kg administered most often once a day, usually in the evening at bedtime due to the sedative effect; optional division of the daily dose into two doses
- ◆ The dose is usually increased gradually

- ◆ Common side effects include dizziness, drowsiness, constipation, blurred vision, dry mouth
- ◆ Caution is recommended in patients with cardiac disease and sensitive to anticholinergic effects; monitoring for suicidal ideation

Duloxetine [16,36]

- ◆ Suitable for management of neuropathic pain with concomitant generalized anxiety disorder in children over 7 years of age and treatment of fibromyalgia in children over 13 years of age
- ◆ Oral administration
- ◆ Starting dose—30 mg once daily
- ◆ After 2 weeks—increase of the dose to 60 mg once daily
- ◆ Blood pressure monitoring and monitoring for suicidal ideation are recommended
- ◆ Withdrawal symptoms are possible upon discontinuation of therapy.

Tapentadol [20,21]

- ◆ Suitable for treatment of acute postoperative pain in children over 6 years of age with a body weight of over 16 kg
- ◆ Short duration of administration—up to 3 days
- ◆ Oral administration
- ◆ For children under 40 kg—1–1.25 mg/kg every 4 hours; maximum daily dose—7.5 mg/kg
- ◆ For children over 40 kg—50 mg every 4 hours; maximum single dose—100 mg; maximum daily dose—600 mg
- ◆ It is recommended to use the minimum effective dose; the dose should be reduced if pain subsides
- ◆ Adverse effects include the typical side effects and risks of opioid analgesics; careful monitoring and reporting of adverse effects, as well as adherence to an opioid-sparing strategy are recommended

Methadone [11]

- ◆ Suitable for mixed nociceptive and neuropathic pain in pediatric oncology patients
- ◆ Oral or intravenous administration
- ◆ Wide range of doses depending on pain intensity and clinical indication
- ◆ Doses—from 0.06 mg/kg/day orally (low-dose therapy; half the standard analgesic dose) to 33 mg/kg/day intravenously (extremely high dose)

- ◆ It is optional to divide the daily dose into several doses at 4- to 12-hour intervals
- ◆ QT prolongation is possible; careful monitoring and reporting of adverse effects, especially in patients with rhythm disturbances, as well as adherence to an opioid-sparing strategy are recommended
- ◆ Caution is required to prevent potential clinically significant drug interactions

Lidocaine [11, 37]

- ◆ Application in the form of patches with 5% lidocaine to affect localized neuropathic pain in children
 - ✓ 1 patch every 12 hours
 - ✓ Suitable for long-term use
 - ✓ Very good tolerability and safety, almost complete absence of side effects
- ◆ Administration as an intravenous infusion
 - ✓ Infusion rate—in most cases 1–2 mg/kg over 30 min, followed by 1–2 mg/kg/h; doses around 3–3.5 mg/kg/h usually do not lead to adverse effects
 - ✓ Different infusion duration depending on the clinical indication (from 2 to 8 hours)
 - ✓ Need for therapeutic monitoring—plasma concentrations should be maintained below 5 mcg/mL to avoid risk of toxicity
 - ✓ If adverse effects occur, the infusion is discontinued or its rate is reduced

Non-Pharmacological Interventions

In addition to pharmacological therapy, it should not be neglected that non-pharmacological interventions play a key role in the treatment of neuropathic pain in children. Physical therapeutic methods, such as thermotherapy, ultrasound therapy, massage and electrical stimulation, contribute to improving blood circulation in the affected tissues, reducing muscle tension and accelerating the recovery process. These techniques not only relieve pain, but also improve the functionality and mobility of patients, which is of particular importance for the pediatric population.

Psychotherapeutic approaches have also been shown to be extremely helpful in pain management. Cognitive behavioral therapy and relaxation techniques have been shown to be beneficial in reducing

stress and improving pain thresholds. This aspect of treatment is important because the patient's psychoemotional state often plays a crucial role in the overall effectiveness of therapeutic interventions [6].

A Treatment Approach Based on Pain Phenotyping

The traditional trial-and-error approach to pharmacological management of neuropathic pain in children and adolescents is not recommended, as it can be not only ineffective but also potentially harmful due to the use of drugs with severe side effects. The lack of evidence-based recommendations further complicates the management of this condition, which requires a precise and individualized approach. In recent years, attention has been paid to implementation of combined strategies for management of neuropathic pain through determining its phenotype by using quantitative sensory testing (QST) and assessment of conditioned pain modulation (CPM). These strategies show the potential to transform clinical algorithms by shifting the focus from traditional diagnosis to personalized medicine that is based on the individual mechanism of pain generation. The QST/CPM assessment allows identification of sensory processing disorders underlying neuropathic pain, and thus suggests a possible mechanism of its occurrence. This approach has been shown to reduce polypharmacy and the need for interventional procedures without reducing the effectiveness of treatment. According to the proposed strategy, neuropathic pain can be phenotyped into three different types that are preferably treated with different pharmacological therapy—gabapentinoids for phenotype A, topical therapy or NSAIDs for phenotype B, and tricyclic antidepressants for phenotype C [2,38].

A QST/CPM assessment provides a precise and individualized approach but it is complicated and time consuming, thus necessitating the development of simplified protocols for routine clinical use. However, individualizing treatment based on pain phenotype offers a promising opportunity to improve care and reduce harm in children and adolescents.

CONCLUSION

The optimal approach to the treatment of neuropathic pain in children requires a multimodal and interdisciplinary strategy that combines pharma-

cological and non-pharmacological methods. The unique mechanisms of development of neuropathic pain and the limitations of the available data on the efficacy of drug therapy must be taken into account. *Gabapentin* is the pharmacological agent of first choice and the most commonly used drug for the treatment of neuropathic pain in the pediatric population. For localized pain, the use of *lidocaine* patches is appropriate, as they are characterized with very good tolerability and safety profile. In patients with concomitant depressive or anxiety disorders, neuropathic pain can be successfully treated with some antidepressants. Most opioid analgesics have no role in the treatment of neuropathic pain. However, some of them have additional mechanisms of action, which makes them useful for patients with mixed nociceptive and neuropathic pain, especially in the field of pediatric oncology. *Lidocaine* therapy in the form of intravenous infusions seems promising for the pediatric population in terms of effectiveness. Its obvious disadvantages are the route of administration and the need for drug monitoring.

Performing quantitative sensory testing or other methods to assess pain phenotype can aid in the selection of pharmacological strategies, allowing for a more precise and individualized approach to the treatment of neuropathic pain.

Despite advances in the understanding and treatment of neuropathic pain in children, significant gaps in the scientific evidence regarding the effectiveness and safety of different therapeutic approaches remain. Additional large randomized clinical trials are needed to evaluate the long-term outcomes of pharmacological and non-pharmacological interventions, as well as to develop more precise guidelines for their combination. Future research should focus on optimizing multimodal therapeutic strategies and advancing personalized medicine in the context of pediatric neuropathic pain.

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