

Acute pain in children: A reappraisal on the modalities of grade evaluation and on treatment strategies (Review)

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Abstract. The present review aimed to provide a summary of practical clinical approaches to the evaluation of the pain grades and modalities of treatment for pediatric patients with acute pain. For this purpose, a literature review was conducted from January, 2000 to December, 2022, which included comprehensive articles from online bibliographic databases (i.e., MEDLINE, Embase, PubMed, Cochrane Central and Scopus) covering the principal topics of pain and children OR therapeutic strategies OR pharmacological treatments OR opioid medication OR pain and nonpharmacological therapies. Different scales were used to grade acute pediatric pain, as this can range from mild to severe and may be disguised by children. In addition, non-pharmacological and pharmacological treatment modalities were reported according to the different underlying causes and types of pain. Furthermore, a list of the most well-known modalities used to measure the presence and grade of acute pain in children was compiled, and the various types of pharmacological and non-pharmacological treatments administered to children with acute pain are discussed. A flowchart for the management of children with severe pain is also presented. Acute pain in pediatric patients is a common event and a reason for concern. The causes of acute pain in children need to be carefully evaluated and appropriate treatment should be administered according to the

real presence, consistency, and duration of the pain and body organ collocation.

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1. Introduction

Children commonly present with acute pain that is either localized or generalized in the body. The pain may occasionally be underrated and thus inadequately treated with the possible consequence of significant issues for the health of the affected child. The revised International Association for the Study of Pain defines pain as an unpleasant sensory and emotional experience associated with or resembling that associated with actual or potential tissue damage (1). The clinical assessment of pain in pediatric patients must include several aspects, such as the psychological history of the child and their family, a thorough physical examination, and when necessary, laboratory analyses and radiological findings. Clinical indications should be drawn from the quality, location, duration, frequency and intensity of the pain. Pain is regarded as a symptom of an underlying condition, and perceptions of pain may be felt in accordance with different factors, such as the age, cognition, sex, previous pain experiences, temperament and psychological attitude of each patient (1). Pain has been temporally distinguished as acute and chronic and arbitrarily

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defined as acute when it lasts for 3 months and chronic when the duration is 6 months (2,3). Acute pain may also be referred to as a painful episode that is transitory and only lasts until the noxious stimulus ends or the underlying damage or pathological event(s) have been removed. Acute pain may further be a temporal manifestation of a chronic disorder.

Pain is a subjective experience (4). Despite the development and greater awareness of instruments, guidelines, and educational and training strategies, recent studies have shown that clinicians still do not pay sufficient attention to pain management, particularly in children. Inadequate clinical evaluations, inappropriate scale measurements and the treatment of acute pain in various situations have been clearly identified as contributing to this issue (5). In children who are <2 years of age, the situation is more pronounced, as the pain, even if treated, is sometimes managed with incorrect or inadequate dosages (5). Acute pediatric pain evaluations must include the pain quality, characteristics, location, onset, duration, aggravating and alleviating factors, and the impact on function (6-9). In children and adolescents, the intensity and quality of pain may be assessed using self-report measures, such as drawings, images of faces, graded color intensities and other systems (8). The aim of the present review was therefore to report the modalities used to measure the presence and grades of acute pain in children, and the different strategies to approach and treat such pain in different clinical situations. A flowchart for the management of children with severe pain is presented in Fig. 1.

2. Literature search methods

A literature review was conducted by collecting articles, including clinical trials, primary research articles and reviews from online bibliographic databases (i.e., MEDLINE, Embase, PubMed, Cochrane Central and Scopus) covering the period from January, 2000 to December, 2022. The key words used for the search were derived from medical subject heading terms, namely 'pain and children (pediatric)', 'pediatric', 'child', 'infant', 'toddler' OR pain therapeutic strategies ('analgesic' or 'analgesia') OR pain pharmacological treatments OR opioid medications OR pain and nonpharmacological therapies. Relevant studies were examined manually and are included in the present reference list. As the subject of the present study was notably wide, the literature data that were included were those that were, in the authors' opinion, more representative.

Once the initial results had been collected, two reviewers analyzed the titles and abstracts and screened them for the inclusion criteria, which were studies with any level of evidence that reported clinical results published over the past 22 years (2000-2022). Comparative, cross-sectional, retrospective, prospective and survey studies, case series, and case reports on the pediatric population were included. All the articles written in languages other than English were excluded. Articles that dealt with different topics, had poor scientific methodologies, or were without an accessible abstract were also excluded. In addition, articles that did not match the inclusion criteria were ruled out. After removing the duplicate records, the main search articles that related to the study were included.

3. Acute pain in children

Diverse events cause acute pain in children, which affects various body organs and requires treatment by different types of specialists. Numerous clinical studies have addressed scale measurements of pain and clinical trials for pain treatment. However, to the best of our knowledge, no common agreement has been reached on the methods to use to measure pain in children or treatment strategies, although several options have been proposed for each topic. The present literature review indicates that a wide range of scales are used to measure acute pediatric pain, with different options employed for pharmacological and non-pharmacological treatment strategies.

The causes and treatment of acute pain are significant challenges, particularly among children and adolescents. Current guidelines recommend assessing and relieving (1,3,8) pain in all children in all instances; yet in clinical practice, particularly in the pediatric population, management is suboptimal and not completed (5). In a survey of acute pain management in children that involved 929 Italian pediatricians, Marseglia *et al* (10) reported the results obtained for 6,335 patients with a uniform distribution of different types of acute pain. Pain was more frequently found to be of moderate intensity (42.2%, $P < 0.001$) and a short duration (within a few days: 98.4%, $P < 0.001$). Only 50.1% of the respondents used an algometric scale to measure pain, and 60.5% always prescribed a treatment. In the group of children with mild to moderate pain ($n = 4,438$), the most commonly used first-line nonopioid treatments were ibuprofen (53.3%) and acetaminophen (44.4%) (10). In the authors' experience, analgesics can be used without causing complications; however, the side-effects of these analgesics should be taken into consideration, as these can aggravate issues that already present in patients with comorbidities. For example, non-steroidal anti-inflammatory drugs (NSAIDs), cause gastric toxicity, which adds to basic reflux, and a reduction in renal flow, which adds to the poor intake of water. The hepatotoxic effect of paracetamol can contribute to malnutrition and the effects of cytochrome inhibitor drugs. Opioids can worsen constipation, nausea and dystonia and can cause itching, which the child will not be able to scratch, as well as urinary retention (globus vesicalis), particularly if the child is receiving glycopyrrolate therapy.

The World Health Organization (WHO) recommends a step approach, with pain divided into mild, moderate and severe (11). In the case of mild pain, the suggested treatment is non-opioid medications. For moderate pain, weak opioids should be used, with strong opioids used for severe pain. The most difficult task in the evaluation is the individuation of the pain condition and the application of the appropriate therapy.

In the assessment of acute pain in children, among the other key factors, are the evaluation of the grade of the pain and the correct treatment required for its attenuation or cessation.

4. Scales for pain grade measurement in pediatric patients

Various tools are available to measure the grades of acute pain in children. A list of scales to measure the properties of self-reported pain intensity is presented in Table I. No single scale is advocated as optimal for use with all types of pain or across the developmental age span. Scales must be applied

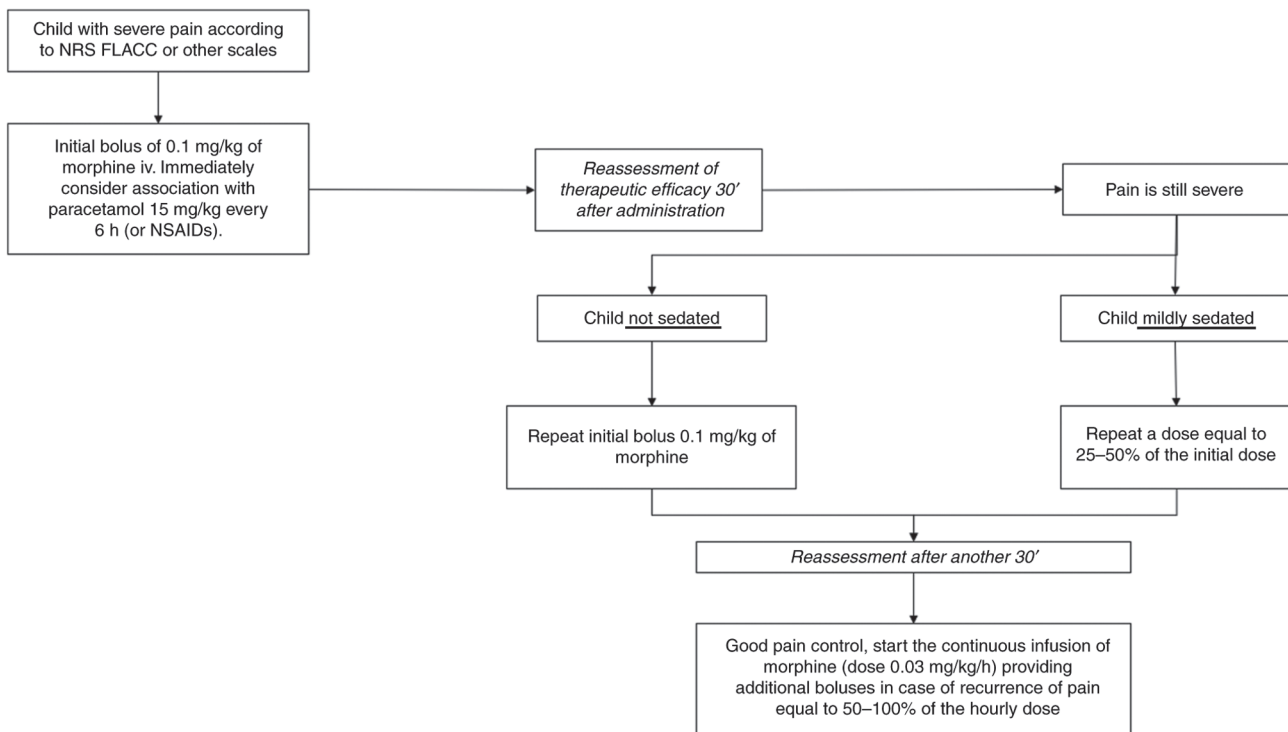


Figure 1. Flow chart depicting the management of a child with severe pain. NRS, Numerical Rating Scale; FLACC, Face, Legs, Activity, Cry, and Consolability (FLACC) scale; NSAIDs, non-steroidal anti-inflammatory drugs.

with due consideration of several factors, including the age of the child, the clinical localization and severity of the pain, and the cognitive and psychological structure of the child (9,12-14). In children with neurocognitive disabilities and in the context of emergency rooms/urgent situations, the measurement of the severity of pain becomes more complex and difficult. The inability/difficulty of children to communicate verbally or non-verbally, the presence of stereotyped or involuntary movements, altered facial and body expressiveness, and sensory disabilities may limit the validity of pain measurement.

5. Therapeutic strategies

Various types of acute pediatric treatments are available depending on the age of the patient, the intensity of the pain, and the characteristics and types of organs affected. As the topic is extremely wide, the present review summarizes the treatment strategies more frequently used. The therapeutic strategies can be divided into non-pharmacological techniques and pharmacological drugs. The use of several other analgesics is not considered (e.g., nitrous oxide, methoxyflurane, ketamine, diamorphine) as this was beyond the scope of the present review.

Non-pharmacological techniques. Research has shown that non-pharmacological options, including physical and psychological strategies, may be helpful in treating pain. Children may benefit from cognitive behavioral strategies, such as the use of imagery or relaxation. The application of non-pharmacological techniques has been employed to control pain, stress, and anxiety in children and their parents (9). The present review provides a summary of some of the suggested

non-pharmacological strategies aimed at the attenuation or cessation of acute pain in children. In their review of 39 trials with 3,394 participants, Uman *et al* (15) examined the effects of psychological interventions on needle-related procedural pain and distress in children and adolescents aged 2-19 years. They found strong evidence in support of distraction and hypnosis for needle-related pain and distress in this population (15). Similarly, Accardi and Milling (16) reported the effectiveness of hypnosis in reducing procedure-related pain in children. A systematic literature search on non-pharmacological interventions used for pain management in children in emergency departments was conducted by Wente (9). Among the 14 articles examined, distraction was used in 10 studies, sucrose in two studies, cold application in one study, and parental holding and positioning in one study. Furthermore, decreased pain, distress and anxiety in the parent, child, and/or observer were noted when these procedures were used (9). Cognitive-behavioral strategies should be related to the age and degree of cognitive development of the patient: The oral administration of sucrose and glucose, kangaroo care, tactile stimulation, rocking, singing and soft music, and an environment with soft, fused lights can be effective for infants. For children of school age, the application of cold spray, ice, hot moist packs, massaging and pressure can be useful and satisfying. Furthermore, the use of bandages, dressings and splints are other simple systems that can be used to reduce pain symptoms and anxiety, as these cover the view of the 'wound' that is causing psychophysical distress in the child (2). A study involving 98 children and 97 control children/parents examined the beliefs of parents about pain and the efficacy of a parental educational intervention on pain intensity in children and the experience of pain-related

Table I. Acute pain scales.

Scale name	Type of scale	Age	Scoring system	Scale	Indications
Faces Pain Rating Scale	Self-evaluation	4-8 years	Picture-based scale where child select 1 of 6 faces to represent their pain experience	0-10 (0-3 mild, 4-6 moderate, 7-10 severe)	Cognitively adequate child with motor impairment
Numerical Rating Scale (NRS)		>8 years	Ask the patient to assign a number to their pain (0 no pain, 10 worst pain ever)	0-10 (0-3 mild, 4-6 moderate, 7-10 severe)	Cognitively adequate child without motor impairment
FLACC (Face Legs Activity Cry Consolability)	Hetero-valuation	0-3 years	5 Behaviour items each scored from 0 to 2 to a total of 10 points	0-10 (0-3 mild, 4-6 moderate, 7-10 severe)	
FLACC-R (Revised)		2 months-7 years or any age nonverbal or with intellectual impairment	Compared to 'FLACC' includes additional pain behaviours often found in children who are non-verbal or with cognitive impairment	0-10 (0-3 mild, 4-6 moderate, ≥ 7 severe)	
NCCPC-R (Non-Communicating Children's Pain Checklist-Revised)		3-18 years	Scale with 30 total items with 7 subscales (vocal, social, facial, activity, body and limbs, physiological, and eating/sleeping) each item scored from 0 to 3 according to the frequency of its occurrence.	Total score of ≥ 7 indicates pain.	Children with cognitive impairment, non-verbal or unable by age to provide pain self-assessment
PPP (Pediatric Pain Profile)		1-18 years	Two-part individualized measure allowing caregivers to describe their child's pain behaviours on good days and bad days and complete a 20-item measure scored on a 0-3 scale	Total score of ≥ 14 indicates clinically significant pain, 10-19 is mild, 20-29 is moderate, 30-39 is severe, and >40 is very severe pain.	
EVENDOL (EValuation ENfant DOuLeur)		0-7 years	Five items (vocal or verbal expression, Facial expression, movements, postures, interaction with the environment) evaluated at rest and at mobilization, Gradations in colour, area and length so as to easily associate scale positions with diffused levels of pain intensity	Total score ranges from 0 to 15. Treatment threshold ≥ 4	
Color Analogue Scale (CAS)		4-10 years		The back of the tool has a numerical rating scale providing a means to assign a numerical pain score between 1 and 10 cm in 0,25 cm increment	

The information listed in the table has been obtained from previous studies (1,3,8).

Table II. Non-pharmacological therapy.

Type of method	Age
Physical methods	
Comforting touch (cuddles, stroking, holding)	All ages
Comfort positioning	All ages
Cutaneous stimulation	>1 months
Pressure/massage	All ages
Hot/cold treatments	All ages
Pacifier and sucrose solution	<1 years
Cognitive-behavioral methods	
Information/communication	>6 years
Psychological preparations	>6 years
Direct involvement in pain management/assessment	>6 years
Distraction tools (music, videos, apps, toys with light/sounds)	All ages
Desensitization	>2 years
View/imagery (story-telling, guided imagery, favor activity)	>6 years
Relaxation (deep breathing, music, muscles relaxing)	All ages
Breathing out/controlled breathing	Teenagers

unpleasantness at 24 h post-discharge from the emergency department (17). According to the researchers, the active participation of parents in their child's pain management may be more effective than a passive educational intervention (17). Music therapy has also been shown to be a form of distraction that alleviates some types of pain and distress experienced by children undergoing medical procedures in a pediatric emergency department (18). In a previous comprehensive review that included 13 studies and involved 778 patients, the effects of music therapy and opioid treatment on pain anxiety among patients who underwent orthopedic surgery were evaluated. Significant differences were found between the two groups regarding the use of music therapy to reduce pain; however, no statistically significant differences were found in the use of opioids and physiological variables between the two groups. The authors maintained that the timing, duration, and type of music intervention can be modified in relation to specific clinical settings and medical teams (19). A summary of the non-pharmacological techniques used for pain management in children is presented in Table II.

Criticism has been expressed as regards the use of non-pharmacological treatments in the context of acute pediatric pain where pharmacological, physical (splint, ice) and psychological (distraction, breathing) treatments may be more effective. In addition, the literature provides evidence of the difficulties faced by nurses in applying non-pharmacological treatments due to inadequate cooperation from physicians, the heavy workloads of nurses and multiple responsibilities, the low ratio of nurses per patient, and the unfavorable attitudes of nurses to non-pharmacological pain management (20).

Pharmacological strategies. Pharmacological therapies are the most commonly used types of treatments for any type of pain. The drugs commonly utilized, as well as the routes of administration, doses and indications on their use are summarized in Table III.

Non-opioid medications. The non-opioid pain medications most commonly used are NSAIDs, which act via their inhibitory actions on cyclooxygenase (COX)-2 enzymes. COX-2 enzymes facilitate the production of pro-inflammatory prostaglandins; thus, prostaglandin production is inhibited to obtain an analgesic effect. Among the most commonly used NSAIDs is ibuprofen. Other COX-2 inhibitors, such as indomethacin, meloxicam and Celebrex, are more frequently used to treat inflammatory and rheumatological disorders than acute pain (20,21). A previous randomized controlled trial of acetaminophen, ibuprofen and codeine treatment for acute pain in children with musculoskeletal trauma conducted by Clark *et al* (21) involved 336 pediatric patients with 100 children in each treatment group. According to the authors of that study, ibuprofen provided the optimal analgesic effect of the three medications studied. In another study, a group of children presenting with uncomplicated extremity fractures was treated in a randomized trial with the oral administration of either morphine or ibuprofen (22). In that trial, 66 children were in the morphine group and 68 in the ibuprofen group. No significant differences in analgesic efficacy were reported between the groups, although morphine was associated with a significantly greater number of adverse effects. The authors of that study maintained that ibuprofen remains safe and effective for outpatient pain management in children with uncomplicated fractures (22). In another randomized clinical trial performed by Chang *et al* (23), of 411 patients with acute extremity pain (mean score, 8.7 on an 11-point numerical rating scale) in an emergency department, no significant differences in pain reduction at 2 h were found. The main pain scores decreased by 4.3 with ibuprofen and acetaminophen, 4.4 with oxycodone and acetaminophen, 3.5 with hydrocodone and acetaminophen, and 3.9 with codeine and acetaminophen. According to the authors of that study, the analgesic effects of NSAIDs were equally efficacious as opioids when treating musculoskeletal pain in adult patients (23).

As is well known, the use of ibuprofen is not recommended for patients with hemorrhagic pathologies, significant dehydration, gastrointestinal disorders and impaired renal function. Jelinek (24) demonstrated that the intravenous administration of ketorolac exhibited an equivalent efficacy in reducing moderate to severe pain as intravenous morphine, although with fewer side-effects. Marzuillo *et al* (25) reviewed the pharmacokinetics of ketorolac and confirmed its efficacy without severe side-effects, if used for a short period of time. Recently, a pilot single central randomized controlled trial demonstrated that ketorolac had comparable results to morphine when used in children aged 6-17 years with suspected appendicitis (26). The use of ketorolac sublingually as a valid alternative in the absence of intravenous access was also suggested (26). Neri *et al* (27) demonstrated that sublingual ketorolac and tramadol were equally effective. In cases of suspected bone fractures, studies have shown that sublingual ketorolac and tramadol are effective analgesics for pain management in children aged 4-17 years (25,26).

Table III. Pharmacological therapies for acute pain.

Drug	Route of administration	Single dose	Maximum dose	Indications
Non-opioids				
Paracetamol	<i>Per os</i>	10-15 mg/kg, every 4-6 h	60-75 mg/kg/die (4 g/die)	From birth
	Rectal i.v.	15-20 mg/kg, every 4-6 h <i>Per os</i>	60-90 mg/kg/die 90 g/kg/die	
NSAIDs				
Ibuprofen	<i>Per os</i>	5-10 mg/kg, every 6-8 h	20-30 mg/kg/die	>3 months
Ketoprofen	<i>Per os</i>	1-3 mg/kg, every 8-12 h	4-9 mg/kg/die	>6 years
Ketorolac	<i>Per os</i>	0.5 mg/kg, every 6-8 h	3 g/kg/die	>16 years
Naproxen sodium	<i>Per os</i>	1 mg/kg, every 8 h	3 g/kg/die	>14 years
Acetylsalicylic acid	i.v.	5-10 mg/kg, every 8-12 h	20 g/kg/die	Not indicated in pediatric age. If necessary >2 years
Opioids				
Weak				
Codeine	<i>Per os</i> or rectal	0.5-1 mg/kg, every 6-8 h	240 mg/die	>12 years
Tramadol hydrochloride	<i>Per os</i>	1-2 mg/kg, every 6-8 h	400 mg/die	>1 year
Strong				
Fast-release morphine sulfate	i.v.	0.15-0.3 mg/kg, every 4 h		>1 year
Morphine hydrochloride	i.v.	Bolus 0.05-0.1 mg/kg, every 2-4 h CI 0.02-0.03 mg/kg/h	5 mg/dose	From birth
Fentanyl	Intra nasal injections i.v.	1-2 µg/kg/dose (repeatable after 30-60 min) Bolus 0.001-0.002 mg/kg; CI 0.001 mg/kg/h	100 µg	>2 years

The information listed in the table has been obtained from previous studies (31-37).

Paracetamol has been cited in numerous studies as the first-line analgesic agent in emergency departments. Its efficacy is valuable at the correct dose (15 mg/kg) in the treatment of mild to moderate pain. It is characterized by its rapid action and the possibility of different routes of administration (28). A previous meta-analysis revealed that the safety and tolerability profiles of paracetamol and ibuprofen were similar in terms of their efficacy for both pain and fever, and they were rarely associated with severe side-effects (28). In instances of mild or moderate pain, it is preferable to administer paracetamol *per os* to achieve fairly rapid action and excellent tolerance in the majority of children. By contrast, the rectal route is burdened by slow absorption and unpredictable efficacy both with respect to action time and analgesic capacity (29). In a multicenter emergency department study in 2018, Benini *et al* (7) found that both paracetamol and ibuprofen were inappropriately used in 83 and 63% of pediatric cases, respectively.

Ketamine, a drug that blocks the effects of glutamate, has been shown to be an effective analgesic in children when administered at sub-dissociative doses (30). Back pain, headache, extremity or musculoskeletal pain, acute abdominal pain and renal colic

are controlled by the intravenous administration of ketamine when used appropriately (31,32). In recent years, two systematic reviews and meta-analyses demonstrated that ketamine was non-inferior to opioid medications for acute pain management, as it had a similar analgesic effect and safety profile (33,34).

Opioid medications. Opioid infusion is usually indicated for patients with chronic pain. Of note, a bolus of an intravenous opioid is advised for patients with sudden-onset severe pain or reserved for breakthrough pain for patients who are already receiving opioid infusions. Researchers have recommended that the starting opioid in opioid-naïve patients should be morphine or hydromorphone (30). Typically, immediate-release oral opioids are ordered for pain at intervals of 3-4 h to minimize breakthrough pain and opioid side-effects (30). Additional smaller doses can be administered every 2 h for breakthrough doses. In general, oral use is preferred over intravenous administration, except in cases of poor absorption or an inability to administer drugs enterally (i.e., colitis, mucositis, vomiting). The sublingual route of administration is safe and efficacious both for ketorolac and opioids (34,35). In the trauma setting, intranasal sufentanil or

diamorphine administration have both been reported as highly efficacious in the treatment of severe pain (36,37).

6. Conclusion

The role of the pediatricians in the treatment of acute pain is extremely complex due to the poor collaboration of and difficulties encountered by the children and their parents to correctly indicate the duration, intensity and localization of the pain. The task of pediatricians consists of carefully evaluating the underlying cause for acute pain in children to consequently administer appropriate treatment. The list of methodologies used to reveal the scales of acute pain and the type of treatment to be used for specific causes of acute pain is wide. Thus, treatment needs to be carried out according to the duration, localization and severity of the pain, reflecting the experience of the single pediatric specialist.

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Authors' contributions

PP, RF, LM, MCF and ADN conceived and designed the study. GT and ADS performed the literature search. CM, LS and MCF analyzed the data obtained from the literature. PP, AP and RF wrote the manuscript. All authors (ADN, LS, MCF, GT, CM, ADS, SS, AP, MC, RF, LM and PP) were involved in the preparation of the final draft and in the revision of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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