DOI: https://doi.org/10.2298/SARH180917019S
UDC: 615.212-053.2; 616-083-053.2

REVIEW ARTICLE / ПРЕГЛЕД ЛИТЕРАТУРЕ

Analgesia in the palliative care of children

Dušica Simić[1,2], Ana Vlajković[1], Ivana Budić[3,4], Miodrag Milenović[2,5], Marija Stević[1,2]

[1]University Children's Hospital, Belgrade, Serbia;
[2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[3]Niš Clinical Centre, Centre for Anesthesiology and Reanimatology, Niš, Serbia;
[4]University of Niš, Faculty of Medicine, Niš, Serbia;
[5]Clinical Center of Serbia, Emergency Center, Anesthesiology and Intensive Care Medicine, Belgrade, Serbia

SUMMARY
Due to the increasing incidence of terminal illnesses in children, there is great urgency within pediatric medicine to give these patients the best palliative care possible. The main focus of palliative care is to alleviate suffering resulting from the psychophysical condition of the child, which is mostly due to physical pain. The first phase of managing pain in palliative care is quantifying and qualifying pain levels, although this is sometimes difficult to do with pediatric patients. In addition to implementing strategies that alleviate or remove pain for patients, it is also crucial to give patients and their families a feeling of full control over pain.
In practice, non-pharmacological and pharmacological methods of analgesia are present. Pharmacological methods include non-opioid and opioid analgesics, followed by co-analgesics as well as methods of regional anesthesia.
In order to give these patients the best care possible, it is necessary that the approach be individual, multimodal, multidisciplinary, and considerate of every detail.
Keywords: pain; palliative care; pediatric patients; analgesia

INTRODUCTION

Terminal illnesses that affect children are a major issue within the medical community. Pediatricians are most often faced with malignant diseases where the survival rate is increasing, and where more than 80% of children diagnosed with malignant tumors can survive for more than five years due to advances in diagnostics, therapy, and supportive care [1]. By improving palliative care methods, pediatricians are able to increase the lifespans of these terminally ill children. Palliative care is defined by the World Health Organization as an "approach to improve the quality of life of patients and families who face life-threatening illness, by providing pain and symptom relief, spiritual and psychosocial support from diagnosis to the end of life and bereavement" [2]. Because pain is the main cause of anxiety, emotional, and behavioral problems with pediatric patients, the main focus of palliative care is to prevent and stop pain, so that patients and their families can have a better quality of life [3, 4, 5].

The World Health Organization defines pain as an unpleasant sensory or emotional experience associated with actual or potential tissue damage [6]. According to this definition, it is clear that pain does not have to be linked to existing tissue damage and that emotional and cognitive components are an important component of the identification of pain. As a result, although this may be more difficult with younger children, patients should be encouraged to complain about pain in order minimize potential tissue damage [7, 8].

In order to create an effective treatment plan to stop and prevent the development of pain, pediatricians must account for the child's age, the psychophysical condition of the child, as well as the characteristic of the pain. The first step in treating pain is recognizing it, then qualifying and quantifying it. The second step is finding the best pharmacological and/or non-pharmacological method to treat the pain, and as such, pain therapy requires a multidisciplinary and multimodal approach [9–12].

TYPES OF PAIN IN CHILDREN

Using pain duration as a basis, pain can be divided into two types: acute and chronic. Acute pain begins suddenly, is associated with a painful stimulus, and is short-lived. Chronic pain can be the result of inadequately treated acute pain or may be chronic from the outset. Chronic pain significantly impairs the quality of life.

Based on the pathophysiological mechanism of pain, pain is divided into nociceptive and neuropathic [13]. Nociceptive pain includes somatic and visceral pain. Somatic nociceptive pain is localized, constant, described as dull or sharp, worsens with movement, and is caused by tissue injury or inflammation. Visceral pain is caused by injury or inflammation of internal organs and can be constant if the pain

Received • Примљено: September 17, 2018
Revised • Ревизија: March 18, 2020
Accepted • Прихваћено: March 19, 2020
Online first: April 23, 2020

Correspondence to:
Ana VLAJKOVIĆ
University Children's Hospital
Tiršova 10
11000 Belgrade, Serbia
anavlajkovic1@gmail.com

originates from a solid organ, or intermittent in the form of cramps, or colic as a result of obstructions in hollow organs. Neuropathic pain is caused by injury, inflammation, or dysfunction of the central or peripheral nervous system [14]. Patients may have mixed pain consisting of somatic, visceral, and neuropathic pain all at the same time or each separately at different times.

Breakthrough pain is a transient strengthening of a constant or controlled pain. There are three types of breakthrough pain: incidental, spontaneous, and pain at the end of a dosing interval [15, 16].

Cancer pain can also be acute and chronic. Acute pain is developed as a consequence of a tumor mass invading surrounding anatomical structures, which leads to their damage, compression, rupture, inflammation, or as a result of diagnostic and therapeutic procedures. Chronic pain is the consequence of the development of the tumor mass itself, metastases in other parts of the body, as well as a result of diagnostic and therapeutic procedures [17, 18].

Until recently, it was thought that neonates did not feel pain or felt less pain compared to older children and adults, but new research within the last decade has concluded that they do feel pain. In fact, fetuses can begin to feel pain from the 26th week of development [19].

ASSESSMENT OF THE PAIN

There are three basic methods for assessing pain: self-reporting, physiological indicators, and by observing the child's behavior. Often, there is disagreement between objective estimates of the severity of the patient's difficulty and assessment, so the standard in assessing the existence of pain is to ask the child whether he/she feels pain (self-reporting) [20, 21]. In younger children, this can be difficult due to problems in understanding. Preschoolers may verbalize the intensity of pain. School-age children may verbalize pain and use an objective measurement of pain. Adolescents should be able to locate and verbalize pain levels.

The second method of assessing pain is to measure physiological reactions to pain, which can be tracked through indicators such as pulse, blood pressure, breathing, redness, paleness, and increased sweating [22, 23].

The third method is observing the behavior of the patient, although this is not a specific pain indicator [24]. The behavior of the child must be interpreted in accordance with its age. Infants who feel pain will cry, scream, refuse food, sleep poorly, make grimaces, or exhibit hypersensitivity or irritability. Facial expression measures appear most useful and specific in neonates. Toddlers may be verbally aggressive, cry, exhibit regressive behavior or withdraw, guard painful areas of body, or be unable to sleep. Preschoolers may attempt to push a stimulus away before it is applied, be uncooperative, see the pain as a punishment, cling to a parent or nurse, or may request emotional support. School-age children experience nightmares related to pain, have muscular rigidity, exhibit body stiffness, closed eyes, wrinkled forehead, as well as engage in the same behaviors listed for preschoolers and toddlers. Adolescents may deny pain in the presence of peers, have changes in sleep patterns and appetite, or display regressive behaviors in the presence of their family.

PAIN SCALES

The most used scales for newborns are the Premature Infant Pain Profile and the CRIES Postoperative Pain Scales [25, 26]. Between the ages of two months and seven years the FLACC (Face, Legs, Activity, Cry, Consolability) scale is used for postoperative pain assessment [27]. Well established self-report pain scales for preschoolers include the Poker Chip Scale, Wong-Baker Faces Scale, and Faces Pain Scale – Revised (FPS-R) [28]. School-age children and adolescents can usually use verbal scales or visual analog pain scales [29]. As for the assessment of pain for children with cognitive impairment, the Non-communicating Child's Pain Checklist – Postoperative Version is recommended [30, 31]. The greater the degree of cognitive impairment, the greater is the likelihood that the child feels less pain.

METHODS OF ANALGESIA

Methods of analgesia include non-pharmacological and pharmacological methods that include the use of non-opioid and opioid analgesics with the use of co-analgesics or adjuvants, as well as methods of regional anesthesia. Developmental differences in response to pain and analgesic efficacy should be taken into account when planning analgesia [32].

NON-PHARMACOLOGICAL METHODS

There is evidence that supports the use of psychological intervention for a variety of pain indications that include physiological, behavioral, and cognitive techniques aimed at reducing pain and pain-related distress through the modulation of thoughts, behaviors, and sensory information [32]. Non-pharmacological methods include various ways of distracting the child's attention through cognitive methods, emotional support, presence of the parents during painful procedures, massage therapy, acupuncture, as well as physical techniques that promote muscle relaxation, transcutaneous electrical nerve stimulation, or hypnosis [33, 34]. The methods listed here are incredibly helpful and are seldom harmful.

PHARMACOLOGICAL METHODS

In order to choose the appropriate medications and their doses, it is necessary to confirm that the child's organs are anatomically developed, although their organ function will not be fully developed until later on, as it takes three months for organs to reach maturity [35]. The most

Table 1. Non-opioid analgesics for the relief of pain in neonates, infants, and children according to WHO recommendations [32]

	Dose (oral route)			
Medicine	Neonates 0–29 days	Infants from 30 days to 3 months	Infants 3–12 months or children 1–12 years	Maximum daily dose
Paracetamol	5–10 mg/kg every 6–8 hours[a]	10 mg/kg every 4–6 hours[a]	10–15 mg/kg every 4–6 hours[a,b]	Neonates, infants, and children max. 4 doses/daily
Ibuprofen	/	/	5–10 mg/kg every 6–8 hours	Child: 40 mg/kg

[a]Children who are malnourished or in a poor nutritional state are more likely to be susceptible to toxicity at standard dose regimens due to reduced natural detoxifying glutathione enzyme;
[b]maximum of 1 g at a time

important factors to consider for the metabolism of drugs are immature liver enzymes and decreased renal function (reduced glomerular filtration) [36]. Glomerular filtration rate has a range of only ½ of adult values at birth, and tubular secretion rates are only 20% of adult capacities. There are also some significant differences in the structure and function of the child's body at birth when they have a higher percentage of body water and less fat compared with older children. Age-related differences in protein binding with drugs also exist. The effects of drugs may vary with age, and dosages must be changed to anticipate and avoid side effects [37].

Before administering analgesics, guidelines must be consulted and pediatricians must strive to achieve maximum efficacy with the chosen method of analgesia. According to the two-step scale of pain from the World Health Organization, the first stage of pain is mild, and it requires the administration of non-opioid analgesics like paracetamol or ibuprofen, with or without co-analgesics. The second stage of pain is moderate to severe, and opioid analgesics should be used with or without co-analgesics [38]. Drugs should be given according to a schedule, not on demand, because in practice this means that the child will not receive the medicine. The administration of the drug should try to be non-invasive, preferably given orally. Therapy must be individually adapted to each patient [38]. It is extremely important to monitor the child and its reaction to the medication at all times, and if necessary, make changes to the therapy.

Non-opioid analgesics are used in the first stage of pain, according to the World Health Organization. Non-steroid anti-inflammatory drugs like ibuprofen and paracetamol are used. These medications work by blocking cyclooxygenase, where ibuprofen drugs work peripherally, while paracetamol leads to the central blockage of enzymes [39].

Opioid analgesics are used in the second, more severe, stage of pain. They can be administered orally, subcutaneously, intravenously, with a continuous infusion, or a PCA (patient-controlled analgesia) pump [40]. The advantage of the PCA is that it eliminates high peaks and low troughs by allowing the patient to press the demand button when they begin to feel pain [41]. Opioid analgesics bind to opioid receptors in the central nervous system, but their use requires monitoring because depression of the respiratory center can occur. Cardiorespiratory monitoring and observation is recommended when opioids are administered to infants less than 2–3 months of age.

NON-OPIOID ANALGESICS

Paracetamol and ibuprofen are used to alleviate mild pain. For children up to three months of age, the only recommended drug for mild pain is paracetamol, while ibuprofen can be used with older infants. Routes for administration are oral (tablets, syrups), rectal (suppositories), or intravenous. Paracetamol is a well-tolerated drug and produces few side effects in the gastrointestinal tract, but there is a risk of hepatotoxicity and acute overdose [42, 43]. In addition, having an analgesic effect, ibuprofen also has an anti-inflammatory and antithrombotic effect. Like the entire NSAID group of drugs, there are significant adverse effects for the mucosa of the gastrointestinal tract when ibuprofen is used [44]. There is a plateau for the analgesic effect of these drugs, but not for their side effects.

OPIOID ANALGESICS

In cases of moderate to severe pain, there is a variety of opioid analgesics that can be used. Of opioid analgesics, morphine is always the medication of choice, while others are considered and used when the side effects of morphine begin to appear [45]. Morphine is dosed gradually until pain is alleviated and there is no maximal dose because the pain acts as an antidote for respiratory depression, unlike non-opioid analgesics (Tables 1–4). Dosages should be adjusted to the patient following his/her pain level indication. The range of effective doses is very wide among children and can differ significantly for one child at different times. Opioid rotation is defined as the practice of changing between different opioids in a set schedule to prevent potential adverse effects and limit dose escalation [46]. The oral route of administration is recommended for the use of opioid analgesics, while the intramuscular route of administration is very unpleasant for children and should be avoided.

When administering opiates, the risks of tolerance, addiction, and withdrawal syndrome must be taken into consideration [47]. Tolerance to opioids occurs when the body becomes accustomed to a certain dose and an increased dose is required to obtain the same effect. Addiction is the creation of psychological and physical dependence on a drug, creating an irresistible need to take the medication again, regardless of possible consequences. Withdrawal syndrome is characterized by symptoms like agitation, insomnia, tremors, gastrointestinal symptoms like nausea,

Table 2. Starting dosages for opioid analgesics for opioid-naive neonates according to WHO recommendations [32]

Medicine	Route of administration	Starting dose
Morphine	IV injection[a]	25–50 mcg/kg every 6 hours
	SC injection	
	IV infusion	Initial IV dose 25–50 mcg/kg, then 5–10 mcg/kg/hour 100 mcg/kg every 6 or 4 hrs
Fentanyl	IV injection[b]	1–2 mcg/kg every 2–4 hours[c]
	IV infusion[b]	Initial IV dose 1–2 mcg/kg, then 0.5–1 mcg/kg/hour

[a]Administer IV morphine slowly over at least 5 minutes;
[b]intravenous doses for neonates are based on acute pain management and sedation dosing information; lower doses are required for non-ventilated neonates;
[c]administer IV fentanyl slowly over 3–5 minutes

Table 3. Starting dosages for opioid analgesics in opioid-naive infants (1 month – 1 year) according to WHO recommendations [32]

Medicine	Route of administration	Starting dose
Morphine	Oral (immediate release)	80–200 mcg/kg every 4 hours
	IV injection[a]	1–6 months: 100 mcg/kg every 6 hours 6–12 months: 100 mcg/kg every 4 hours (max. 2.5 mg/dose)
	SC injection	
	IV infusion[a]	1–6 months: initial IV dose: 50 mcg/kg, then: 10–30 mcg/kg/hour 6–12 months: initial IV dose: 100–200 mcg/kg, then: 20–30 mcg/kg/hour
	SC infusion	1–3 months: 10 mcg/kg/hour 3–12 months: 20 mcg/kg/hour
Fentanyl[b]	IV injection	1–2 mcg/kg every 2–4 hours[c]
	IV infusion	Initial IV dose 1–2 mcg/kg[c], then 0.5–1 mcg/kg/hour
Oxycodone	Oral (immediate release)	50–125 mcg/kg every 4 hours

[a]Administer IV morphine slowly over at least 5 minutes;
[b]intravenous doses of fentanyl for infants are based on acute pain management and sedation dosing information;
[c]administer IV fentanyl slowly over 3–5 minutes

Table 4. Starting dosages for opioid analgesics in opioid-naive children (1–12 years) according to WHO recommendations [32]

Medicine	Route of administration	Starting dose
Morphine	Oral (immediate release)	1–2 years: 200–400 mcg/kg every 4 hours 2–12 years: 200–500 mcg/kg every 4 hours (max. 5 mg)
	Oral (prolonged release)	200–800 mcg/kg every 12 hrs
	IV injection[a]	1–2 years: 100 mcg/kg every 4 hours 2–12 years: 100–200 mcg/kg every 4 hours (max. 2.5 mg
	SC injection	
	IV infusion	Initial IV dose: 100–200mcg/kg[a], then 20–30 mcg/kg/hour
	SC infusion	20 mcg/kg/hour
Fentanyl	IV injection	1–2 mcg/kg[b], repeated every 30–60 minutes
	IV infusion	Initial IV dose 1–2 mcg/kg[b], then 1 mcg/kg/hour
Hydromorphone[c]	Oral (immediate release)	30–80 mcg/kg every 3–4 hrs (max. 2 mg/dose)
	IV injection[d]or SC injection	15 mcg/kg every 3–6 hours
Methadone[e]	Oral (immediate release)	100–200 mcg/kg every 4 hours for the first 2–3 doses, then every 6–12 hours (max 5 mg/dose initially)[f]
	IV injection[g] or SC injection	
Oxycodone	Oral (immediate release)	125–200 mcg/kg every 4 hours (max. 5 mg/dose)
	Oral (prolonged release)	5 mg every 12 hours

[a]Administer IV morphine slowly over at least 5 minutes;
[b]administer IV fentanyl slowly over 3–5 minutes;
[c]hydromorphone is a potent opioid and significant differences exist between oral and intravenous dosing; use extreme caution when converting from one route to another; when converting from parenteral hydromorphone to oral hydromorphone, doses may need to be titrated up to 5 times the IV dose;
[d]administer IV hydromorphone slowly over 2–3 minutes;
[e]due to the complex nature and wide interindividual variation in the pharmacokinetics of methadone, it should only be used by practitioners experienced with its use;
[f]methadone should initially be titrated like other strong opioids; the dosage may need to be reduced by 50% 2–3 days after the effective dose has been found to prevent adverse effects due to methadone accumulation; from then on, dosage increases should be performed at intervals of one week or more and with a maximum increase of 50%;
[g]administer IV methadone slowly over 3–5 minutes

vomiting, poor appetite, tachycardia, tachypnea, hypertension, and fever. Children who have been on opiates for a long time and at high dosages require gradual reduction of opiate use in order to prevent the development of addiction. If opioid therapy lasted for 7–14 days, the dose can be decreased by 10–20% of the original dose every 8 hours. In the case of a long-term therapy protocol, the dose should not be reduced more than 10–20% per week [38]. When opioid overdose occurs, central respiratory depression develops, which can lead to a coma. Naloxone can be administered to a patient to stop the immediate opioid overdose, but opioid addiction and the development of withdrawal syndrome cannot be cured by Naloxone, so further treatment will be needed to treat the addiction [48].

ADJUVANT CO-ANALGESICS

Co-analgesics have a primary purpose other than pain management, but they can be used in addition to analgesics to better control pain relief. Corticosteroids, bisphosphonates, antidepressants, anticonvulsants, and ketamine can be used as co-analgesics, but there are still no recommendations for their use in pediatric patients.

METHODS OF REGIONAL ANESTHESIA

The application of regional anesthesia in childhood depends on the physiological specifications of their age, as well as on the technical capabilities of the anesthesiologist [49]. The effect of the block is short-term, and for long-term effects, catheter techniques are used. The use of catheter techniques improves the control of postoperative pain, reduces the use of analgesics and opioids, postoperative

nausea and vomiting, time spent in the hospital, as well as costs, all of which improves the satisfaction of the patients and their families with the procedure [50].

CONCLUSION

The primary goal of treating terminally ill children of all ages is giving them life without pain. It is necessary to keep in mind that a child often cannot adequately interpret the pain he/she feels, so it is necessary to monitor the child at all times and adjust the therapy accordingly. Pain therapy in palliative care should always be multimodal and multidisciplinary because this will improve efficacy and minimize side effects.

Conflict of interest: None declared

REFERENCES

1. Armstrong GT, Liu Q, Yasui Y, Neglia JP, Leisenring W, Robison LL, et al. Late mortality among 5-year survivors of childhood cancer: a summary from the Childhood Cancer Survivor Study. J Clin Oncol. 2009;27(14):2328–38.
2. Bakula DM, Sharkey CM, Perez MN, Espeleta HC, Gamwell KL, Baudino M, et al. The Relationship Between Parent Distress and Child Quality of Life in Pediatric Cancer: A Meta-Analysis. J Pediatr Nurs. 2020;50:14–9.
3. Snaman JM, Kaye EC, Baker JN, Wolfe J. Pediatric palliative oncology: the state of the science and art of caring for children with cancer. Curr Opin Pediatr. 2018;30(1):40–8.
4. Nunes MDR, Nascimento LC, Fernandes AM, Batalha L, De Campos C, Gonçalves A, et al. Pain, sleep patterns and health-related quality of life in paediatric patients with cancer. Eur J Cancer Care (Engl). 2019;28(4):e13029.
5. Vervoort T, Karos K, Johnson D, Sütterlin S, Van Ryckeghem D. Parental emotion and pain control behaviour when faced with child's pain: the emotion regulatory role of parental pain-related attention-set shifting and heart rate variability. Pain. 2019;160(2):322–33.
6. Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. Br J Anaesth. 2019;123(2):e273–83.
7. Kaye EC, Gushue CA, DeMarsh S, Jerkins J, Sykes A, Lu Z, et al. Illness and end-of-life experiences of children with cancer who receive palliative care. Pediatr Blood Cancer. 2018;65(4):10.1002/pbc.26895.
8. Tutelman PR, Chambers CT, Urquhart R, Fernandez CV, Heathcote LC, Noel Melanie, et al. When "a headache is not just a headache": A qualitative examination of parent and child experiences of pain after childhood cancer. Psychooncology. 2019;28(9):1901–9.
9. Madi D, Clinton M. Pain and its Impact on the Functional Ability in Children Treated at the Children's Cancer Center of Lebanon. J Pediatr Nurs. 2018;39:e11–e20.
10. Forgeron PA, Stinson J. Fundamentals of chronic pain in children and young people. Part 2. Nurs Child Young People. 2014;26(9):31–6.
11. Fortier MA, Wahi A, Bruce C, Maurer EL, Stevenson R. Pain management at home in children with cancer: a daily diary study. Pediatr Blood Cancer. 2014;61(6):1029–33. Erratum in: Pediatr Blood Cancer. 2016 Jul;63(7):1316.
12. Simons LE, Sieberg CB, Conroy C, Randall ET, Shulman J, Borsook D, et al. Children With Chronic Pain: Response Trajectories After Intensive Pain Rehabilitation Treatment. J Pain. 2018;19(2):207–18.
13. Dunne FJ, Getachew H, Cullenbrooke F, Dunne C. Pain and pain syndromes. Br J Hosp Med (Lond). 2018;79(8):449–53.
14. Xu N, Wu MZ, Deng XT, Ma PC, Li ZH, Liang L, et al. Inhibition of YAP/TAZ Activity in Spinal Cord Suppresses Neuropathic Pain. J Neurosci. 2016;36(39):10128–40.
15. Bedard G, Davies A, McDonald R, Hawley P, Buchanan A, Popovic M, et al. Breakthrough cancer pain: a comparison of surveys with European and Canadian patients. Support Care Cancer. 2015;23(3):791–6.
16. Gonella S, Conti A, Campagna S. Breakthrough cancer pain: guida alla valutazione [Breakthrough cancer pain: A guide towards assessment]. Assist Inferm Ric. 2019;38(4):200–11.
17. Larue F, Colleau SM, Brasseur L, Cleeland CS. Multicentre study of cancer pain and its treatment in France. BMJ. 1995;310(6986):1034–7.
18. Fleisch J, Dahan A. Pijn bij kanker [Pain in cancer]. Ned Tijdschr Geneeskd. 2018;161:D1447.
19. Bellieni CV. Pain assessment in human fetus and infants. AAPS J. 2012;14(3):456–61.
20. Vlajković A, Vilotijević M, Polovina M. Assessment of the association between quality of life in patients with atrial fibrilation and cardiovascular outcomes during the one-year follow-up. Med Podml. 2017;68(3):8–16.
21. Landry BW, Fischer PR, Driscoll SW, Koch KM, Harbeck-Weber C, Mack KJ, et al. Managing Chronic Pain in Children and Adolescents: A Clinical Review. PM R. 2015;7(11 Suppl):S295–S315.
22. Olsen RB, Bruehl S, Nielsen CS, Rosseland LA, Eggen AE, Stubhaug A. Chronic pain and cardiovascular stress responses in a general population: the Tromsø Study. J Behav Med. 2014;37(6):1193–201.
23. Stone AL, Walker LS, Heathcote LC, Hernandez JM, Basch MC, Wilson AC, et al. Somatic Symptoms in Pediatric Patients With Chronic Pain: Proposed Clinical Reference Points for the Children's Somatic Symptoms Inventory (Formerly the Children's Somatization Inventory). J Pain. 2019;20(8):932–40.
24. Monina E, Falzetti G, Firetto V, Mariani L, Caputi CA. Behavioural evaluation in patients affected by chronic pain: a preliminary study. J Headache Pain. 2006;7(6):395–402.
25. Motta Gde C, Schardosim JM, Cunha ML. Neonatal Infant Pain Scale: Cross-Cultural Adaptation and Validation in Brazil. J Pain Symptom Manage. 2015;50(3):394–401.
26. Krechel SW, Bildner J. CRIES: a new neonatal postoperative pain measurement score. Initial testing of validity and reliability. Paediatr Anaesth. 1995;5(1):53–61.
27. Crellin DJ, Harrison D, Santamaria N, Babl FE. Systematic review of the Face, Legs, Activity, Cry and Consolability scale for assessing pain in infants and children: is it reliable, valid, and feasible for use? Pain. 2015;156(11):2132–51.
28. von Baeyer CL, Chambers CT, Forsyth SJ, Eisen S, Parker JA. Developmental data supporting simplification of self-report pain scales for preschool-age children. J Pain. 2013;14(10):1116–21.
29. Martins PC, Couto TE, Gama AC. Auditory-perceptual evaluation of the degree of vocal deviation: correlation between the Visual Analogue Scale and Numerical Scale. Codas. 2015;27(3):279–84.
30. Massaro M, Ronfani L, Ferrara G, Badina L, Giorgi R, D'Osualdo F, et al. A comparison of three scales for measuring pain in children with cognitive impairment. Acta Paediatr. 2014;103(11):e495–500.
31. Murgia M, Izzo R, Bettinelli A, Di Maggio C, De Angelis M, Mangone M, et al. Validity and reliability of Italian version of the Non-Communicating Children's Pain Checklist: revised version. Eur J Phys Rehabil Med. 2019;55(1):89–94.
32. Simić D, Mitrović M, Stević M, Simić I, Marjanović V, Budić I. Procedural pain management in children of all ages. Pain Medicine Journal. 2017;2(1):21–7.
33. Loh J, Gulati A. The use of transcutaneous electrical nerve stimulation (TENS) in a major cancer center for the treatment of severe cancer-related pain and associated disability. Pain Med. 2015;16(6):1204–10.
34. Song Y, Oh M, Park S, Park M, Kim K, Lee U, et al. The Methodological Quality of Systematic Reviews and Meta-Analyses on the Effectiveness of Non-pharmacological Cancer Pain Management. Pain Manag Nurs. 2015;16(5):781–91.
35. Strolin Benedetti M, Whomsley R, Baltes EL. Differences in absorption, distribution, metabolism and excretion of xenobiotics between the paediatric and adult populations. Expert Opin Drug MetabToxicol. 2005;1(3):447–71.
36. Strassburg CP, Strassburg A, Kneip S, Barut A, Tukey RH, Rodeck B, et al. Developmental aspects of human hepatic

drug glucuronidation in young children and adults. Gut. 2002;50(2):259–65.
37. Petrov-Bojičić I, Milojević I, Simić D, Stević M, Kalezić N. Fiziološke razlike između dece i odraslih. SJAIT. 2013;35(7–8):347–54.
38. World Health Organisation. WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses. Geneva, 2012.
39. Zamir Q, Nadeem A. Non-steroidal anti-inflammatory drugs vs. Paracetamol: drug availability, patients' preference and knowledge of toxicity. J Ayub Med Coll Abbottabad. 2016;28(4):746–9.
40. Simić D, Budić I, Simić I, Stanković Z, Milenović M, Stević M. Patient-controlled analgesia for infants and children. Pain Medicine Journal. 2017;2(3):19–24
41. Ocay DD, Otis A, Teles AR, Ferland CE. Safety of Patient-Controlled Analgesia After Surgery in Children And Adolescents: Concerns And Potential Solutions. Front Pediatr. 2018;6:336.
42. Chiew AL, Gluud C, Brok J, Buckley NA. Interventions for paracetamol (acetaminophen) overdose. Cochrane Database Syst Rev. 2018;2(2):CD003328.
43. Tong HY, Medrano N, Borobia AM, Ruiz JA, Martínez AM, Martín J, et al. Hepatotoxicity induced by acute and chronic paracetamol overdose in children: Where do we stand? World J Pediatr. 2017;13(1):76–83.
44. Bianciotto M, Chiappini E, Raffaldi I, Gabiano C, Tovo PA, Sollai S, et al. Italian Multicenter Study Group for Drug and Vaccine Safety in Children. Drug use and upper gastrointestinal complications in children: a case-control study. Arch Dis Child. 2013;98(3):218–21.
45. Sverrisdóttir E, Lund TM, Olesen AE, Drewes AM, Christrup LL, Kreilgaard M. A review of morphine and morphine-6-glucuronide's pharmacokinetic-pharmacodynamic relationships in experimental and clinical pain. Eur J Pharm Sci. 2015;74:45–62.
46. Kim HJ, Kim YS, Park SH. Opioid rotation versus combination for cancer patients with chronic uncontrolled pain: a randomized study. BMC Palliat Care. 2015;14:41.
47. Bhalla S, Andurkar SV, Gulati A. Neurobiology of opioid withdrawal: Role of the endothelin system. Life Sci. 2016;159:34–42.
48. Kerensky T, Walley AY. Opioid overdose prevention and naloxone rescue kits: what we know and what we don't know. Addict Sci Clin Pract. 2017;12(1):4.
49. Novaković D, Budić I, Simić D, Abašer N, Slavković A, Živanović D. Periferni nervni blokovi u pedijatrijskoj anesteziji. Srp Arh Celok Lek. 2009;137(9–10):497–501.
50. Simić I, Simić D, Stanković Z, Petrov I, Stević M, Dučić S. The use of perineural catheters in pediatric population. Pain Medicine Journal. 2017;2(3):7–11.

Аналгезија у палијативном збрињавању деце

Душица Симић[1,2], Ана Влајковић[1], Ивана Будић[3,4], Миодраг Миленовић[2,5], Марија Стевић[1,2]

[1]Универзитетска дечја клиника, Београд, Србија;
[2]Универзитет у Београду, Медицински факултет, Београд, Србија;
[3]Клинички центар Ниш, Центар за анестезиологију и реаниматологију, Ниш, Србија;
[4]Универзитет у Нишу, Медицински факултет, Ниш, Србија;
[5]Клинички центар Србије, Ургентни центар, Анестезија и интензивно лечење, Београд, Србија

САЖЕТАК

Услед све већег пораста броја деце оболеле од неизлечивих болести, велики значај у педијатријској медицини је палијативно збрињавање ове деце. Главни задатак палијативног збрињавања је ублажавање патње која произилази из психофизичког стања детета, а највећим делом из бола. Понекад је изузетно тешко препознати, квантификовати и квалификовати бол код педијатријских болесника, а то је управо прва фаза у проналажењу најбољег начина за ублажавање патње. Кључно је пронаћи најбољи начин за ублажавање или уклањање бола, али начин који ће како детету тако и родитељу пружити осећај потпуне контроле над болом.

У пракси су заступљене нефармаколошке и фармаколошке методе аналгезије. Фармаколошке методе укључују неопиоидне и опиоидне аналгетике, потом коаналгетике, као и методе регионалне анестезије.

Да бисмо на најбољи начин збринули ову децу, неопходно је да приступ буде индивидуалан, мултимодалан, мултидисциплинаран, и мора се посветити пажња сваком детаљу.

Кључне речи: бол; палијативно збрињавање; педијатријски болесници; аналгезија