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Maria Beatriz Bernardo Marques

Postoperative Pain Assessment Methods for Infants and Young Children: a Review

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Postoperative pain assessment methods for infants and young children: a review

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Postoperative pain assessment methods for infants and young children: a review

ORIENTADOR

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Dedico este trabalho às pessoas que mais contribuíram para o meu percurso académico.

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Postoperative pain assessment methods for infants and young children: a review.

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Abstract

Purpose: Pain assessment in pediatric postoperative setting has always been challenging, due to the lack of insight about pain mechanisms in newborns, infants and young children. Several research works about this subject were conducted over the years, and such studies contradict what was postulated for many years and demonstrate that infants do feel pain stimuli, even more so than older children or adults.

For this reason, it is important for health care providers to be familiar with appropriate pediatric pain assessment tools, accordingly to age, cognitive development and context of the pain.

Methods: This paper will focus on the diverse available scales and parameters used, as well as their advantages and limitations. Additionally, some recent developed technologies are briefly mentioned, some of which could translate a solution for this problem in the future.

Results: We still lack a gold standard for pain assessment in all clinical settings and pediatric age groups. Self-report, behavioral and physiological scales can be used for such purpose, although none of these methods has proven to be superior nor demonstrated excellent accuracy.

Conclusions: Further research is needed in order to find and validate an objective and easy to use pain assessment instrument that could become a gold standard for worldwide use.

The question about the best pain assessment method for infants and young children remains unanswered, being necessary to adapt the pain assessment process to each specific child and context.

Keywords: Pain, Assessment, Postoperative Period, Behavioral, Self-report, Physiological, Scales, Infants, Children.

Introduction

For a long period of time, it was believed that newborns and infants didn't feel as much pain as older children and adults, as it was thought their nervous system wasn't completely developed yet.

However, it is long known that peripheral nerve myelination is indeed concluded at the time of birth. Therefore, every newborn and, subsequently, infants and children, are capable of feeling pain and of establishing *motor responses* to these unpleasant stimuli [1]. On the contrary, the pain inhibitory pathways are undeveloped, which actually translates into a more exuberant pain sensation, due to the *overdrive* of the excitatory mechanisms. In other words, younger children may actually feel more pain in response to a lower-intensity noxious stimulus [2,3]. There are increased central effects, such as tissue damaging by noxious stimuli, which may lead to long time structural and functional *damage* in pain pathways, causing chronic pain and increased sensitivity to pain stimuli later in life [4]. Physiological responses, such as increased heart rate, blood pressure and oxygen demand, can happen at the time of the noxious stimuli and these may be detrimental to debilitated children, worsening postoperative outcomes [5] as well as psychological adverse effects, such as fear, anxiety and depression [6].

On the other hand, when pain is overestimated the child is exposed to overmedication, which can potentially cause adverse effects [7].

Postoperative pain management in children is still far from ideal. Reportedly, only 25% of children subjected to surgical procedures are pain free on the day of the intervention and 13% find themselves under severe pain [8]. Usually, there is a tendency for *oligoanalgesia*, and lack of an implemented guideline for pain assessment is often reported as the cause, along with ineffective pain measurement tools [9].

It has always been a challenge to effectively determine pain intensity in pediatric patients. When assessing pain in children, certain factors such as age, cognitive level, disabilities, type of pain and situation upon which the pain emerges must be considered [10]. Pain assessment is the first step to pain management. Currently, most health care providers base pain assessment on behavioral and self-report pain scales, although there is no evidence that a single scale proves to be indeed more accurate than others, giving way to worldwide discordance in actual clinical practice.

In order to provide optimal medical care to children, it is mandatory to improve the accuracy of pain assessment, by applying the best assessment tools to the patient at hand.

For the reasons mentioned above, the doubt about the best pain assessment method in infants and young children remains, being the aim of this paper to review the most commonly used pain assessment tools, as well as their advantages and limitations.

Self-Report Scales

Nowadays, self-report scales are the *gold standard* for pain assessment in children over six years old, whenever its application is possible [11].

These scales can be verbal or nonverbal. However, they always require a certain degree of cognition and communication skills, both being improved by increasing age and experience, as it depends on the child's development. As an example, facial expression scales are favored when dealing with younger children [12].

The most commonly used self-report scales are the Faces Pain Scales Revised (FPS-R), Numerical Rating Scales (NRS) and Visual Analogue Scales (VAS). *Table 1* summarizes the most commonly used self-repot scales.

Self-Report scales' application may actually be possible by the fourth year of age, but it depends greatly on the maturity of the child (both cognitive and emotional) and it can only be applied to verbal children who don't present a cognitive disability [13]. Therefore, it cannot be used as a clinical standard method for pain assessment at such young ages.

The Numerical Rating Scales (NRS) are also difficult to use with children younger than 8 years old. They demand the ability to understand numeracy and to have the skill to express oneself. Being able to count (in younger children) does not suffice, as it is also required an ability to understand quantitative significance of numbers, translating a higher level of cognitive development. Among these scales, the most commonly used is the NRS-11, scored from 0 to 10 [14]. It has also been postulated that children tend to provide a higher level of pain when using the NRS, in comparison to the VAS or the FPS-R.

The FPS-R, presents different facial expressions portraying various degrees of pain, by demonstrating different feelings, to which the children should identify themselves with (*figure 1*) [15]. This method doesn't demand such a refined cognitive development, which makes it more adequate to younger children [16]. Moreover, studies show that children favor these scales when compared to the VAS [17], while a study by Tovar supported the use of the FPS-R in children aged older than five, remaining the doubt about younger children and the best evaluation method [18].

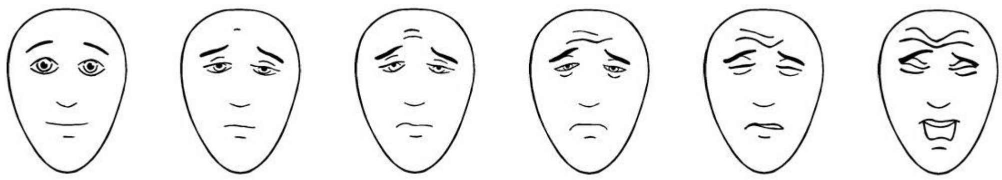

Figure 1 The Faces Pain Scale - Revised: scored from 0 to 10 (0-2-4-6-8-10) or from 0 to 5. The child must point to the face that shows how much pain they are feeling *[Copyright of the FPS-R is held by the International Association for the Study of Pain (IASP) ©2001. This material may be photocopied for non-commercial clinical, educational and research use, pending permission for journal publication at this date]*

VAS depicts a 10 cm line, representing a continuous pain dimension, either vertical or horizontal, in which the child must mark the point that corresponds to their pain. The ends of the line are the extreme limits of pain. The index of pain severity is given by the length in centimeters from the low extreme of the line to the patient's mark. They are often used in clinical practice and several studies have proven its validity and sensitivity for use in children as young as three years old [19].

When it comes to construct validity, VAS shows good to moderate correlation with other self-report pain measures, for instance with the FPS [20] and it is the most recommended of self-report scales for children aged four to six years old, being the vertical version the most suitable [21].

According to Birnie [11], the Numerical Rating Scale (NRS-11), the revised Faces Pain Scale (FPS-R) and the Color Analogue Scale (CAS) (a specific type of VAS, where 0.25 cm intervals are colored with a gradual color scheme from white to red, filling the 0 to 10 cm line [22], exhibited in *figure 2* [23]) are recommended for acute pain, showing better performance than the other analyzed self-report scales.

According to Baeyer [24], the revised Faces Pain Scale can be used for children as young as 4 years old, and the CAS starting from five years old.

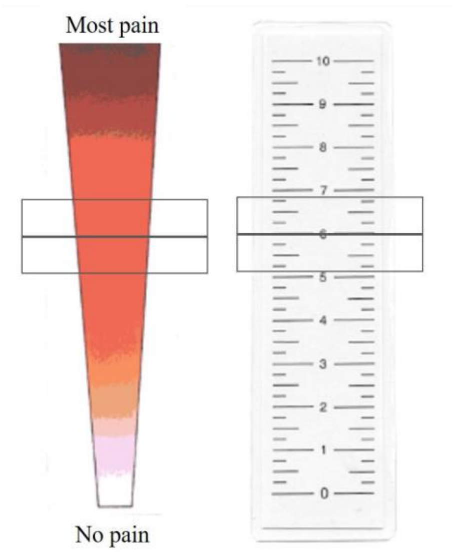

Figure 2 Color Analog Scale (CAS), with the permission of Kathy Speechly. It depicts a band, 10 cm of length, with a gradual color pattern, going from dark red to white [23]

However, these tools didn't provide strong results for their use in postoperative or chronic pain settings. Moreover, there wasn't any self-report scale reliable enough to measure pain in children younger than six years, which is also proved by further studies.

All the self-report scales share a common problem, which lies on the child's understanding of which level of pain they are feeling. Indeed, when facing the task of choosing a face, a number or a point in the crescendo line of pain, they are told which extremity is "no pain at all" and the other "the worst pain imaginable". What happens is that the amount of pain the children have experienced previously in their lives will determine the way they choose the level of the present noxious feeling. It is known, for instance, that *hospitalized children* describe pain differently from the others, for instance, they are more likely to cry and to describe pain in combination with fear and tension [25]. Therefore, it may not correctly reflect the true intensity of the pain.

Furthermore, younger children (below five years of age) show a tendency to choose the extremes of the scales. This happens due to the fact that they don't understand the scale as being gradual but dichotomous [26]. Although these scales are largely used in most clinical settings, their accuracy doesn't seem to be as good in post-operative and chronic pain situations. In fact, for these specific settings, there are only weak recommendations considering the use of self-report tools. Also, no self-report measure is ultimately recommended for children younger than six years of age [14], which makes the problem of accurate pain assessment in this age group stand.

Tool	Age group	Advantages	Disadvantages	Observations
Self Report Scales	**Recommended > 6 years**	Greater accuracy than the other tools. Quick assessment time.	Requires cognition and communication skills (not applicable to young or disbaled children)	Prefered pain assessment method
NRS	> 8 years	Simple and easy to use scale.	Demands higher cognitive skills. Only possible to use with older children.	Prefered tool for older children
FPS-R	> 5 years	Children reportedly favor this scale. More intuitive and easy to understand by younger children.	Not enough evidence for its use below the age of 5. Limited for children with cognitive or visual impairment.	Conforms closely to a linear interval scale
VAS	≥3 years	Potentially applicable to younger children. Continuous pain dimension.	Only good to moderate correlation with FPS	Vertical version is prefered

Table 1 Summary of Self Report Scales and their main advantages and disadvantages. NRS: Numerical Rating Scale, FPS-R: Faces Pain Scale revised, VAS: Visual Analog Scale

Behavioral scales

No behavioral pain assessment system has yet been universally accepted in clinical practice, due to contradictory findings about their specificity, sensitivity, reliability or validation. Another reason frequently pointed out, is the lack of *feasibility* in a hospital setting, given the long time usually required for patient examination, being too impracticable for regular assessments, as it is necessary in a postoperative setting. [27]. The expression of pain in children younger than six years old is essentially non-verbal and consists primarily in body movements and facial expressions

When there is the need to assess pain in younger age groups (newborns, infants and small children), self-report scales cannot be applied, due to the patient's immature cognitive and language development, as mentioned before. In these cases, other pain measures must be put into action, being behavioral scales, the most validated tools in clinical practice, at least for now. These scales are based on the measure of facial expressions, body movements as well as crying, among other features [28]. Most times, a combination of all these features is calculated, in order to achieve a better assessment.

Some researches show behavioral methods, most specifically, *facial expressions*, are the most reliable tools in the pediatric pain assessment field, having the highest sensitivity and sensibility in infants [29]. However, the specificity and sensitivity of these scales are disappointing, being influenced by other distress factors, such as fear, anxiety, hunger, or even physiological states, like fever [30].

Nowadays, it is possible to say that behavioral pain assessment methods are more accurate when applied to newborns and young infants. Regarding toddlers (mostly between two and four years old), this task appears to be more difficult, as their facial expressions and body movements are not so specific for pain (they can express fear or anxiety as well). As was concluded in the study by Goodenough [31], no facial expression scale could be proved to be superior to the others.

The most commonly used scales are the COMFORT and the FLACC scales [32], which will be described below and are summarized in *table 2*, along with some others of the most used behavioral scales.

The FLACC (Face, Legs, Activity, Cry, Consolability) scale is validated for children aged two months to seven years old, comprising five categories, as follows: facial expression, leg movement, activity, cry and consolability. It showed excellent correlation between observers and intraobservers [33]. Its usefulness furthers into cognitive impaired children, proving to be a reliable method in this population (mostly the revised FLACC [34]. It doesn't require a long observational time, lasting only up to five minutes [35].

The FLACC scale is one of the most widely used behavioral scales, although there is not enough evidence that allows recommendations for the application of this scale to all the contexts and age groups. It was designed in order to provide health care professionals with a simpler and quicker observational tool to evaluate pain in children. Therefore, it focuses on five behaviors, each scoring from 0 to 2, adding up to a maximum of 10 points.

The FLACC scale has proved to be a good measurement tool in a recent study, exhibiting excellent sensitivity (89.94% - 95%CI: 78.48-96.83%) and sensibility (87.82% - 95%CI: 78.6-95.23) [36].

The COMFORT Scale, on the other hand, is composed of six behavioral factors (alertness, level of agitation, body movement, muscle tone, facial tension, respiratory response) and two physiological parameters (heart rate and blood pressure). It is validated for the assessment of pain in children between newborns and three years old, in postoperative setting [37].

Surprisingly, the two most objective measures of the scale (heart rate and blood pressure) are the ones that showed lowest interrater correlation, as opposed to four subjective measures (alertness, calmness, respiratory response and movement), which exhibited the highest agreement levels [38]. This scale is especially useful to assess pain in sedated or unconscious children, from birth to adolescence, being recommended in such contexts [22].

In postoperative settings, children are often ventilated, sedated, which makes behavior assessment difficult. Although promising at first, Cury demonstrated that this scale proved insufficient to properly guide analgesic administration in children following heart surgery, suggesting the need to develop a more accurate tool [39]. There is also a new modified COMFORT scale, which has been developed, but still needs further studies to be validated [40].

The Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) is also validated for assessment of postoperative pain, in children from one to five years of age (some studies even recommend its application until 7 years old [41]). Judging six pain behaviors (Cry, facial expression, verbal expression, torso position, touch and leg position), it proved to have good sensitivity and sensibility, which, together with its simple and quick application, makes it a good assessment tool in this age group [42]. Moreover, it has great correlation with VAS score, as well as excellent inter and intraobserver reliability.

The Objective Pain Scale (OPS) can be used starting from the 18th month until the child is twelve years old. It was initially formulated based on six parameters, including blood pressure, crying, movement, agitation, posture and complaints (when the age is appropriate). However, the later developed modified OPS, omitted the blood pressure analysis and showed great reliability and validity [34].

The FLACC scale only accomplished moderate to good validity with Objective Pain Scale (OPS) and Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) [33].

The Behavioral Observational Pain Scale (BOPS) has been developed for children aged one to seven years old and it focuses on three specific behaviors: facial expression, verbalization and body position. A positive correlation between this scale and the CHEOPS was found, regarding construct validity, as well as a good interobserver reliability [43].

There is also the CRIES scale (crying, requires oxygen, increased vital signs, expression, sleeplessness) and it can be used from newborns to infants aged 6 months. This scale is valid until 72 hours post-surgery and exhibits excellent interobserver reliability [44].

The EVENDOL (*Evaluation Enfant Douleur*) has been validated to use in postoperative pain assessment of children since birth to seven years old, and can be used when self-reporting scales are not an option [45]. This method is not influenced by fever, fear or hunger and it comprises four behavioral features as well as one environmental factor.

It is also worth mentioning the CHIPPS scale (Children and Infants Postoperative Pain Scale), which comprises four items in its assessment: crying, facial expression, trunk's posture, legs' posture and motor restlessness, which of each can be scored from 0 to 2 points. The higher the CHIPPS score, the higher the level of pain the child is experiencing. A great advantage of this scale is the short time it takes to assess the score, an observation time of only fifteen seconds. It has been validated for pain assessment in the post-operative period for newborns, toddlers and young children (until five years of age) [46].

Among all the behavioral scales used at the present time, the EVENDOL and the CHIPPS show the widest array of applications and are reliable for use on children younger than 1 year of age. The CRIES scale can be used for newborns and infants up until 6 months old. However, its validity didn't prove to be as strong as EVENDOL's and CHIPPS' [37].

When it comes to pain assessment in cognitive impaired children, the task is even more challenging. Not only do they share the usual confounding factors as the other children, but they also add some new difficulties, due to cognitive disabilities. For this reason, special scales were developed, as a result of a poor analgesic management in this target population following surgery, which resulted in undertreated patients. Non-communicating Children's Pain Checklist Postoperative Version (NCCPC-PV), FLACC, revised FLACC and Individualized Numerical Rating Scales (INRS) can and should be used under these special circumstances [42].

Besides the physicians and caregivers' direct assessment using these pain scales, the future lies on video analysis of the children's facial expressions, thanks to machine learning algorithms, already put into practice, for instance, by Mansor [47] achieving 90.77% accuracy [12].

It is also important to recognize that behavioral pain scales are time consuming and require a good education on the subject, by the health care providers, a fact many times neglected in clinical practice [48].

A study by Slater [49] has concluded there can be cortical response to noxious stimuli without a change in facial expression or overall behavior. These lack of motor response to pain, may happen due to the immaturity of the neuronal motor circuit, which translates into an absence of muscle contraction. Therefore, even in the absence of a motor response, expressed by body movements or variation in face expression, there can be no certainty that the child is not under pain. This discovery represents a big limitation to the accuracy of behavioral scales.

Another *limitation* is related to the fact that younger children exhibit lower stimuli threshold for spinal motor responses, such as reflexes (withdrawing from a noxious stimulus) [50] but, when it comes to facial expressions and body movements, they present less variations, when compared to older children [51]. These findings suggest that the *emotional reaction* to pain develops later in life, while the sensory-motor response is visible right at the beginning of life, which makes it difficult to apply the same scale in different ages.

Tool	Age group	Advantages	Disadvantages	Observations
Behavioural Scales	**Recommended** **< 6 years**	Allow for a more reliable pain assessment in younger children.	Influenced by several distress factos. Impractible for regular assessments. Demands highly trained professionals.	Lack of an universally adopted method.
FLAAC	2 months to 7 years	Quick assessment time. Can be used with disabled children.	Lack of evidence to be applied to all contexts and age groups.	Analyses 5 behavior components.
COMFORT	Newborn to 3 years	Validated for postoperative settings. Suited for sedated or unconscious patients.	Accuracy not proved for conscious patients.	Comprises 6 behavioral and 2 physiological parameters.
CHEOPS	1 to 5 years	Validated for postoperative pain assessment. Simple and quick application.	Narrow age group applicability.	Composed of 6 behavior factos.
OPS	18 months to 12 years	Wide age range.	Assessed parameters are not very specific.	Combines physiological and behavioral factos.
BOPS	1 to 7 years	Showed a good correlation with CHEOPS. Easy and quick assessment.	Potentially more inaccurate than the FLAAC scale.	Focuses only on 3 behavior patterns (derived from FLAAC scale).
CRIES	Newborn to 6 months	Excellent interobserver reliability	Valid only up to 72h post-surgery. Very small age group applicability.	Validity not as strong comaring to EVENDOL and CHIPPS.
EVENDOL	Newborn to 7 years	Validated for postoperative settings. Not very influenced by distress factors.	Lack of satisfatory validation for children aged 2 to 6 months.	Evaluates 4 behavioral componets and 1 environmental factor.
CHIPPS	Newborn to 5 years	Short observation time needed.	Only validated for postoperative setting.	4 behavioral items.

Table 2 Summary of Behavioral Pain Assessment Scales and their main advantages and disadvantages. FLACC: Face, Legs, Activity, Cry, Consolability Scale, OPS: Objective Pain Scale, BOPS: Behavioral Observational Pain Scale, CRIES: Crying, Requires oxygen, Increased vital signs, Expression, Sleeplessness, EVENDOL: Evaluation Enfant Douleur, CHIPPS: Children and Infants Postoperative Pain Scale

Physiological Measures

Among the physiological parameters usually analyzed for pain measurement are heart rate, respiratory rate, transcutaneous oxygen levels and blood pressure. Because all of these factors can also change due to other causes of distress, and not necessarily noxious stimuli, there is not a single physiological measure able to determine accurately pain intensity in children [52] and several studies support the idea that physiological measures should be used in *combination* with other parameters, as they are not reliable enough for individual use [53].

Moreover, some studies also mention intracranial pressure, cerebral blood flow, palmar sweating, decrease in oxygen saturation and vagal tone, for instance, as physiological pain indicators. However, as mentioned before, they are *not specific* to painful stimuli and their sensibility is also lacking. They are greatly affected by several clinical conditions, as sepsis, hypoxemia or even fever. Therefore, they are not reliable enough to translate pain intensity [54].

Mainly based on physiological factors, the *Cardiac Analgesia Assessment Scale* (CAAS) comprises four indicators: pupillary size, heart rate, blood pressure and respiratory and motor response. This scale is consistent in reflecting pain over time and it reported to be a more consistent measure than VAS [55]. It is especially useful when evaluating an invasively ventilated patient subjected to high doses of sedatives and muscle relaxants, when motor responses are not exuberant.

On the other hand, bio factors, translating autonomic nervous system responses, such as ECG, photoplethysmography (PPG), electrodermal activity (EDA), galvanic skin response (GSR), surgical pleth index (SPI), pupillary dilating reflex (PDR) and skin temperature, for instance, have been studied for measuring pain in children during painful procedures, general anesthesia or postoperative period. Nevertheless, the results were disappointing, and it has been understood that using exclusively physiological factors to determine pain does not translate satisfactory accuracy. Therefore, they should be included in scales together with behavioral factors, producing a better outcome [56].

SPI, for instance, has been studied on its post-operative application. Although it shows a direct relation to pain during general anesthesia, these results don't seem as promising when the patient is awake [57]. PDR proved to be a more sensitive index of noxious stimulation than the commonly used variables of HR and arterial BP in anaesthetized children and it is also independent of age, which facilitates its use in clinical practice [58].

Infrared thermal imaging may be helpful in analyzing thermic variations in pain processing. Mostly regarding neuropathic pain, it can measure not only superficial (skin) temperatures, but also in-depth variations. This method has proven to obtain good results, combining normal thermographs with altered temperature patterns in patients under painful stimuli [59]. However, this study was not conducted on children and the results are not sufficient to estimate good performance for its use in this setting.

Regarding the *Analgesia Nociception Index* (ANI), contradictory studies exist. On one hand, Ledowski et al concluded it didn't perform as well as physiological parameters (blood pressure and heart rate) when measuring pain during a surgical procedure [60]. On the other hand, Boselli and Jeanne found a significant negative correlation between these two scales, when specifically assessing postoperative pain [61]. Meanwhile, Sabourdin concluded that the ANI might provide a more sensitive assessment of nociception in anesthetized children than hemodynamic parameters or skin conductance [62].

The ANI bases itself on calculating heart rate variability, through a continuous ECG analysis, which correlates with parasympathetic activity. It has shown good inverse correlation with NRS [63] and its interpretation is both easy and quick. Indeed, it is translated by a number (from 0 to 100, where 0 means absence of analgesia and 100 absence of pain), both as an average value for a period of time or as a instant measure [64].

A study by Funcke has shown promising results regarding the ANI, SPI and PDR, finding them highly sensitive and specific for pain assessment. Although this study was conducted in adults during general anesthesia, it implies a good correlation between these factors and noxious stimuli, findings that may be applied to children, also in postoperative settings [65].

Although the ANI already promoted good expectations, it also presented some limitations when dealing with infants and very young children, due to their differences in heart rate variability. For this reason, the Newborn Infant Parasympathetic Evaluation Index (NIPE) was developed [66].

However, limited research has been lead, and this new tool lacks yet validation to be implemented in clinical practice. Nevertheless, Faye et al found correlation between the NIPE and the *Échelle Douleur Inconfort Nouveauné* (EDIN), a scale for postoperative neonatal pain [67], which provides promising results that should lead to further studies.

Conclusions

As the most validated pain assessment tools cannot be applied to all age groups, alternatives to the self-report scales are necessary in order to improve health care in postoperative pediatric settings. Even though self-report scales are considered the gold standard for children over six years of age, in some cases their application is not possible, due to cognitive impairment or in sedated patients for instance, which compromises pain assessment even in older children.

Although behavioral scales are widely used, there is evidence about the absence of behavioral pain manifestation even when cortical pain pathways are activated, which translates into a lack of sensibility of behavioral measures. For this reason, a child scoring a low value on behavioral scales may not, indeed, be pain free. Furthermore, these scales lack universal validity, and require highly trained observers, being subjective and with high intra and interobserver variability, which represents a problem in terms of reliability.

In postoperative setting, where children may be under sedation and invasive ventilation, specific problems may arise (such as reduced muscular responses to pain), for which behavioral methods are not so accurate and should be used with care.

Physiological scales prove not to be reliable when used as a single assessment method. It is postulated, by the American Society of Pain Management, that a combination of behavioral and physiological features is beneficial.

There is not a unique observation method recommended for pain assessment across all ages and contexts. The lack of a global cut-off point from a pain scale for pain treatment puts the patients at risk for overmedication or undertreated pain, with severe consequences, as mentioned before, and it constitutes a great problem left unsolved in pediatric intensive care units all over the world.

Therefore, further research in this area is needed, due to the frequent inability to accurately assess pain in clinical practice in postoperative pediatric intensive care units and to be able to provide optimal analgesia to children in such settings.

Several studies are already underway, such as neuroimaging and machine learning algorithms to evaluate facial expressions, among others. It is also important to wait for more studies to validate recently developed methods, such as the ANI and NIPE, so that they can be properly implemented in clinical practice. Meanwhile, health care providers should be familiar with the different available tools and be informed about the recommendations for each age group and clinical setting.

References

1. Rose JB, Logan DE (2004) Pediatric pain assessment. In: Litman RS (ed) Pediatric Anesthesia. The Requisites in Anesthesiology, 1st edn. Philadelphia, pp 191–195.
2. Fitzgerald M, Howard RF (2002) The neurobiologic basis of paediatric pain. In: Zchecter NL, Berde CB, Yaster M (ed) Pain in Infants, Children and Adolescent. Baltimore, pp 19–42.
3. Fitzgeral M (2005) The development of nociceptive circuits. Nat Rev Neurosci 6(7): 507-520. https://doi.org/10.1038/nrn1701
4. Fitzgeral M, Beggs S (2001) The neurobiology of pain: developmental aspects. Neuroscientist 7(3): 246-257. https://doi.org/10.1177/107385840100700309
5. Anand KJ, Aranda JV, Berde CB, Buckman S, Capparelli EV, Carlo W, Hummel P, Johnston CC, Lantos J, Tutag-Lehr V, Lynn AM, Maxwell LG, Oberlander TF, Raju TN, Soriano SG, Taddio A, Walco GA (2006). Summary proceedings from the neonatal pain-control group. Pediatrics. 117(3 Pt 2): 9–22.
6. Linton, S. J. and W. S. Shaw (2011). "Impact of psychological factors in the experience of pain." Phys Ther 91(5): 700-711. https://doi.org/10.2522/ptj.20100330
7. Strassels, SA, (2014) Opioids in clinical practice. In: McGrath PJ, Stevens BJ, Walker SM, Zempsky WT (ed) Oxford Textbook of Paediatric Pain. Oxford University Press, Oxford, pp. 457–473.

8. Mather L, Mackie J (1984) The Incidence of Postoperative Pain in Children. Pain, 28(4): 328-329.
9. Karling, M. , Renström, M. and Ljungman, G (2002) Acute and postoperative pain in children: a Swedish nationwide survey. Acta Pædiatrica, 91(6): 660-666. doi:10.1111/j.1651-2227.2002.tb03298.x.
10. Chiaretti A, Pierri F, Valentini P, Russo I, Gargiullo L, Riccardi R (2013) Current practice and recent advances in pediatric pain management. Eur. Rev. Med. Pharmacol. Sci. 17(Suppl. 1): 112–126.
11. Birnie KA, Hundert AS, Lalloo C, Nguyen C, Stinson JN (2019) Recommendations for selection of self-report pain intensity measures in children and adolescents. Pain, 160(1): 5-18. doi:10.1097/j.pain.0000000000001377.
12. Subramaniam SD, Doss B, Chanderasekar LD, Madhavan A, Rosary AM (2018) Scope of physiological and behavioural pain assessment techniques in children – a review. *Healthcare Technology Letters* 5(4): 124-129, doi: 10.1049/htl.2017.0108.
13. McGrath PA, Seifert CE, Speechley KN et al (1996) A new analogue scale for assessing children’s pain: an initial validation study. Pain, 64(3): 435–443.
14. Gaffney A, McGrath P, Dick B (2003) Measuring pain in children: Developmental and instrument issues. In: Schechter N, Berde CB, Yaster M (ed) Pain in Infants, Children and Adolescents, 2nd edn. Philadelphia: Lippincott Williams & Wilkins, pp 128-41.
15. Hicks CL, Baeyer CL, Spafford PA, Korlaar IV, Goodenough B (2001) The Faces Pain Scale – Revised: Toward a common metric in pediatric pain measurement. Pain, 93(2): 173-183. doi:10.1016/s0304-3959(01)00314-1
16. Champion GD, Goodenough B, von Baeyer CL, Thomas W (1998) Measurement of pain by self-report. In: Finley GA, McGrath (ed) Measurement of Pain in Infants and Children. Seattle, pp 123-60.
17. Luffy R, Grove SK (2003) Examining the validity, reliability, and preference of three pediatric pain measurement tools in African American children. Pediatr Nurs 29(1):54-9.
18. Tovar C, von Baeyer CL, Wood C, Alibeu JP, Houfani M, Arvieux C (2010) Postoperative Self-Report of Pain in Children: Interscale Agreement, Response to Analgesic, and Preference for a Faces Scale and a Visual Analogue Scale. Pain Research and Management 15(3): 163-168, https://doi.org/10.1155/2010/475907.
19. Stinson JN, Kavanagh T, Yamada J, Gill N, Stevens B (2006) Systematic review of the psychometric properties, interpretability and feasibility of self-report pain intensity measures for use in clinical trials in children and adolescents. Pain, 125(1): 143-157. doi:10.1016/j.pain.2006.05.006.
20. Aradine CR, Beyer JE, Tompkins JM (1998) Children's pain perception before and after analgesia: a study of instrument construct validity and related issues. J Pediatr Nurs 3(1) 11-23.
21. Beltramini A, Milojevic K, Pateron D (2017) Pain Assessment in Newborns, Infants, and Children. Pediatric Annals 46(10): 387-395. doi:10.3928/19382359-20170921-03.
22. Bulloch B, Garcia-Filion P, Notricia D, Bryson M, Mcconahay T (2009) Reliability of the Color Analog Scale: Repeatability of Scores in Traumatic and Nontraumatic Injuries. Academic Emergency Medicine 16(5): 465-469. doi:10.1111/j.1553-2712.2009.00404.x
23. Mcgrath PA, Seifert CE, Speechley KN, Booth JC, Stitt L, Gibson MC (1996) A new analogue scale for assessing children’s pain: An initial validation study. Pain 64(3): 435-443. doi:10.1016/0304-3959(95)00171-9
24. Baeyer CL (2006) Children’s Self-Reports of Pain Intensity: Scale Selection, Limitations and Interpretation. Pain Research and Management 11(3): 157-162. doi:10.1155/2006/197616.
25. Savedra M, Gibbons P, Tesler M, Ward J, Wegner C (1982) How do children describe pain? A tentative assessment. Pain 14(2): 95-104. doi:10.1016/0304-3959(82)90091-4.

26. Chambers CT, Johnston C (2002) Developmental differences in children's use of rating scales. J Pediatr Psychol 27(1): 27-36.
27. Franck LS, Greenberg CS, Stevens B (2000) Pain assessment in infants and children. Pediatr Clin North Am; 47(3): 487–512.
28. Buttner W, Finke W (2000) Analysis of behavioural and physiological parameters for the assessment of postoperative analgesic demand in newborns, infants and young children: a comprehensive report on seven consecutive studies. Paediatr Anaesth 10(3): 303–318.
29. Craig KD, Whitfield MF, Grunau RV, Linton J, Hadjistavropoulos HD (1999) Pain in the preterm neonate: behavioural and physiological indices. Pain 52(3): 287–299.
30. Lamontagne LL, Hepworth JT, Salisbury MH (2001) Anxiety and postoperative pain in children who undergo major orthopedic surgery. Appl Nurs Res; 14(3): 119–124.
31. Goodenough TB, Perrott DA, Champion GD, Thomas W (2000) Painful pricks and prickle pains: is there a relation between children's ratings of venipuncture pain and parental assessments of usual reaction to other pains? Clin J Pain 16(2): 135–43.
32. Oakes, L (2011) Compact clinical guide to infant and child pain management. New York.
33. Suraseranivongse S, Santawat U, Kraiprasit K et al (2001) Cross-validation of a composite pain scale for preschool children within 24 h of surgery. Br J Anaesth 87(3): 400–405.
34. Voepel-Lewis T, Merkel S, Tait AR, Trzcinka A, Malviya S (2002) The reliability and validity of the Face, Legs, Activity, Cry, Consolability observational tool as a measure of pain in children with cognitive impairment. Anesth Analg. 95(5): 1224-1229.
35. Merkel SI, Voepel-Lewis T, Shayevitz JR et al 1997. The FLACC: a behavioral scale for scoring postoperative pain in young children. Pediatr Nurs 23(3): 293–297.
36. Ge X, Tao JR, Wang J, Pan SM, Wang YW (2015) Bayesian estimation on diagnostic performance of Face, Legs, Activity, Cry, and Consolability and Neonatal Infant Pain Scale for infant pain assessment in the absence of a gold standard. Paediatr Anaesth 25(8): 834–839.
37. Van Dijk M, De Boer J, Koot H, et al (2000) The reliability and validity of the COMFORT scale as a postoperative pain instrument in 0 to 3-year old infants. Pain 84(2-3): pp 367–377.
38. Ambuel B, Hamlett KW, Marx CM, Blumer JL (1992) Assessing Distress in Pediatric Intensive Care Environments: The COMFORT Scale. Journal of Pediatric Psychology, 17(1): 95-109. doi:10.1093/jpepsy/17.1.95.
39. Cury MR, Martinez FE, Carlotti AP (2012) Pain assessment in neonates and infants in the post-operative period following cardiac surgery. Postgraduate Medical Journal, 89(1048): 63-67. doi:10.1136/postgradmedj-2012-130808.
40. Hartrick CT, Kovan JP (2002) Pain assessment following general anesthesia using the Toddler-Preschooler Postoperative Pain Scale: a comparative study. J Clin Anesth 14(6): 411–415.
41. Ghai B, Makkar JK, Wig J (2008) Postoperative pain assessment in preverbal children and children with cognitive impairment. Paediatr Anesth, 18(6): 462-477. doi:10.1111/j.1460-9592.2008.02433.x.
42. McGrath PJ, Johnson G, Goodman JT, Dunn J, Chapman J (1985) CHEOPS: a behavioral scale rating postoperative pain in children. In: Fields HL, Dubner R, Cervero F (ed) Advances in Pain Research and Therapy. New York, pp 395-402.
43. Hesselgard K, Larsson S, Romner B, Stromblad L, Reinstrup P (2007) Validity and reliability of the Behavioural Observational Pain Scale for postoperative pain measurement in children 1-7 years of age. Pediatric Critical Care Medicine 8(2): 102-108. doi:10.1097/01.pcc.0000257098.32268.aa.

44. McNair C, Ballantyne M, Dionne K et al (2004) Postoperative pain assessment in the neonatal intensive care unit. Arch Dis Child Fetal Neonatal 89(6): 537–541.

45. Fournier-Charrière E, Tourniaire B, Carbajal R, et al (2012) EVENDOL, a new behavioral pain scale for children ages 0 to 7 years in the emergency department: design and validation. Pain 153(8): 1573-1582. doi:10.1016/j. pain.2012.02.024.

46. Büttner W, Finke W (2000). Analysis of behavioural and physiological parameters for the assessment of postoperative analgesic demand in newborns, infants and young children: A comprehensive report on seven consecutive studies. Paediatr Anesth 10(3): 303-318. doi:10.1046/j.1460-9592.2000.00530.

47. Mansor MN, Syam SHF, Rejab MN et al (2012) AR model for infant pain anxiety recognition using fuzzy k-NN'. Proc. Int. Symp. on Instrumentation and Measurement, Sensor Network and Automation (IMSNA) 2(1): 374–376.

48. Bandstra N, Chambers C (2008) Pain assessment in children. In: H. Breivik, M. Nicholas, W. Campbell, & T. Newton-John (ed) Clinical pain management second edition: Practice and procedures, Florida, pp. 447–461.

49. Slater R, Cantarella A, Franck L, Meek J, Fitzgerald M (2008) How Well Do Clinical Pain Assessment Tools Reflect Pain in Infants? PLoS Med 5(6): e129 doi:10.1371/journal.pmed.0050129.

50. Andrews K, Fitzgerald M (1994) The cutaneous withdrawal reflex in human neonates: sensitization, receptive fields, and the effects of contralateral stimulation. Pain 56(1): 95–101.

51. Johnston CC, Stevens B, Craig KD, Grunau RV (1993) Development changes in pain expression in premature, full term, two and four month-old infants. Pain 52(2): 201–228.

52. McGrath PJ, Unruh AM (1994) Measurement and assessment of paediatric pain. In: Wall PD, Melzack R (ed) Textbook of pain. Edinburgh, pp 303–313.

53. Sweet SD, McGrath PJ (1998) Physiological measures of pain. In: Finey GA, MacGrath PJ (ed) Measurement of Pain in Infants and Children. Seattle, pp 59-81.

54. Finley GA, McGrath PJ (1998) Measurement of Pain in Infants and Children (ed) Progress in Pain Research and Management, pp 59–82.

55. Suominen P, Caffin C, Linton S, McKinley D, Ragg P, Davie G, Eyres R (2004) The Cardiac Analgesic Assessment Scale (CAAS): a pain assessment tool for intubated and ventilated children after cardiac surgery. Pediatr Anesth, 14(4): 336–343.

56. McGrath PA, Gillespie J (2001) Pain assessment in children and adolescents, In: Turk DC, Melzack R(ed) Handbook of pain assessment. New York, pp. 97–118.

57. Thee C, Ilies C, Gruenewald M, Kleinschmidt A, Steinfath M, Bein B (2015) Reliability of the surgical pleth index for assessment of postoperative pain. Eur. J. Anaesthesiol, 32(1): 44–48.

58. Constant I, Nghe MC, Boudet L, Berniere J, Schrayer S, Seeman R, Murat I (2006) Reflex pupillary dilatation in response to skin incision and alfentanil in children anaesthetized with sevoflurane: a more sensitive measure of noxious stimulation than the commonly used variables. Br. J. Anaesth, 96(5): 614–619.

59. Frize M, Herry C, Scales N (2003) Processing thermal images to detect breast cancer and assess pain. Proc. IEEE/EMBS Region 8 Int. Conf. on Information Technology Applications in Biomedicine (ITAB), Birmingham, pp 234–237.

60. Ledowski T, Averhoff L, Tiong WS, Lee C (2013) Analgesia Nociception Index (ANI) to predict intraoperative haemodynamic changes: Results of a pilot investigation. Acta Anaesthesiologica Scandinavica, 58(1): 74-79. doi:10.1111/aas.12216.

61. Boselli E, Jeanne M (2014) Analgesia/nociception index for the assessment of acute postoperative pain. Br. J. Anaesth. 112(5): 936–937.

62. Sabourdin N, Arnaout M, Louvet N, Guye ML, Piana F, Constant I (2013) Pain monitoring in anesthetized children: first assessment of skin conductance and analgesia-nociception index at different infusion rates of remifentanil. Paediatr. Anaesth 23(2): 149–155.

63. Gerbershagen H, Rothaug J, Kalkman C, Meissner W (2011) Determination of moderate-to-severe postoperative pain on the numeric rating scale: A cut-off point analysis applying four different methods. British Journal of Anaesthesia 107(4): 619-626. doi:10.1093/bja/aer195.

64. Daccache G, Jeanne M, Fletcher D (2017) The Analgesia Nociception Index. Anesthesia & Analgesia, 125(1): 15-17. doi:10.1213/ane.0000000000002145.

65. Funcke S, Sauerlaender S, Pinnschmidt HO, Saugel B, Bremer K, Reuter DA, Nitzschke R (2017) Validation of Innovative Techniques for Monitoring Nociception during General Anesthesia. Anesthesiology, 127(2): 272-283. doi:10.1097/aln.0000000000001670.

66. Javorka K, Lehotska Z, Kozar M, Uheikova Z, Javorka M, Zibolen M (2017) Heart Rate variability in newborns. Physiol Res 66(2): 203-S214.

67. Faye PM, Jonckheere JD, Logier R, Kuissi E, Jeanne M, Rakza T, Storme L (2010) Newborn Infant Pain Assessment Using Heart Rate Variability Analysis. The Clinical Journal of Pain, 26(9): 777-782. doi:10.1097/ajp.0b013e3181ed1058.

Annexes

Publication Guidelines – Child's Nervous System, Springer

Types of papers

Review articles and invited papers

Review papers may be narrative or systematic and are subject to the peer review process. They should offer exhaustive information on a given subject. The Editor will invite experts in the various fields of the neurosciences to publish Invited papers, although unsolicited reviews may also be considered. The Abstract must not be structured and the text may be arranged freely. The contribution should not be signed by more than 7 authors, while the text should not exceed 4000 words. Up to 15 figures or tables and 70 references are allowed. Exceptions at the discretion of the Editor in Chief.

Title Page

The title page should include:
The name(s) of the author(s)
A concise and informative title
The affiliation(s) and address(es) of the author(s)
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Abstract

Please provide a structured abstract of 150 to 250 words which should be divided into the following sections:
Purpose (stating the main purposes and research question)
Methods
Results
Conclusions
Keywords: Please provide 4 to 6 keywords which can be used for indexing purposes.

Text Formatting

Manuscripts should be submitted in Word.
Use a normal, plain font (e.g., 10-point Times Roman) for text.
Use italics for emphasis.
Use the automatic page numbering function to number the pages.
Do not use field functions.
Use tab stops or other commands for indents, not the space bar.
Use the table function, not spreadsheets, to make tables

References

Citation

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1.Negotiation research spans many disciplines [3].
2. This result was later contradicted by Becker and Seligman [5].
3. This effect has been widely studied [1-3, 7].

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text. Do not use footnotes or endnotes as a substitute for a reference list. Reference list entries should be alphabetized by the last names of the first author of each work and numbered consecutively.

Tables

All tables are to be numbered using Arabic numerals.

Tables should always be cited in text in consecutive numerical order.

For each table, please supply a table caption (title) explaining the components of the table.

Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.

Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

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Figure captions begin with the term Fig. in bold type, followed by the figure number, also in bold type.

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