Pediatric Pain Management

Assessment and treatment of pain in pediatric patients.

Abstract

Pediatric patients experience pain which is more difficult to assess and treat relatively to adults. Evidence demonstrates that controlling pain in the pediatrics age period is beneficial, improving physiologic, behavioral, and hormonal outcomes. Multiple validated scoring systems exist to assess pain in pediatrics; however, there is no standardized or universal approach for pain management. Healthcare facilities should establish pediatrics pain control program. This review summaries a collection of pain assessment tools and management practices in different facilities. This systematic approach should decrease pediatric pain and poor outcomes as well as improve provider and parent satisfaction.

Keywords: Pain, Pain assessment, Pain management, Pediatric patients.

Introduction

According to the International Association for the Study of Pain (IASP) Pain is "an un-pleasant sensory and emotional experience associated with actual and potential tissue damage". Pain has also been defined as "existing whenever they say it does rather than whatever the experiencing person says" [1-4]. It is one of the most dreading and devastating symptom commonly propagated in people with advanced chronic conditions including cancer patients. Pediatric patients are the most under treated and present to hospital for pain compared to adults; because of the wrong belief that they neither suffer pain nor they remember painful experiences [5]. The quality of life experienced by the patient can greatly reduce, regardless of their basic diagnosis. Thus, if pain will be poorly managed, it can reflect the influence on family and careers causing different which may leads to increased rates of hospital admission [5,6]. Uncontrolled pain has also direct impact on health outcomes and more than a few effects on all areas of life. The emotional, cognitive, and behavioral components of pediatric patient are also important to assess pain and to simplify the management practices [7,8].

A long-term negative effect of untreated pain on pain sensitivity, immune functioning, neurophysiology, attitudes, and health care behavior are supported with numerous evidences. Health care professionals' who care for children are mainly responsible for abolishing or assuaging pain and suffering when possible [5,7,9]. The practice of pediatric pain treatment protocol has made great progress in the last decade with the development and validation of pain valuation tools specific to pediatric patients. Almost all the major children hospitals now have dedicated pain services to provide evaluation and immediate treatment of pain in any child [10,11].

In pediatric age, it is more difficult to assess and treat pain effectively relatively to adults. The lack of ability to notice pain, immaturity of remembering painful experiences and other reasons are the reflection of persistence of myths related to the infant's ability to perceive pain [12]. However, the treatment of pain in childhood is like the adult management practice which includes pharmacological and non-pharmacological interventions. On the other hand, it critically depends on an in-depth understand of the developmental and environmental factors that influence nociceptive processing, pain perception and the response to treatment during maturation from infancy to adolescence [13,14].

The practice of assessing pain and its management in pediatric patients can show a discrepancy based on the different countries and their respective health institutions. So, this review focused on the contemporary practice and new advances in pediatric pain assessment and its management.

Classification of Pain

Many classification systems are used to describe the different types of pain. The most common classification schemes refer to pain as acute or chronic; malignant or nonmalignant; and nociceptive or neuropathic [15]. Most studies are agreed with the following classification of pain (Table 1).

Table 1. *The general classification of pain in pediatrics [3,4,8,15-20]*

Category	Sub-classification	Description
Pathophysiological	Nociceptive pain	This type of pain arises as the tissue injury activates specific pain receptors named nociceptors, which are sensitive to noxious stimuli. These receptors' can respond to different stimulus and chemical substances released from tissues in response to oxygen deprivation, tissue disruption or inflammation. It can be **somatic** or **visceral** pain based on the site of the activated receptors.
	Neuropathic pain	This type of pain arises when the abnormal processing of sensory input recognized by the peripheral or central nervous system.
Etiologically	Non-malignant	It includes the pain due to chronic musculoskeletal pains, neuropathic pains, visceral pain (like distension of hollow viscera and colic pain) and chronic pain in some specific anemia. Rehabilitation care is there main treatment protocol.
	Malignant	This is the pain in potentially life-limiting diseases such as multiple sclerosis cancer, HIV/AIDS, end stage organ failure, amyotrophic lateral sclerosis, advanced chronic obstructive pulmonary disease, Parkinsonism and advanced congestive heart failure. These illnesses are indicating for similar pain treatment that emphases more on symptom control than function.
Based on duration	Acute	This is pain of recent onset and probable limited duration. It usually has an identifiable temporal and causal relationship to injury or disease. Most acute pain resolves as the body heals after injury.
	Chronic	It is the pain which lasts a long time mostly 6 months, which commonly persisting beyond the time of curing of an injury and may be without any clearly identifiable cause.
Based on location		When Pain is often classified by body site (e.g. on head, on the back or neck) or it can be the anatomic function of the affected tissue (e.g. vascular, rheumatic, myofascial, skeletal, and neurological). It does not provide a background to resolve pain, but it can be useful for differential diagnoses.

Assessment of Pain in Pediatrics

Pain is often referred to as the "fifth vital sign" and it should be assessed and recorded as often as other vital signs. The appropriate intervention of pain is planned based on the accurate valuation of pain. Organized and routine pain assessment by using the standardized and validated measures is accepted as a corner stone for effective pain management in patients, unrelatedly to the age or other conditions [21]. A study in Brazil suggests that consistent accomplishment of assessments of pain using ordinary scales, such as Face, Legs, Activity, Cry and Consolability score and other bodily parameters are mandatory to optimize pain management in pediatric intensive care units [22]. As pain is a subjective experience, individual self-reporting is the favorite method for assessing pain. However, when valid self-report is not available as in children who cannot communicate due to age or developmental status, the observational and behavioral assessment tools are acceptable substitutions [5,7,22].

The use of the pain management algorism on Stollery children's hospital shows significant improvement for assessment of pain in pediatrics. The pre and post analysis indicated in a staff (n=17) given that a feedback of 41.2% felt that the algorism improved their ability to assess and manage pain in children equally, 35% felt that it increased their capacity to communicate a child's pain with other health care team members, 52.9% felt that the algorism should be further applied on other units across the hospital [23]. Even though, the assessment of pain symptoms is easy in adults, selection of appropriate pain assessment tools should consider age, cognitive level and the presence of eventual disability, type of pain and the situation in which pain is occurring in children. Therefore, healthcare professionals need to be aware of their limitations in addition to trained in the use of pain assessment tools [7,24,25].

The assessment in Canadian pediatric teaching hospitals indicated out of 265 children, majority (63%) of them found with a minimum of one documented pain assessment tool, 30% of children had at least two assessment tools, 17% had 3-5 measurement tools and 16% had at least six assessments in 24 h of admission. Most (63%) of the children were find a different document of 666 pain assessment tools, with a median of three assessments per one child [14]. Parent, patient, as well as staff satisfaction is positively associated with accurate assessment of pain in addition to well improvement of pain management. Brief and well validated tools are available for the assessment of pain in non-specialist settings. Nevertheless, each tool cannot be broadly suggested for assessment of pain in all children and across all settings. Individual needs of the children lead to assess and re-evaluate of pain consistently as a mandatory in every situation. On top of that, ethnicity, language, and cultural factors should be under consideration as they may influence pain assessments and its expression [5,12,26].

Most formal and commonly used means of pediatric assessment tools for pain are available and categorized depending the pediatrics age.

Pain Assessment in Neonates

Neonates pain rating scale (NPR-S): Major guidelines indicate that the assessment of pain in neonates (term babies up to 4 weeks of age) had better be use the **C**rying, **R**equires oxygen for saturation above 95%, Increasing vital signs, Expression and Sleepless (CRIES) scale (Table 2) [2,24,27-30].

Several other pain scales have been designed for the objective assessment of neonatal pain, including the COMFORT ("behavior") score, pain assessment tool, scale for use in newborns, distress scale for ventilated newborns and infants. Although these assessments are validated as research tools, the mainstay of appropriate management includes the caregiver's awareness, knowledge of clinical situations where in pain occurs, and sensitivity to the necessity of preventing and controlling pain [31].

Assessment of pain in infants: On a study in Australia hospitals, Infants (1 month to approximately 4 years) were scored using the face, leg, activity, cancelability and cry (FLACC) measuring tool. Scoring should be done by staff after observing the infant for 1 min. Among two observers a reliability of FLACC was established in a total of 30 children in the post anesthetics care unit (PACU) (r=0.94). After analgesic administration, validity was established by demonstrating a proper decrease in FLACC scores. Correspondingly, a high degree of association was found between PACU nurse's global pain rating scale, FLACC scores, and with the objective scores of pains scale. This tool has been established in various settings and in diverse patient populations and finds that as reliable and valuable. It provides a simple background for computing pain behaviors in children who may not be able to put into words the incidence or severity of pain. Lastly, the constructed validity is supported by analgesic administration as the scores decreases significantly. Another recent studies have demonstrated that FLACC was the most chosen in terms of sensible qualities by clinicians at their respective institutions [27,29,32-35]. Although the tool can be used by clinicians, it is more effective with parent input to provide a description of 'baseline' behavior. This is supported by the findings of the Malvinas study, which suggested that the addition of unique descriptors allowed parents to augment the tool with individual behaviors unique to their children. In addition, for infants who show good comprehension and motor skills, this pain assessment tool can be used as an alternative [36]. The FLACC scale has 98% sensitivity and 88% specificity in assessing pain levels [34]. Therefore, those different studies concluded that FLACC scale is the most appropriate measurement tool for pain assessment in infants (Table 3).

Table 2. *Neonatal pain rating scale [27-29]*

Cries Pain Rating Scale			
	0	1	2
Crying	No	high pitched	inconsolable
Requires O_2 for sat >95%	No	<30%	>30%
Increased vital signs	HR and BP <or=pre-op	HR and BP; Increased <20% of pre-op	HR and BP; Increased >20% of pre-op
Expression	None	Grimace	Grimace/grunt
Sleepless	No	Wakes at frequent intervals	Constantly awake

Table 3. *FLACC assessment tool [27,29,32-35]*

FLACC Behavioral Pain Assessment Tool			
	0	**1**	**2**
Face	No particular expression or smile	Occasional grimace/frown withdrawn or disinterested	Frequent/constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless or tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry	Moans or Whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Cancelability	Content or relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Assessment of pain in older children:

Self-report: The single most reliable indicator of the existence and intensity of pain and any resultant distress is the patient's self -report. For older children, the use of a self-reporting scale can be helpful to staff and empowering to the patient [24]. A self-report of pain from a patient with limited verbal and cognitive skills may be a simple yes/no or other vocalizations or gestures, such as hand grasp or eye blink. When self-report is absent or limited, explain why self-report cannot be used and further investigation and observation are needed [4,28]. Myriad guidelines are coming together in using different self-report methods in assessing pain in older children such as the Visual Analogue Scale (VAS) (Figure 1) which is described by a horizontal line with "no pain" at the beginning to "worst possible pain" at the termination and patients draw a line to show their severity of pain. It has several benefits: it avoids imprecise descriptive terms, quick and simple to score, and offers many determining points. However, it can be difficult in post-operatively or in children with neural and psychological disorder as it needs a concentration and coordination [1,12,24,29]. Wong-Baker faces pain rating scale is the other self-report tool mainly used to assess acute pain. Expressed by six line-drawn faces range from no pain at one end to worst pain at the other end and assigns by number with word descriptors to each face to indicate the intensity of pain [11,37].

However, many studies take a type of self-report, face scale method for assessing pain in older children. Below is the Faces scale, currently used by the children's hospital at West Mead:

These faces show how much something can hurt. From no pain to very much pain pointing to the face by the patient him/herself to show how much he/she hurt to simplify pain assessment (Figure 2).

Generally, most institutions approved using the pain assessment tools as their basic instrument for diagnosis and management of the different type of pains encountered in pediatrics.

Management of Pain in Pediatrics

The management of pain in pediatrics is still misunderstood. Explicitly, neonates and infants are not managed for pain effectively, due to the misperception that they are not able to sense pain as adults [16,18]. American academy of pediatrics suggested that the lack of pain assessment and fears of adverse effects of analgesic medications including respiratory depression and addiction are the main barriers to the treatment of pain in children [9]. As the underlying disease is expected to advance a continuous adjustment of pain therapy is required. A study in Toronto hospitals shows that out of the total 265 children, 58.9% received a minimum of one documented intervention of pain management. Out of 66 children with recognized pain (mild, moderate or severe), 55 of them received an intervention for their pain [14]. It extends beyond pain relief, encompassing the patient's quality of life and ability to work productively and to enjoy recreation. Pain management is a joint responsibility among the members of the health care team. This includes addressing pain status of each patient daily on inpatient unit rounds or with each patient visit, consultation if pain treatment is ineffective, and discharge planning for continuing pain management needs [3,15,38].

Generally, on consideration of the above challenges Managements of pain in pediatrics encompass the use of pharmacological and non-pharmacological interventions to control the patient's identified pain.

Non-Pharmacological Interventions

Non-pharmacological measures should be favored as base line for both adults and children intervention of pain. in conjunction with pharmacological options to help lower levels of anxiety, pain and distress, the psychological comfort measures such as relaxation techniques and distraction as well as physical interventions including the use of massage repositioning or heat and/or cold compresses are useful Strategies [3,4,15,19,24,39]. According to the guidelines for clinical practice of the American pain society, pain education such as the interventions and options for pain relief during the pre-

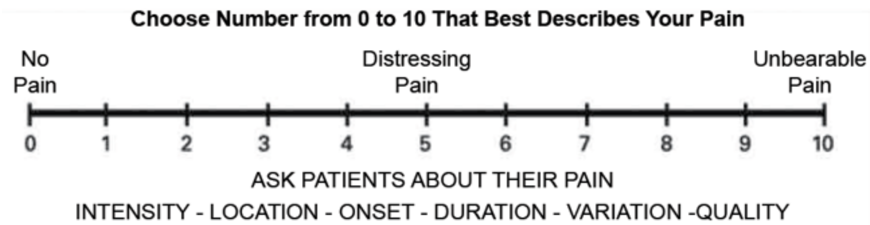

Figure 1. *Visual analogue scale [21,25]*

Figure 2. *Face scale assessment tool [27]*

surgical visit for patients and their families is important to develop their perception towards pain management [40]. A study by Lm Zhu et al. in Canadian pediatric teaching hospitals indicated that out of the 55 (83.3%) children who take pain management intervention, six of them received a physical treatment and five children received a psychological intervention [14].

General the following interventions are considered as non-pharmacological treatment of pain based on the recent and numerous studies.

Sucrose

Concentrated sucrose solutions (2 ml of 24% solution) may be used as a pain relief measure in preterm and term newborns up to 1 month of age as its analgesic effect lasts approximately 3 to 5 min. It promotes natural pain relief by activating endogenous opioids in contact with the oral mucosa. The effectiveness of sucrose solution enhanced by allowing the infant to continue sucking on a pacifier or breastfeed [41]. A randomized controlled clinical trial found that a single dose oral sucrose is effective and safe for minimizing physiological response to a painful stimulus and behavioral expressions in preterm infants [37]. The proposed hypothesis initiated from the endogenous opioid release can cause by taking oral 20-30% glucose through unknown mechanism. Therefore, Several studies recommended to considered oral sucrose as one of the non-pharmacological interventions of pain [30,31,37].

Distraction

Distraction involves engaging a child in a wide variety of pleasant activities that help focus attention on something other than pain and the anxiety. Examples of distraction activities are listening to music, singing a song, blowing bubbles, playing a game, watching television or a video, and focusing on a picture while counting. Guided imagery and breathing techniques may be forms of distraction for school-age children and adolescents [42]. A randomized control trial suggested that a virtual reality games were found to be effective distraction for children with acute burn injuries [43].

Breast Feeding

Breast milk is the best alternative to no intervention or to the use of sucrose in patient suffering with a single painful procedure. During venipunctures and heel stick procedures, neonates who were breastfed showed a substantial decrease in the variability of physiologic response as compared to other non-pharmacological interventions [30,39,44].

Skin-to-Skin Contact

Skin to skin contact demonstrated as effective non-pharmacological intervention in reduction of pain especially when used as adjunctive therapy to breastfeeding or other sweet solutions. Canadian medical association demonstrated that skin-to-skin contact principally Kangaroo care plays its own role in reducing and caring their children as the care giver and the baby have a direct physical contact [4,30].

Pharmacological Management of Pain

The current pharmacologic treatment protocol of pain for children is primarily extrapolated from adult intervention without any evidence of value in children [32]. High-quality pediatric experimental researches are needed to demonstrate efficacy and safety of analgesics for innumerable pain conditions in children to avoid continued use of analgesics empirically [8]. The development of age-appropriate pain assessment tools leads to improvement in the management of pain in children in the last two decades. Depending on the severity of pain, non-opioids and opioids are the most common analgesic agents used a “step-wise” approach in management of pain in both children and adults [19,24,28]. It is important that pain be reassessed soon after any pharmacological intervention to guide further interventions and to ensure the achievement of pain relief ensured by reassessment of pain regularly after any pharmacological intervention. Multimodal analgesia practice should be considered in patients with pain by concomitant use of the opioids, NSAIDs and other adjuvant therapies [14].

Generally, World Health Organization (WHO) demonstrated three-step analgesic ladder for treatment of pain (Figure 3) [45].

Non-Opioids Used for Management of Pain in Pediatrics

***Acetaminophen*:** It is the most frequently used pain-relieving agent in pediatric patients. It has lack of significant side effects and excellent safety profile with benefit to all levels of pain in children [39]. In common to the guideline of different institutions (Table 4), initially a loading dose of 30 mg/kg should be given, then 10-15 mg/kg every four to six hours as maintenance with maximum dose of 90 mg/kg/day for children. But, for term neonates of less than ten days 60 mg/kg and 45 mg/kg for premature infants. Neonates have a slower clearance rate so the drug must be given less frequently. Acetaminophen is manly used for mild to moderate pain independently and in combination of opioids for patients with severe pain for example acetaminophen with codeine) [24,37,45]. Rectal preparations of this analgesics used for infants and toddlers who are unable or unwilling to take orally. However, several studies have confirmed that rectal absorption comparatively inefficient and slow. Hepatotoxicity is not associated with single rectal doses of 30 to 45 mg/kg produced plasma concentrations that were generally in the effective range [46].

In relative to oral doses rectal doses are slowly decline in plasma concentrations. Based on a day pharmacokinetic study, the dosing interval for rectal dose extended to at least 6 h [29]. Acetaminophen toxicity can result when the

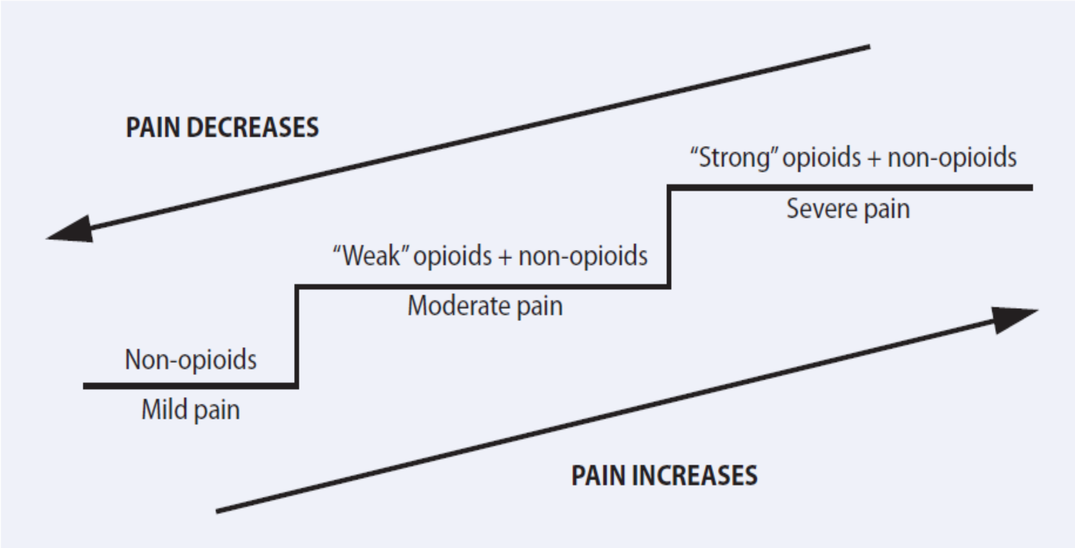

Figure 3. *The WHO analgesic ladder [15,24,45]*

Table 4. *Dosage guidelines for the common non-opioids used in the management of pain in pediatrics [12,48]*

Drug	Oral peak time	Usual Pediatric dosage	Usual Adult dosage	Comments
Acetaminophen	0.5–2 h	10–15 mg/kg every 4 h orally 20-40 mg every 6 h rectally	650–1000 mg every 4 h	Lacks the peripheral anti-inflammatory activity of other NSAIDs
Choline magnesium trisalicylate (Trilisate)	2 h	25 mg/kg every 12 h	1000–1500 mg every 12 h	Does not increase bleeding time like other NSAIDs; available as oral liquid
Ibuprofen	0.5 h	6–10 mg/kg every 6–8 h	200–400 mg every 4–6 h	Fewer GI effects than other non-selective NSAIDs
Naproxen	2–4 h	5 mg/kg every 12 h	250–500 mg every 6–8 h	Delayed-release tablets are not recommended for initial treatment of acute pain
Ketorolac	0.75–1 h	0.25–0.5 mg/kg IV or IM, every 6 h	30 mg IV loading dose, then 15–30 mg every 6 h	IV or IM use only in children less than 50 kg; should not be used for children with bleeding disorder or at risk for bleeding complications
Celecoxib	3-6 h	1-2 mg/kg	100-200 mg every 12 h	sparing of COX-1 reduces the risk of serious GI side effects and renal toxicity Also, no effects on platelet aggregation

toxic metabolite acetyl-p-benzoquinone-imine (NAPQI) is produced in high quantities. This may lead infants and children to hepatotoxicity. However, rodent study compared weanling to adult rats and suggested that infants produce high levels of sulfhydryl group of glutathione (GSH) to bind NAPQI as a part of hepatic growth and this may provide some protection against the hepatotoxicity produced by overdose [7].

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

NSAIDs are commonly used analgesics with less contraindication in relative to opioids. Mainly these are used as analgesic regimen in mild and moderate pain by preventing the conversion of arachidonic acid to prostaglandins and thromboxane. Prostaglandins are pro inflammatory mediators that sensitize nociceptors to increase afferent nociceptive signal to pain. Diclofenac, ketoprofen and ibuprofen commonly used NSAIDs in pediatric practice [7]. An observational study on the use of non-steroidal anti-inflammatory drugs (NSAIDs) was done in a sample of 51 patients in Italy resulted that ibuprofen was the most (68.6%) used NSAID followed by ketoprofen 9.8% and acetylsalicylic acid 7.8% for pain management of in pediatrics. The use of NSAIDs is now well established in clinical pain management [47].

This show to decrease morphine consumption and improve the quality of analgesia without increasing the incidence of side effects. These drugs are now a standard peri-operative analgesic agent in many pediatric institutions. Ibuprofen mainly used is available in oral suspension, infant drops, tablet and intravenous formulations. It is used to close patent ductus arteriosus (PDA) and as pain reliever in perioperative in neonates and children weighing greater than 7 kg. It is available as different dosage form such as oral suspensions, tablets, infant drops and intravenous preparations with a dose of 30 mg/kg in 3-4 divided doses. Besides, diclofenac is available like ibuprofen dosage forms with the recommended dose to children at a dose of 0.3–1 mg/kg with a maximum dose of 50 mg 3 times daily. However, ketorolac is not approved for use in children under 16 years of age. It only used for short term interventions of acute post-operative pain at a dose of 10-40 mg every 4-6 h for a maximum of 7 days [7,12,48].

Meta-analysis of studies comparing ibuprofen and diclofenac reveal that both drugs work well and that choosing between them is an issue of dose, safety and cost. An oral ibuprofen dose of 30-40 mg/kg per day appears to render equivalent analgesia to oral/rectal diclofenac 2-3 mg/kg per day. No difference in safety has been documented in these dose ranges [27]. Clinical pharmacology understanding for non-opioid analgesics is required for optimal administration. Because, for patients with post-operative pain, the minimal effective for analgesic dose and toxic dose is not known certainly. These doses may be higher or lower than the usual dose ranges recommended for the drug involved. On top of that, NSAIDs and acetylsalicylic acid have a potential toxicity, most commonly bleeding diathesis due to inhibition of platelet aggregation, renal impairment and gastro duodenopathy due to prostaglandin inhibition [12].

Opioids

Like adult population, management of acute pain in pediatric is also targeted with opioids. The analgesic effect comes through binding the mu-opioid receptor which is widely distributed at sites of peripheral inflammation and throughout the CNS. The variation in pharmacological response of opioids in pediatrics leads to adjustment based on clinical response, age and presence of side effects [7,27]. The indications for opioids include postoperative pain, pain due to sickle cell disease, and pain due to cancer [49]. A study in the Canadian teaching hospitals confirms that opioids are mainly used in severe pain and shows an improvement in all patients from the their experience of severe pain received an opioid treatment [14]. Most currently practiced guidelines in recent advanced pediatric hospitals are commonly used the following opioids in the management moderate to severe pain in pediatrics (Tables 5-7).

Morphine: It is the most commonly used phenanthrene derivative opioid in children with severe pain. Pharmacokinetics disparity (Table 5) exists for this drug between age groups. Because the plasma concentrations of morphine in neonates and infants display a prolonged half-lives (2-3fold) difference even with administration of constant infusion [7,12,27].

Codeine: It is a prodrug which activated to morphine by the enzyme cytochrome CYP2D6. However, the activity of this enzyme is highly variable and shows inter-individual variation which leads to a variation in analgesic effect of codeine [7,10]. Caucasian population are considered as **'Super Metabolizers'** whose approximately carry 10% of this variant. Therefore, even low dose codeine put them at risk of respiratory depression and excess sedation. Indeed, codeine is now infrequently prescribed in Australia [7,27].

Tramadol: It is structurally related to morphine which has a central analgesic effect by the formation of O-desmethyl-tramadol with a mu-opioid receptor affinity 200 times greater due to biotransformation in the liver by cytochrome P450(10). A dose of 50–100 mg every 4 h to a maximum of 400 mg per day is recommended to children between 12–18 years [7]. However, now a day's tramadol does not recommend for pediatrics under 12 years of age.

Fentanyl: Even though it is metabolized to inactive metabolites, fentanyl has 100 times more effect of analgesic than morphine. Commonly it used by the trans mucosal, intravenous, inhalational or intra-nasal and transdermal routes for procedural related pains in surgery due to its rapid onset and offset [7]. Case series and outcome studies of children not undergoing intubation suggest a higher frequency of opioid-induced respiratory depression among neonates than among infants over six months of age or older children [27]. In addition to the use of naloxone 10-20 mcg /kg for urgent situations, deep breath encouragement, awakening of the patient and withholding further doses may manage mild respiratory depression in children. Non-respiratory side effects of opioids, including nausea, ileus, itching, and urinary retention, are common among infants and children and may cause considerable distress. Many opioid side effects can be ameliorated by drug therapy directed at the side effect (e.g. antiemetic's to treat nausea and vomiting, antihistamines to treat itching and laxatives to treat constipation) [12,49].

Generally, WHO guideline recommends analgesic treatment in two steps according to the child's level of pain severity [15,24,48].

Table 5. *Pharmacokinetics of morphine [27]*

Age Group	Volume of Distribution (l/kg)	Clearance (ml/kg/min)	Half Life (Hours)
Preterm neonate	1.8-5.2	2.7-9.6	7.4-10.6
Term neonate	2.9-3.4	2.3-20	6.7-13.9
1-8 Years	1.4-3.1	6.2-56.2	0.8-1.2
Adult	1.1-2.1	Dec 34	1.4-3

Table 6. *Dose administration of morphine [7,12]*

Age	Appropriate Initial Dose
1-6 Month	50-150 μg/Kg every 4 h
6 Month-12 years	100-300 μg/Kg every 4 h
12-18 years	3-20 mg every 4 h

Table 7. *Opioids commonly used in pediatric pain management [12,50,51]*

Drugs	Usual Recommended Starting Dose		Comments
	Oral	*Parenteral*	
Morphine	0.3 mg/kg every 3–4 h	0.1 mg/kg every 3–4 h	Used as a standard of comparison for all opioid drugs
Codeine	0.5–1 mg every 3–4 h	Not recommended	Codeine is a pro-drug and not all patients convert it to an active form to achieve analgesia
Oxycodone	0.1–0.2 mg/kg every 3–4 h	Not recommended	Use as first line therapy for severe pain
Methadone	0.2 mg/kg every 4–8 h	0.1 mg/kg every 4–8 h	0.1mg/kg commonly used for acute pain 0.2-0.4 mg/kg commonly used for chronic pain
Fentanyl	5–15 mcg/kg Oralet	1 mcg/kg every 1–2 h	The Oralet is not widely used because of nausea and vomiting side effects

Indication Based on Pain Intensity

- Stage 1 – Non-opioid +/- adjuvant agent for mild pain
- Stage 2 – Opioid +/- non-opioid +/- adjuvant agent. For moderate to severe pain or pain uncontrolled after Step 1.

Common Analgesic Adjuvant

When a drug has a primary indication other than pain but is analgesic in some conditions it can be describe as adjuvant analgesic. Such adjuvants mainly used for the treatment of non-malignant pain in combined with primary analgesics to improve the outcome and to maintain the balance between relief and side effect [12]. Moreover, adjuvants can provide independent analgesic activity and treat concurrent symptoms that exacerbate pain for specific types of pain. The most commonly used adjuvants such as anti-depressants (amitriptyline), topical and local anesthetics and anticonvulsants (e.g. gabapentin and pregabaline) for neuropathic pain, steroids in edema induced pains, bisphosphonates and radiation therapy for metastases bone pain, neuroleptics for pain associated with anxiety, restlessness or nausea) [7,27,52].

Conclusion

In summary, numerous clinical practice guidelines and policy statements have been published in the last 10 years about pediatric pain. These publications are valuable resources for physical therapists and other health care providers who serve infants, children, and adolescents who have, or are at risk for, pain resulting from diverse etiologies. Improved management is contingent on valid and reliable measurement of pain. Fortunately, there are many excellent pediatric pain measures. Selection of appropriate measures requires an understanding of pain, measurement, and child development. Because, measurement of pain in infants, young children, and children with disabilities who are unable to self-report is particularly challenging and merits increased attention. These assessment tools have a basic benefit to the health care providers who are involved in pediatric health management to control the pain through non-pharmacological and pharmacological interventions. On top of that, pediatric institutions are well positioned to support and implement policy initiatives to improve the identification and management of pediatric pain and to contribute new knowledge through research.

Recommendations

An appropriate pain assessment measurements and techniques are needed to manage pain in pediatric patients and should be applied in every pediatric health care institution. Firstly, high possible standard of pain care for all patients should be provided through a multi modal (non-pharmacological, pharmacological and adjuvants) approach. Secondly, pediatric centers collaboration will be necessary to share the standard treatment protocol. Finally, even though the incidence of pain in children is like that of adults, clinicians should have considered the distinctiveness of children. The Cooperation of the caregivers and families are essential for successful pain assessment and its intervention in pediatric patients.

A Mind–Body Approach to Pediatric Pain Management

Abstract: Pain is a significant public health problem that affects all populations and has significant financial, physical and psychological impact. Opioid medications, once the mainstay of pain therapy across the spectrum, can be associated with significant morbidity and mortality. Centers for Disease and Control (CDC) guidelines recommend that non-opioid pain medications are preferred for chronic pain outside of certain indications (cancer, palliative and end of life care). Mindfulness, hypnosis, acupuncture and yoga are four examples of mind–body techniques that are often used in the adult population for pain and symptom management. In addition to providing significant pain relief, several studies have reported reduced use of opioid medications when mind–body therapies are implemented. Mind–body medicine is another approach that can be used in children with both acute and chronic pain to improve pain management and quality of life.

Keywords: mind–body medicine; pain management; pediatrics; acupuncture; yoga; meditation; hypnosis

1. Introduction

Pain is a significant public health problem leading to lost days of school and increased use of the healthcare system. Pain affects all populations and can significantly impact quality of life [1]. Over 11 million children have special health care needs and about 60% of them have difficulty participating in any activity [2]. In one cross-sectional study of pain prevalence in a pediatric hospital, the authors found that out of 241 patients, 27% had pain at the time of admission and 77% experienced pain at some point during their admission; what is more, pain medication was found to be single-agent and administered irregularly [3].

In recent years, opioid diversion, as well as the overuse and over prescription of opioid medications, have come to the forefront as a significant public health concern. Integrative medicine uses a patient centered approach to combine conventional medicine with evidence-based complementary approaches. Integrative therapies such as mind–body medicine can provide a non-opioid and nontoxic approach to pain management across the spectrum. Even in the case of end-of-life care [4,5], integrative and mind–body therapies are recommended [4,5]. For example, the Hospice and Palliative Nurses Association's most recent position statement supports and encourages the competent practice of complementary therapies for the purpose of promoting holistic end-of-life-care.

2. The Problem

2.1. What Is Pain

Pain can be defined as an unpleasant sensation. In some cases, pain is a warning sign of actual or potential tissue damage. However, dysregulation of the nervous system can also lead to a pain sensation when there is no present danger [6,7]. In addition to the physical sensation, pain behaviors are also influenced by pain perception. In a recent randomized control trial, pain sensitivity was assessed in over 700 adult patients with major depression. It was found that those suffering from major depression had higher pain sensitivity even after adjusting for factors such as poor sleep and physical inactivity [8]. Severity of anxiety also predicted decreased pain threshold.

Chronic pain is known to be associated with changes in not only brain function, but also in brain structure. In 2013, researchers demonstrated that the brain areas that were activated in acute low back pain for example were limited to regions involving acute pain; in the chronic pain group, activity was found in the emotion-related circuitry of the brain [9].

Pain perception and experience in the pediatric population is complex and multi-faceted, including but not limited to the nidus of pain itself, the fear of pain, previously developed pain memories, and familial influence. Acute pain is usually classified as pain lasting less than three months with a sudden onset that is often related to tissue damage. When considering the development of chronic pain in pediatrics, typically defined as pain persisting beyond three months or beyond the expected duration of healing, a fear-avoidance response can emerge, leading to a self-fulfilling cycle made up of pain, emotional distress, and functional disability [10]. In pediatrics, there is also an added complexity when considering developmental stage and parental influence. Not only do parents often have to serve as the surrogate communicator for the patient, parents own magnification, rumination, and anxiety surrounding pain influences the child and vice versa, leading to increased pain sensitivity and fear-avoidance behaviors [11]. It is clear that pain is not as simple as a noxious stimulus to an extremity that sends a danger signal to the brain.

2.2. The Opioid Crisis

Increases in opioid prescriptions have been noted over the past decade [12–14]. The opioid overdose and death rates have also been noted to increase [15–20]. 2016 Centers for Disease and Control (CDC) guidelines state that non-opioid therapy is preferred for chronic pain outside of active cancer, palliative and end-of-life care in patients over the age of 18 years. Inappropriate medication use and dosing can lead to death and disability [15–20]. At times, significant morbidity can result even when recommended dosage ranges are used [15–20]. For example, deaths have been described with the use of codeine despite dosages prescribed in the recommended range. In the case of codeine, the prodrug must be converted into morphine in the liver via the cytochrome P450 2D6 system and drug over or under conversion may be the result of genetic variation [21]. Furthermore, tolerance, withdrawal, and dependence present a problem even in the pediatric population and the neuropsychological effects of opioids may also be a cause for concern [22–25]. Opioid medications can play an important role in the treatment of pain; however, a pain management plan is not complete without including mind–body therapies.

2.3. Pain in Pediatrics

In pediatrics, pain, both acute and chronic, is often under-recognized and under-treated [26]. Studies have shown that up to 40% of children experience pain at least weekly, and conservative estimates say chronic pain affects 20% to 35% of children and adolescents around the globe [27]. Despite this significant prevalence, pain often goes under-addressed. A large-scale study involving eight pediatric hospitals observed inadequate pain assessment and management for patients undergoing painful procedures, reporting that less than one-third of patients had documentation of one or more pain management interventions [28]. When pain becomes chronic, significant physical and psychological tolls are experienced by both the patient and their families. Often the pain itself continues into adulthood, with 17% of adult chronic pain patients reporting a history of chronic pain in childhood/adolescence [29]. In addition, patients with chronic pain are at increased risk for several comorbidities, including many psychiatric disorders, hyperactivity disorders, social disability, and educational/occupational disability [10]. This patient population also has increased use of medical services, with healthcare costs for children with moderate to severe chronic pain averaging 19.5 billion annually [30]. Despite approximately 1.7 million children affected by chronic pain in the US alone with approximately 20% of cases having developed from acute post-operative pain, assessment and management of pain in pediatrics continues to be a challenge [26,31]. Mind–body medicine can provide a different approach. The mind–body approach is one in which the strengths of the patient and family are considered. In addition, this approach focuses on designing a treatment plan that is efficacious and minimizes the need for opioid medications. Mind–body remains a relatively novel approach in medicine. Although most of the current literature focuses on adult populations and on the more conventional psychological therapies (e.g.; cognitive behavioral therapy and dialectical behavioral therapy) that share similar inherent characteristics with mind–body approaches [32–34], there is a growing body of evidence that supports other mind–body therapies as effective and practical treatment approaches in pediatrics [35–39], particularly in the symptomatic treatment of cancer [4,40–45].

3. The Mind–Body Approach to Pain

3.1. The Use of Mind–Body Medicine in Pain Management

The American Academy of Pediatrics' clinical report on Mind–Body Therapies in Children and Youth describes mind–body therapies as those that focus on the interaction between the mind and the body, with the intent to use the mind to influence physical functions and directly affect health [46]. Mind–body therapies show promise as adjunct and at times primary treatment for pain in children and adults, and can be used across the spectrum. For example, diaphragmatic breathing stimulates the vagus nerve and promotes the relaxation response. The vagus nerve, an essential component of the autonomic nervous system, affects many of the body's internal organs including: the heart, lungs, liver, spleen, kidneys and gastrointestinal tract. As with many therapies, a development-based approach is essential. Teens can use complex imagery, while younger children can be taught diaphragmatic breathing techniques with simple imagery, such as blowing a balloon or blowing out candles. A toddler can be encouraged to engage in diaphragmatic breathing with the use of bubbles or pin wheels. For infants or children with severe cognitive disabilities, rocking and rhythmic womb or heartbeat sounds are techniques that can encourage diaphragmatic breathing.

These techniques are well tolerated in children [36,44,47,48] and can be used in a developmentally appropriate manner to serve as adjunct or primary pain management [47,48]. Furthermore, a reduction in opioid use may be seen. One study demonstrated a greater than 60% reduction of opioid-like medication usage following routine surgery when acupuncture was used [49–51]. Although more research is needed in the pediatric population, given the low risk and low cost of many of these techniques [52–54] for patients and potentially for insurance companies as well, their use is encouraged to enhance symptom management whenever feasible. In the next section, we give an overview of selected mind–body therapies and their function and applications in the management of pain in the pediatric population.

3.2. Selected Mind–Body Approaches

3.2.1. Meditation and Mindfulness

Over the past few decades, mindfulness has emerged as a fundamental component of numerous therapies and interventions for a wide spectrum of clinical aliments [55]. Mindfulness, described as "the awareness that emerges through paying attention on purpose, in the present moment, and non-judgmentally to the unfolding of experience moment by moment", is a meditation practice with ancient Buddhist origins that focuses on experiencing the present moment unobstructed by bias or judgmental thinking in an effort to improve cognitive and emotional well-being [56]. One such application of mindfulness is Kabat Zinn's Mindfulness-Based Stress Reduction (MBSR), a group intervention first introduced in 1990 that focuses on mindfulness meditation training as a complimentary therapy to the standard medical treatment of chronic pain and illness [57–64]. Research has suggested that mindfulness can improve symptoms associated with medical illnesses and increase quality of life [65]. From a neuroscientific perspective, magnetic resonance imaging (MRI) and functional magnetic resonance imaging (fMRI) studies have been conducted in hopes of identifying the neural mechanisms that are responsible for the efficacy of mindfulness meditation in pain relief [66–73]. In one study, thirteen skilled Zen mediators, each having had a minimum of 1000 hours of meditation experience, were recruited and experimentally exposed to pain via thermal stimuli while in an MRI [70]. During exposure to pain, the meditators exhibited increased brain activation in the insula, thalamus, and midcingulate cortex; areas associated with the sensory aspect of pain. Additionally, decreases in brain activity were observed within the hippocampus, amygdala, and caudate; areas responsible for the recollection, emotion, and appraisal components of pain, respectively. The authors concluded that the participants were completely aware of the sensation of pain but were able to inhibit the appraisal and emotional responses of pain. In other words, changes in the perception of pain were facilitated through the cognitive and affective components of the pain matrix rather than through the sensory properties of pain. Furthermore, the differences in brain activity were found to be inversely proportional to meditation skill level, establishing a correlation that supports the authors' hypothesis in regards to meditation's therapeutic effect on pain. As for neurophysiological findings, structural MRI results overlapped with the fMRI results: meditators were found to have thicker grey-matter in the same pain-related regions of the brain where changes in functional activity were observed [66,68,69].

In terms of overall clinical outcome research, controlled trials of adults suffering from various forms of chronic pain (chronic low back pain, chronic headache/migraine, chronic neck pain, arthritis, cancer, and fibromyalgia) have indeed demonstrated improved pain ratings in regards to multiple dimensions of pain including intensity, acceptance, functional limitations, quality of life, and psychological well-being [62]. Nonetheless, mindfulness as it relates to pain in children has not been extensively studied and although mindfulness meditation has shown to be beneficial in classroom and school settings for improving psychological distress [74–77], more research is required in order to determine whether the same effects can be translated in children and pediatric medicine.

3.2.2. Hypnosis

Hypnosis as a form of therapy has a long history and has been widely used across various disciplines of health care. While the current research establishes hypnosis as a beneficial treatment for the management of pain in regards to both acute medical conditions, such as trauma and post-operative care, and chronic medical conditions, such as cancer and sickle cell anemia [78–80]; it is only since the 1980s that it has been meaningfully applied to pediatric care [81,82].

In general, hypnosis includes three phases: induction, suggestion, and emergence [82]. During induction, the provider encourages patient relaxation by asking them to imagine a calm and serene setting on which they can focus all of their attention. Next, the patient is given therapeutic suggestions to achieve the desired effect. Lastly, the patient is asked to leave their imagined setting and to return to normal consciousness. Hypnosis for pain management follows this same protocol with a focus on suggestions that either turn down or decrease pain perception or increase pain thresholds [83].

Given the significance of the suggestion stage of hypnosis, an important factor in clinical outcomes is the degree to which an individual is responsive or susceptible to hypnotic suggestions—a trait that is often referred to as hypnotizability. Of note, studies that have attempted to measure hypnotizability among children via the Children's Hypnotic Susceptibility Scale and the Stanford Hypnotic Scale for

Children have shown a positive correlation between hypnotizability [84,85] and age, thus suggesting that hypnosis may be an especially viable form of therapy for pain management in the pediatric population [82].

Taking a neuroscientific approach, neuro-imaging studies have attempted to measure the effects of hypnosis on the neuroanatomy and the neuro-cognitive functions of the brain in the context of pain [85–88]. In other words, many researchers have set out to investigate how hypnosis affects the brain's neural-networks and physiology that in turn, are responsible for the perception of pain within an individual. This "pain matrix", as it has been described, is comprised of specific areas of the brain that collectively produce the experience of pain. In the simplest summary of the current literature, the components of the pain matrix include: the prefrontal cortex, frontal lobes, anterior cingulate cortex, primary and secondary somatosensory cortices, thalamus and insula. The cerebellum, though not technically a component of the pain matrix, also plays a role. Using fMRIs to measure brain activity during hypnosis, researchers have concluded that by influencing activity in the various components of the pain matrix, hypnosis is indeed able to have a collective therapeutic effect on pain.

Research focusing on clinical and experimental outcomes has also yielded positive results. A meta-analysis performed in 2000 of 18 studies found hypnosis to have a moderate to large analgesic effect [78]. When compared to groups receiving standard treatment and groups receiving no treatment, 75% of participants receiving hypnotic suggestion experienced a greater analgesic effect. Furthermore, the effect was seen with both clinical and experimental pain with no significant difference between the two settings.

Hypnosis is a tool that carries minimal risk when used appropriately for pain management. It can be used by patients as well as practitioners. The goal is often to instruct the patient on the hypnotic technique so that hypnosis will become a tool of empowerment that the patient is able to use themselves at appropriate times for symptom management. It is important to note that hypnosis should only be performed by an appropriately trained practitioner and only to treat conditions that the practitioner is competent to treat.

3.2.3. Yoga

Yoga is another mind–body modality that should be considered in the management of pain. In brief, the ancient practice of yoga aims to unite the mind, body, and spirit through different isometric exercises, body poses, and mindful breathing. The goal is to optimize body functioning and reconditioning, skeletal realignment, and blood/lymph flow to the tissues [89]. Beyond the biophysical benefits, yoga is also inexpensive, can be practiced by people of any age and physical skill level, and can be performed almost anywhere. The side effects are minimal, with the most common being musculoskeletal injury, often resulting from inappropriate supervision and/or technique [90].

Growing research has shown yoga to be an effective therapy for chronic pain among adults, but studies remain limited for the pediatric population [91]. In a 2006 meta-analysis, when yoga was incorporated into school curricula, improvements in academic performance, behavior, concentration, emotional balance, and self-esteem were all seen [92]. Regular practice of yoga has been associated with improvement in mood and function in patients suffering from depression [93].

These same techniques can be of great benefit in the management of chronic pain in particular. One pilot study of a yoga program in pediatric patients with Irritable Bowel Syndrome (IBS) and functional abdominal pain, demonstrated significant decreases in pain frequency and intensity, as well as improved quality of life per parents report [94]. A study of 30 children, aged 11–18, with amplified pain syndromes enrolled in an intensive interdisciplinary pain rehabilitation program incorporating 5–6 h of yoga weekly demonstrated improved pain and functioning without the use of pharmacology therapy [95]. Positive effects have also been shown in pediatric patients with rheumatoid arthritis [96]. Current evidence is encouraging, but more large-scale research is still needed to determine the efficacy of yoga in the treatment of pediatric chronic pain [39].

3.2.4. Acupuncture

Acupuncture has been a focus of Traditional Chinese Medicine (TCM) for thousands of years and since its introduction into western medicine, it has become one of the most popular complementary and alternative medical (CAM) therapies in the US [97]. First acknowledged as a medical therapy by the National Institute of Health (NIH) in 1997, the number of licensed acupuncturists in the US has grown exponentially over the decades with over 27,000 licensed acupuncturists in 2013—a one hundred percent increase from 2000—and an estimated one million annual American consumers. In 2001, Battlefield Acupuncture, an auricular acupuncture procedure, was developed by Richard Niemtzow as a simple and effective method for rapid pain relief that can be performed with minimal training by non-licensed acupuncturists [98–100]. Since then, it has since been utilized in emergency rooms and has been taught to US military and North Atlantic Treaty Organization (NATO) personnel for use in both medical and battlefield environments [99,101].

Research into the efficacy of the therapy has also increased over the years with many studies demonstrating acupuncture to be more effective at treating chronic pain than placebo, standard care, and no care [102–112]. Acupuncture is a viable alternative for the treatment and management of acute and chronic pain across various illnesses [22,103,113–115]. One overview of Cochrane reviews concluded that acupuncture demonstrates effectiveness as a treatment for pain associated with migraines, tension headaches, neck disorders, arthritis, and low back pain [104].

Research studies aiming at understanding the physiological and neurological mechanisms that make acupuncture an effective therapy have produced interesting results that have served as the basis for several potential hypotheses [107,116–129]. Many researchers believe that acupuncture stimulates nerves and muscles located within the acupuncture points and trigger a release of neurochemicals endorphins such as serotonin, oxytocin, and endogenous opioid peptides and therefore result in an analgesic effect [117,123,127]. However, while substantial research has shown acupuncture to be an effective therapy for pain among the adult population, there is limited research on acupuncture in regards to the treatment of pain among pediatric patients. Nonetheless, what little research does exist concludes that acupuncture is an effective and feasible therapy option for pain in pediatric populations [48,103,130–134]. One study in the pediatric intensive care unit (PICU) that used acupuncture for acute post-operative pain in children showed that acupuncture was highly accepted and well tolerated without morbidity. In addition, the majority (70%) of patients and families surveyed believed that acupuncture helped their pain. This particular study used the Japanese form of acupuncture with fine needles for older children and Shonishin (a non-needling technique using special tools) for those who were younger than two years of age [135]. A number of other articles have also shown some perceived pain relief without significant adverse effects due to acupuncture. [136,137]

Though acupuncture is safe when administered by appropriately trained and credentialed practitioners, there are some children who have a fear of needles or for medical reasons such as low platelet count or immunodeficiency that may not be recommended to receive acupuncture. For those patients, other techniques such as Shonishin or acupressure can be employed.

4. Discussion: H.O.P.E, A New Paradigm

The use of mind–body techniques in pediatrics can be a powerful adjunct to empower patients and their families and to give them hope for a brighter future with improved quality of life. In partnership with their physicians, families can begin to uncover what is in their tool box for pain and symptom management. One such framework developed by us is the pneumonic: H.O.P.E. We have used H.O.P.E. with success in clinical practice with families as a strategy for approaching pain management. H.O.P.E. addresses four essential components in the evaluation of pain and of the treatment plan. It is described in more detail below.

- H: **How** has the pain affected you and impacted your quality of life? **How** have they addressed the pain in the past and what therapies have been used?

- O: **Observations** about previous management approaches. What have they **observed**? What worked and what did not? What makes the pain perception worse?
- P: **Plan** for the future, set goals and determine the treatment plan.
- E: **Evaluate** the **efficacy** of the plan and manage **expectations.**

In addition to understanding what pharmacologic, non-pharmacological and integrative options are available; it is also important for all parties involved to discuss goals of care. In fully unpacking the child and family's needs, appropriate recommendations for pain management can be made. Recommendations will be different based on the clinical condition and goals of care.

5. Conclusions

Mind–body medicine provides an important approach to the management of both acute and chronic pain in the pediatric population. There are many modalities that are underutilized in pediatrics including mindfulness, hypnosis, yoga and acupuncture. It is important to note that these can be of significant benefit with minimal risk. Mind–body approaches can be used alongside conventional treatment or in some cases as the primary treatment for pain. Though more research is needed; the mind–body approaches discussed are recommended for patients who have no underlying contraindications. As our understanding of pediatric pain and pain management continues to mature, mind–body medicine is an area that is ripe for future studies and investigations.