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PEDIATRIC PALLIATIVE CARE (KS HOEHN, SECTION EDITOR)

Integrative Therapies to Support Pediatric Palliative Care: the Current Evidence

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Abstract

Purpose of Review This review offers an evidence-based introduction to integrative therapies that can be used with children receiving palliative care and suggestions for how to incorporate these therapies into practice.

Recent Findings For each integrative therapy discussed, recent research from both the pediatric and adult literature is summarized.

Summary Integrative medicine offers a patient-centered approach to care that brings together conventional and complementary therapies. Evidence-based integrative therapies exist for many troublesome end-of-life symptoms, including pain, anxiety, nausea, and constipation, and offer the benefits of being low risk and non-invasive. The body of evidence on integrative therapies for pediatric palliative care is still small but interest and use among patients and providers are stimulating increased research efforts which are summarized here.

Keywords Pediatric palliative care · Integrative medicine · Acupuncture · Aromatherapy · Botanicals · Mindfulness · Breastfeeding

Introduction

Integrative medicine is a patient-centered, evidence-based approach to care that brings together conventional and complementary therapies to address the full spectrum of a person's biopsychosocial needs [1, 2••]. Complementary medicine is an umbrella term for a diverse array of therapies developed outside the bounds of conventional medicine and includes biochemical therapies such as herbs, supplements, and diets, mind-body therapies, bioenergetic therapies, biomechanical therapies, and whole medical systems such as Ayurveda and Traditional Chinese Medicine [3].

Integrative medicine is a natural ally in the practice of palliative care. They both share an emphasis on allowing the course of treatment to be defined by the patient's goals and preferences, on understanding the patient's illness within the broader context of their life circumstances, and on using less invasive interventions when possible. Integrative medicine offers palliative care practitioners an expanded toolbox for promoting comfort and managing symptoms as well as an expanded platform for partnering with patients around the health practices and beliefs that are most important to them. When there is a desire to reduce the use of opiates and sedatives, integrative medicine offers an array of non-pharmacologic approaches to pain and symptom management.

The responsibility of the palliative care practitioner vis-à-vis complementary and integrative medicine is twofold. First, palliative care providers must be able and willing to meet patients where they are in terms of their use of complementary

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therapies. Between 40% and 70% of pediatric subspecialty patients and children with chronic illness are using complementary therapies [2••, 4]. Palliative care providers should be asking about the use of these therapies in an open and non-judgmental way with the goal of partnering with patients and families to assess the impact of these therapies, identify any potential interactions with other therapies they are receiving, and integrate these therapies into the patient's treatment plan when appropriate. Given the increasing body of evidence that supports the use of complementary therapies in a diverse array of patient populations and disease processes, it is also the responsibility of palliative care providers to educate themselves in evidence-based integrative approaches that have the potential to benefit their patients and to consider prescribing these therapies in contexts where they have been shown to be helpful.

Our goal in this review is to help palliative care providers meet both of the above imperatives—to become more aware of the complementary therapies that patients may already be using and to begin to integrate evidence-based integrative approaches into their own practice.

Aromatherapy/Essential Oils

Aromatherapy, the use of essential oils for healing, has been used for therapeutic purposes for nearly 6000 years. Essential oils are concentrated extracts taken from roots, leaves, seeds, or blossoms of plants. Aromatherapy massage involves massage using a carrier oil or base oil combined with essential oils such as rose or lavender oil. René-Maurice Gattefosse, a French chemist, established the science of aromatherapy in 1928 [5]. In children, essential oils may be administered via aromatic baths, aromatic compresses, aromatic foot baths, diffusion, gargle, inhalation, oral, pillow, spot treatment, steam inhalation, and sublingual drops [6]. Essential oils have gained popularity in the USA since the 1980s with the first research studies on aromatherapy in pediatric palliative care published in the 1990s [7, 8].

Essential oils are believed to have physical healing and emotional calming properties, both of which are beneficial to pediatric palliative care patients. There are limited studies examining the effectiveness of essential oils. Oils such as lavender and rosemary influence the mental state; improve depression, attention, and cognitive processes; and can improve the perception of pain [9, 10]. Lemon and lavender oil cause measurable, short-lived physiologic changes in conscious and unconscious palliative patients which are notably different from healthy patients [11]. Orange essential oil can reduce salivary cortisol and pulse rate of anxious children during dental treatment [12]. A small palliative care study showed sandalwood oil to be effective in reducing anxiety [13]. Aromatherapy with lavender essence helps reduce pain severity of intravenous catheter insertion in children [14]. Aromatherapy with *Rosa damascena* Mill can be used in postoperative pain in children ages 3–6 years, together with other common treatments without any significant side effects [15]. Aromatherapy had a small non-significant effect size in treating postoperative nausea and vomiting compared with control in one pilot study [16].

Aromatherapy can be beneficial for children at end of life, specifically to reduce anxiety. Lavender is one of the most commonly used essential oils for anxiety in children. Children ages 3–5 years may benefit from a mixture of five drops each of lavender, orange, and cedarwood administered via one drop of the mixture combined with equal parts of carrier oil to the wrists.

According to the Omaha Children's Hospital and Medical Center Housewide Policy for Palliative Care, the following are approved for use: (1) a combination of lavender, orange, juniper berry, patchouli, and ylang-ylang for anxiety, stress, frustration/fear, and pain; (2) a combination of ginger, cardamom, spearmint, and fennel for stomach upset, motion sickness, nausea, emesis; (3) a combination of lemon, orange, bergamot, lavender, and peppermint for lethargy, fatigue, or sense of depletion; (4) a combination of peppermint, rosemary, frankincense, and bergamot for distraction or generalized discomfort; and (5) a combination of lavender, marjoram, tangerine, and ylang-ylang for insomnia [17].

Essential oils are generally considered to be safe, but caution should be used in children because of risk of allergic reactions and skin sensitivity, accidental ingestion, and poisoning. A 2016 meta-analysis of a total of 12 pediatric and adult studies concluded that aromatherapy should be considered a safe addition to current pain management procedures as no adverse effects were reported in any of the included studies [18•]. Though the proper use of essential oils is generally safe, potential reactions with medications are not well studied and should be considered [19]. As pediatric palliative care programs increase in numbers and size, further research on effectiveness and safety of aromatherapy is needed to help guide treatment.

Botanicals, Vitamins, and Dietary Supplements

Botanicals/herbs, vitamins, and dietary supplements can be very helpful in managing pain and other symptoms during end-of-life care and can be especially helpful when used alongside other modalities such as acupuncture, mind-body therapies, or gentle manual therapies, in addition to conventional therapies.

Botanicals/herbs have been used to treat various ailments for centuries by indigenous cultures. Greater interest in "natural" approaches to health over the past decades has increased awareness and use of these products. Herbs have "Generally

Recognized As Safe" (GRAS) status for use in the USA. GRAS is the US Food and Drug Administration (FDA) designation that a chemical or substance is considered safe by experts qualified by scientific training and experience to evaluate their safety so therefore is exempted from the usual Federal Food, Drug, and Cosmetic Act (FFDCA) food additive tolerance requirements. The FDA regulates vitamins and dietary supplements under a different set of regulations than those covering drug products. Under the Dietary Supplement Health and Education Act of 1994 (DSHEA), the FDA is responsible for taking action against any adulterated or misbranded dietary supplement product after it reaches the market [20].

Magnesium is a supplement that is helpful for pain as it is a natural muscle relaxant and pain reliever. It also helps promote sleep and alleviate depression and anxiety through its natural calming effects [21]. In addition, it is an effective treatment for constipation. A typical dose would be 250–500 mg or the lessor of 9 mg/kg orally one to two times a day using magnesium glycinate, gluconate, aspartate, malate, or chloride as these salts are less likely to cause GI upset.

Ginger is also good for pain relief as it has natural anti-inflammatory actions [22]. Ginger is also widely known for its digestive effects and is used as a nausea reliever [23]. Ginger can be used as a tea, as extract, or in capsule form in a dose of 500 mg four to six times a day.

Omega-3 fatty acids, in the form of fish oil/flax oil or eating fatty fish, have been shown to reduce pain and to help alleviate depression in patients with anxiety/depressive symptoms and chronic pain [24]. Anxious and depressive symptoms contribute to worsening pain and chronic pain often contributes to such disorders. Using Omega-3s in doses of 1–3 g per day may help break this cycle of dysfunction.

Chamomile, in the form of tea, extracts, or capsules, can be used for nausea/stomach upset, dyspnea, anxiety, agitation, or insomnia. The active ingredient in chamomile binds to gamma-aminobutyric acid (GABA) receptors to exert anxiolytic effects without sedation [25]. An effective dose is 1 to 3 g taken three to four times daily. Brewing one heaping teaspoon of dried chamomile flowers in one cup boiled water for 10 min yields about 3 g of chamomile.

Valerian root can be used for dyspnea, anxiety, restlessness, agitation, and insomnia [26]. Dosing of 100 to 300 mg 30–60 min before bedtime is recommended for sleep. It can also be dosed on a three-times-a-day schedule for anxiety or dyspnea.

Cannabidiol (CBD oil) has diverse CNS actions with antipsychotic, analgesic, anticonvulsant, antioxidant, and anti-inflammatory properties and has been studied widely in adults as a treatment for anxiety [27]. Dosing starts at 0.5 mg/kg/dose given one to two times a day for children. Dosing can safely be increased every 3 days for optimal effects. For treatment of anxiety in adults, doses of 300–600 mg are used.

Vitamin D treats myalgias/muscle pain, strengthens the immune system, helps promote brain function, and reduces depression [28]. To target a serum 25-hydroxy vitamin D level of 50-80 ng/ml, considered the optimal levels, daily doses of 1000-5000 IU may be needed.

Bach flower remedies (Rescue Remedy™)—flower extracts—are commonly recommended by practitioners for anxiety, dyspnea, and pain without causing sedation. Though there are few controlled prospective trials of Bach flower remedies (BFRs) for psychological problems and pain, BFRs are considered safe [29]. Fifteen to thirty drops can be given as needed for symptom relief.

L-Theanine has been used for its relaxation and anti-anxiety effects and is also good for promoting sleep. L-Theanine reduces anxiety by increasing levels of GABA and serotonin. Excess serotonin manufactures more melatonin [30]. Typical dosing would be 100 to 200 mg once or twice daily.

Acupuncture/Acupressure: Harnessing the Body's Own Healing

Acupuncture is a form of therapy that has been practiced in China for over 2500 years. Based on the concept of Qi (life force) which travels along meridians, acupuncture points can be accessed by needles to balance and remove obstructions along the meridians, and thereby treat ailments. Acupuncture has been used to treat conditions like pain, nausea, and anxiety—common complaints in pediatric palliative care [31, 32]. Up to 20% of children in the USA have used acupuncture [33].

In a 1997 consensus statement, the National Institute of Health reported on the safety of acupuncture and its efficacy for postoperative dental pain and nausea/vomiting in both postoperative recovery and chemotherapy [34]. Since then, acupuncture has been shown to be safe in pediatrics and efficacious in treating nausea, vomiting, and pain [35, 36•, 37, 38]. More recently amidst the opioid epidemic in America, acupuncture has received national attention with the Federal Drug Agency recommending that healthcare providers learn about acupuncture specifically as a non-pharmacological modality to treat pain [39].

While acupuncture's mechanism is not completely elucidated, numerous pathways have been implicated, including endogenous endorphin release reversed by naloxone, connective tissue distortion and its local and downstream effects, cerebral cortex remodeling, and autonomic nervous system modulation [40–44].

Acupuncture/acupressure provides numerous advantages for children in palliative care. Both can be applied to all ages, including infants. Acupuncture can be administered by a physician trained in acupuncture or by a licensed acupuncturist. Acupressure can be taught to both patients and caretakers for administration. Having the hands of a loved one perform

acupressure may bring comfort akin to the benefits of therapeutic touch [45], strengthening their connection, and empowering the caretaker with a therapeutic tool to help relieve the child's discomfort.

Shoni Shin is a form of acupuncture from Japan that is particularly useful in young infants/children as therapeutic effect can be obtained by light strokes applied with shells, stones, or metal objects along the meridians [46]. Auricular acupuncture utilizes points on the auricle, which can be accessed by beads, semi-permanent ear needles, and acupuncture needles [47]. An advantage in using Shoni Shin and auricular acupuncture is that neither form of acupuncture interferes with monitoring leads or indwelling tubes. Another benefit is that children can freely move while receiving these therapies, making them easier to tolerate.

Children in palliative care are often extensively medicated, which may result in drug interactions and detrimental side effects [32]. Unlike pharmaceuticals that could compound symptomology, acupuncture activates the body's inherent mechanisms, avoiding interactions with drugs. Adverse effects from acupuncture are "substantially lower than many drugs, …" [34] and a systematic review concluded "that acupuncture is safe when performed by appropriately trained practitioners" [35].

Although there is a paucity of acupuncture research in pediatric palliative medicine, the published safety, efficacy, and acceptability of acupuncture in children and adults suggest the benefits this therapy can offer to children and families during the entire complex and critical disease trajectory. Acupuncture could be an invaluable treatment option in the field of pediatric palliative medicine, an area ripe for research.

The Impact of Breastfeeding and Breastmilk

Breastfeeding and breastmilk are not always considered in discussions of palliative care. Healthcare providers often refrain from discussing breastfeeding or milk expression with the families of dying infants, worrying that this will be one more burden on the family.

When expectant parents are faced with an infant with a life-threatening diagnosis, perinatal palliative care at birth is often chosen. In preparation for their baby's birth and death, families can plan how they would like to spend the limited time with their newborns, which may include quiet time with skin-to-skin and breastfeeding opportunities. Mothers of sick or dying infants often find solace and satisfaction in the opportunity to provide milk to their infants, rich with antibodies, growth factors, oligosaccharides, and many other anti-inflammatory properties which have the potential to nourish, heal, and soothe. When the opportunity to express milk and the benefits it could provide to the infant are discussed openly, families are often very interested and committed to doing so.

Healthcare providers should develop a level of comfort discussing the imminent onset of lactation with women delivering a live or stillborn infant at any point beyond 16 weeks gestation. The normal progression of lactogenesis will occur following delivery of the infant and placenta with the drop in progesterone and rise in prolactin. Colostrum expression is often possible prior to delivery and milk "comes in" between days 2 and 5 postpartum, regardless of the birth outcome.

While every scenario is different, consideration should be given to placing the palliative care infant skin-to-skin at the breast when feasible as soon as possible after delivery. Substantial literature supports the benefits of kangaroo mother care (KMC), originally defined as skin-to-skin contact, prone and upright, on the chest of the mother, father, or other caregiver. Stabilization of vital signs and blood sugar are some of the physiologic rewards from this low-tech activity [48]. In addition, KMC provides an excellent chance for quality intimate time for family members with the infant. Direct breastfeeding if possible is ideal; however, infants can be put to the expressed breast to suckle for comfort if direct feeding is not an option. Nasogastric tube feeds of expressed breastmilk can be provided to the stable infant while being held in KMC by any family member. Oxytocin plays a role for all participants in KMC with regard to bonding, attachment, relaxation, and effect on mood. These are precious heartwarming moments to be shared by families and offering them can be an immensely sacred opportunity.

Preparing the grieving mother of a stillborn or a very preterm infant for lactogenesis will allow her to be proactive in anticipating milk leakage, alleviating engorgement, and establishing full lactation if desired. The postpartum period of separation if the infant is sent to a neonatal intensive care unit, for example, is an important time to begin milk expression. Drops of colostrum can be collected and used on an oral swab for the NPO ventilated infant. In the case of prenatal loss, the problems that mothers encounter extend beyond the pain of breast engorgement and leakage; every drop of leaked milk may be a reminder of the loss [49].

In the event of infant death, surplus milk stored at home or in the hospital can be donated to benefit other sick or preterm infants. Many of the non-profit donor human milk banks across the USA will screen bereaved moms and arrange for direct overnight shipping of surplus frozen breast milk at no cost. Upon receipt of the frozen milk, it is thawed, pooled, pasteurized, and refrozen by the milk bank to be provided to other sick or preterm infants in need.

Many families note that the opportunity to donate their infant's previous milk to another sick or preterm infant plays a large comforting role in their healing process. Some women find this to provide such a positive sense of purpose, remembrance, and gratification they choose to continue to express their milk as a legacy to their infant—offering an incredible ongoing gift of donor human milk treatments to other infants in need [50].

Mind-Body Therapies

Mind-body therapies capitalize on the connection between the mind and the body to influence physiology; improve physical, mental, and emotional functioning; and increase wellbeing [51]. Some commonly used mind-body therapies are mindfulness or meditation, yoga, biofeedback, guided imagery, and clinical hypnosis or hypnotherapy. Mind-body therapies can be adapted to the developmental needs of children and adolescents of all ages, including infants and children with developmental disabilities, whose autonomic responses can be affected by rhythmic movements and sounds [52]. In the palliative care setting, mind-body therapies can be used to help children and adolescents reduce pain and anxiety and better cope with painful procedures, and can also be used to help caregivers better cope with the stress of caring for an ill child.

Biofeedback

In biofeedback, individuals use real-time feedback to strengthen their ability to regulate autonomic processes. During a biofeedback session, the individual practices a skill like deep breathing or progressive muscle relaxation while connected to a monitor that allows them to track their success using physiologic measurements, such as a heart rate, EEG waves, or temperature. Outcomes of biofeedback that are relevant to palliative care include improvement in coping with chronic pain and reduced anxiety [53, 54]. Biofeedback can also help reduce anxiety associated with painful procedures. In one relevant example, children with cancer underwent a series of biofeedback sessions prior to painful procedures using the HeartMath emWave device to give them feedback on their heart rate variability during performance of a belly breathing relaxation exercise. The majority of patients in this small study reported reduced fear of a planned painful procedure following this intervention [55]. Certified biofeedback providers can be found through the Biofeedback Certification International Alliance [56] but there are also an increasing number of consumer-directed devices and apps that can be used at home and which may appeal to children's interest in technology [51].

Meditation and Mindfulness

Meditation and mindfulness are practices that strengthen the individual's ability to attend to a chosen point of focus with the goal of being more consistently aware of present-moment experience [57]. During meditation, individuals focus on an attentional anchor such as the breath, sound, movement, or a repetitive phrase (*mantra*) and practice returning to the point of focus when their attention wanders. Meditation has been part of religious and cultural traditions across the world for thousands of years but has been adapted for secular audiences as the practice of mindfulness. Jon-Kabat Zinn developed mindfulness-based stress reduction (MBSR) as an 8-week curriculum [58, 59] that has demonstrated benefit in a wide variety of well and ill adults and children. There is also a growing body of evidence supporting the effectiveness of more brief mindfulness practices, including two pilot studies of 5-min mindfulness interventions in adult palliative care patients and their caregivers that showed reductions in distress [60, 61]. In meta-analyses of the effects of mindfulness on diverse populations of adults, the outcomes most relevant to palliative care include reductions in pain, anxiety, stress, and depression, as well as improvement in physical functioning and quality of life [62–64]. Research on meditation and mindfulness in children has focused largely on school-based populations and there is a dearth of evidence on these techniques in ill children. While further research is needed to assess the efficacy of meditation and mindfulness in pediatric palliative care patients, these interventions are low risk. There are many mindfulness apps that include practices for children and can be used by patients, families, and providers.

Caregiver Stress

Watching a child suffer can be overwhelming for caregivers, leading them to inadvertently compound the child's pain perception or catastrophizing through an empathic response. Caregivers may repeatedly verbalize feelings of anxiety, anger, and sense of urgency to "fix the problem" in the child's presence. Working with stressed parents and caretakers in this situation can be extremely demanding and at the same time offers clinicians an important opportunity to buffer the child's suffering by guiding caretakers towards techniques to address their own stress and suffering in more constructive ways.

First steps include acknowledgment of the adult's distress, confidence to introduce the topic in a compassionate manner, and familiarity with evidence-based resources that may offer new coping options. Depending on the parent's interests and available resources, any of the mind-body tools from simple breath work to a more complex meditation practice have potential to be helpful. Some of the most robust literature in this area comes from the pediatric oncology literature where parental stress and its impact on children have been widely recognized [65].

For example, in a group survey of 125 families whose child was undergoing treatment for cancer, more than 95% of parents reported post-traumatic stress symptoms [66]. Work is underway to develop reliable scales to help clinicians identify those caretakers in most need [67], and in offering caretakers new insights into perspective taking and how to decrease their burnout in these very challenging circumstances [68].

Interventions are beginning to be evaluated for efficacy. In a study examining the effectiveness of guided imagery and progressive muscle relaxation (PMR) as a tool to reduce stress

and improve mood in parents of children hospitalized for malignancies, the treatment group ($n = 29$ parents, control $n = 25$ parents) received individualized 25-min sessions once weekly for 3 weeks using PMR and guided imagery scripts tailored to the intervention. Recordings in CD form were also given to the parents for continued use. Results showed statistically significant improvement in anxiety ($p = 0.008$) and reduction in tension ($p = 0.027$) and a decrease in sadness ($p = 0.001$) versus the control group [69].

Mindfulness is another mind-body technique under active study and can be taught in a variety of ways. Online delivery of a mindfulness curriculum has been shown to be effective in adults [70] and has been piloted with parents of pediatric oncology survivors with promising results. Therapies such as mindfulness can also be harnessed by clinicians to buffer their own stress, an area of very active study [71].

Conclusions

Integrative medicine offers a variety of therapies that can help children receiving palliative care reduce pain and anxiety, manage troublesome symptoms, and strengthen their connection to their caregivers. Caregivers can also benefit from integrative therapies to help them cope with the stress of caring for an ill child. The integrative therapies presented are low risk with few reported adverse effects, and while current evidence is limited in the pediatric palliative care population, the existing evidence supports their safe use in children. Further research is needed to fully elucidate the efficacy of integrative therapies in pediatric palliative care.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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