Pediatric Palliative Pain and Symptom Management

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Many children with life-limiting conditions have distressing symptoms not just at the end of life, but throughout the course of their illnesses, which may run years after the initial diagnosis. Because pediatricians treat these children throughout their disease trajectory, it is important to have the basic skills to assess and treat pain and other distressing symptoms. This article reviews pain and symptom assessment and management.

Several studies have shown a high degree of symptom burden in pediatric populations with terminal illness in the last few weeks of life. Some commonly reported symptoms include pain, dyspnea, fatigue, poor appetite, nausea, vomiting, constipation, and change in sleep patterns. While much of the focus in the medical literature has been on end of life symptoms, many children living with life-limiting conditions experience distressing symptoms throughout their illness. The perception of suffering as a result of these symptoms may be different for each child and family. However, the need for pain and symptom management is clear. Good pain and symptom control, especially in the last days and weeks of life, can have a lasting positive impact on families; failure to achieve good symptom control, on the other hand, is associated with complicated grief and bereavement. For most children, symptom control can be achieved using standard dosing protocols with well-known medications such as opioids and benzodiazepines. Klick and Hauer identify several guiding principles for symptom management, which are outlined in Sidebar 1 (see page 330).

PAIN ASSESSMENT AND CONTROL

Assessment

Treatment of pain starts with its multifaceted assessment. For young or non-verbal children, we often rely on the caregiver’s report. Pain may manifest as changes in behavior, irritability, or fatigue. A complete pain history includes namely: location of the pain; and then for each site the quality, exacerbating/relieving factors, onset, associated symptoms, temporal pattern, impact on daily life/activities, and response to treatments. An initial pain assessment should also include a discussion of the child or family’s history with pain, pain medications, and what they perceive as barriers to...
good pain management. It is important to understand that pain is a complex experience impacted not only by physical factors, but also psychological, social, spiritual, and environmental factors as well.8

There are multiple pain assessment tools for both verbal and nonverbal children. Some common examples of pain scales include the following: the Infant FLACC tool (Face, Legs, Activity, Cry, and Consolability) using behavioral observation for infants; the Faces Pain Scale using visual images of faces representing levels of pain for school age children; and the Visual Analogue Scale using rating of a single line with descriptors of pain at each end for children and adolescents.9 Pain assessment guides the ongoing treatment, as the goal is resolution of pain. Thus, once a useful tool is picked for an individual patient, that same tool should be used to determine the efficacy of the treatment; much like a blood sugar level is rechecked to evaluate the effect of the insulin dose prescribed. It is also important to remember that pain assessment tools should be used in the context of treatment, reassessment, and review of other factors influencing pain.

Barriers to Pain Management

Misconceptions and myths surround the use of pain medications, creating barriers to adequate pain control. Some commonly misunderstood terms and their meaning are reviewed in Sidebar 2. Additional myths include disproportionate fear of respiratory depression and hastening death, or the belief that children do not experience pain as much as adults do.12,13 Adequate pain management does not hasten death, but on the contrary can improve and prolong the child’s quality and even duration of life.14

Treatment of Pain

The treatment of pain for a child with a life-limiting condition depends on the comfort of the child as reported by the child or family caregiver. Many times, control of pain can be achieved simply by using nonpharmacologic techniques, including positioning, distraction, application of heat and ice, as well as prescribing medications well-known to the pediatrician. Usual starting doses, as found in commonly used references, such as the drug dosing formulary in The Harriet Lane Handbook, are often sufficient for mild to moderate pain, but titration may be needed for more severe pain.15 Medication doses for severe pain should be titrated until good pain control is achieved or significant side effects are manifest. Side effects are the only limitation to dosing for pure opioid medications, as opposed to non-opioid medications, which usually have a clear upper limit. It is critical to keep in mind that the final goal is improved comfort.

Recommendations for pain management can be found in the World Health Organization (WHO) guidelines. Basic principles are outlined in Sidebar 3 (see page 331).16 New WHO guidelines have eliminated step two medications (codeine and tramadol) moving from a three-step ladder to a two-step approach. Due to concerns about the safety, efficacy, and variable metabolism of codeine, its use is no longer recommended. The guidelines called for additional research with tramadol to determine its safety and efficacy in children. The safety of using low dose strong opioids, such as morphine, for moderate pain was felt to be safer than use of the previous step two medications. The choice of which opioid to start depends on factors such as severity and type of pain, medication history, preferred route, and preferred schedule.

SIDEBAR 1.

Guiding Principles for Symptom Management

• Partner with the child and family to establish clear goals of therapy. Focus on improved physical and psychosocial function, and decreased suffering.
• Recognize that emotional, spiritual, and social suffering can significantly affect the experience of symptoms.
• A child’s report of symptoms is the “gold standard” of assessment. Parental report, physiologic indicators, and behavioral indicators are alternate assessments.
• Use developmentally appropriate communication and assessment tools.
• Anticipate symptoms, respond to them quickly, and re-evaluate the efficacy of treatment often until the symptom distress is resolved.
• Consider early referral to a pain or palliative care specialist for refractory symptoms.

Source: Klick JC, Hauer J

SIDEBAR 2.

Commonly Misunderstood Terms

• Addiction — compulsive behaviors of seeking out a drug despite adverse consequences or self-harm. Extremely uncommon in patients receiving palliative care in the absence of a pre-existing addiction disorder.
• Pseudoaddiction — behaviors such as clock-watching, loud moaning, or multiple requests for pain medications that may be mistaken for addiction, but are actually a response to inadequate pain control. Titration of medication to resolution of distress extinguishes this behavior.
• Tolerance — a physiologic need for increased dose of a drug to achieve the same clinical effect due to receptor down-regulation.
• Dependence — a physiologic response of the body with long-term medication use, leading to withdrawal if the medication is suddenly stopped, reversed, or if the dose is tapered too rapidly. It is not the same as addiction and can be avoided by slowly tapering the medication.

Source: Weissman D10,11
**Morphine**

Morphine is the WHO-preferred analgesic and is most frequently prescribed worldwide for moderate to severe pain. It has been well studied in children and can be given by multiple routes including oral, intravenous, subcutaneous, rectal, peridural, and spinal. In addition, morphine is inexpensive, readily available, and can be given in long-acting form if needed. Morphine is metabolized by the liver and excreted by the kidney. Dose adjustment or use of an alternate opioid should be considered in the face of severe renal insufficiency or failure since poor renal clearance leads to buildup of toxic morphine metabolites, resulting in irritability, myoclonus, seizures, increased pain and rarely respiratory depression.

**Oxycodone**

Oxycodone is another commonly used opioid. There is no intravenous preparation of oxycodone in the United States, but long acting oral forms are available. Compared to morphine, it has a slightly longer half-life; for some patients every 6-hour dosing may be possible. In addition, it is more expensive and in some settings may be less available than morphine. The conversion ratio from morphine to oxycodone is approximately 1:2:1, which means the equivalent daily dose of oxycodone would be 50% to 100% of the daily morphine dose. Clearance of oxycodone is also affected by severe renal insufficiency or failure.

**Hydromorphone**

Hydromorphone is 5 to 7.5 times more potent than morphine, meaning much lower doses are needed to obtain the same analgesic efficacy. Hydromorphone may be administered by all routes other than rectally. There is no long-acting form of hydromorphone available for pediatric use in the US. Hydromorphone is a good alternative if morphine or oxycodone is not well tolerated.

**Fentanyl**

Fentanyl is available in intravenous, transdermal, intranasal, and transbuccal routes and is useful in patients with renal insufficiency or failure. The transdermal patch cannot be titrated quickly nor does it give quick pain relief at time of initiation due to its long half-life and slow absorption, respectively. Other analgesic medications, such as morphine or oxycodone should first be titrated to relief prior to conversion to a transdermal patch for chronic, stable pain control. Transbuccal or intranasal routes can be used for acute or breakthrough pain. These medication delivery systems can be expensive and are not widely available; therefore, use of a complementary medication, such as morphine, for breakthrough pain, is often a reasonable option. Appropriate doses must be calculated.

**Methadone**

Methadone is a long-acting, inexpensive opioid. It is available as an oral and parenteral medication and it acts on numerous classes of pain receptors; it can therefore be very useful in refractory, chronic, or neuropathic pain. Methadone should be prescribed carefully and by an experienced practitioner. Frequent communication with the patient must be, especially in the first weeks of treatment, until a stable regimen is reached. Consultation with a pain or palliative care specialist is recommended for those unfamiliar with methadone and its side effects.

**Correct Dosage**

Starting doses for commonly used opioids are outlined in the Table (see page 332), along with dosing tips in Sidebar 4. Changing from one opioid to another to reduce the build-up of metabolites (“opioid rotation”) can be accomplished using equianalgesic dosing charts. Dose adjustment for opioid rotation can be confusing because they account for incomplete cross-tolerance, meaning that the reduced efficacy of a medication over time that is related to tolerance does not translate completely to the new alternate medication, rendering it more potent than predicted when using the standard conversion table. If a practitioner is inexperienced with this paradigm, consulting

**WHO Principles of Pain Management in Children**

**Analgesic Two-Step Approach**

- Step 1 – Nonopioids (acetaminophen, ibuprofen)
- Step 2 – Opioids (morphine, oxycodone, fentanyl, hydromorphone)

*Consider adjunct medications when appropriate.*

**Principles of Pain Management**

- By the clock: at a regular interval
- By the child: based on child’s pain level and response to treatment
- By the appropriate route: use least invasive route possible

** WHO = World Health Organization.

Source: World Health Organization

**Dosing Tips for Opioids**

- Consider scheduled medications, plus breakthrough (prn) doses if pain is expected for some duration of time.
- The easiest and least invasive route is always preferred.
- For infants less than 6 months of age, decrease starting dose by 30%-50%.
- Consider lower end of starting doses for an opioid-naïve child.
- Rescue doses can be given for breakthrough pain at 25%-50% of the scheduled interval dose or (alternatively) 10% of the total daily dose.
- If there is an indwelling IV catheter consider using it. Subcutaneous administration is an option for many medications if no other route is possible.
- Avoid intramuscular dosing.

Source: Shaw TM

**SIDEBAR 3.**

**WHO Principles of Pain Management in Children**

**SIDEBAR 4.**

**Dosing Tips for Opioids**
with a pain or palliative care specialist may be beneficial.

Combination medications, such as acetaminophen with codeine or oxycodone and acetaminophen with hydrocodone should be used with caution, if at all, in children. It is easy to exceed maximal recommended doses of the acetaminophen and ibuprofen when using these. Optimally, the nonopioid analgesic will be prescribed concurrently but separately from the opioid to ensure safe dosing of each medication. In addition, use of hydrocodone in the pediatric population carries concerns similar to codeine regarding safety and efficacy.

**Side Effects of Opioids**

**Constipation**

The most common side effect of opioid treatment, constipation, should be managed proactively. A bowel regimen including a stool softener and an osmotic or motility agent should be started at the initiation of opioid treatment unless the patient is experiencing diarrhea. As opioid doses escalate, so must the intensity of the bowel regimen.

**Pruritis**

Often mistaken for an allergic reaction, pruritis is an expected side effect of opioids due to their histamine releasing properties; the itching usually resolves within a few days of treatment initiation or increased dosage. Treatment with diphenhydramine or hydroxyzine can be helpful until resolution. If pruritis is severe or refractory to treatment consider rotating to another opioid.

**Nausea and vomiting**

Nausea and vomiting usually are temporary symptoms occurring at the time of initiation or escalation of opioid medication doses and can be treated with antiemetics until resolution. Sedatives such as promethazine should be avoided if possible.

**Urinary retention**

An uncommon side effect of opioid treatment, urinary retention can be managed with nonpharmacologic techniques such as running water, manual pressure on the bladder (Crede’s maneuver) or, if needed, intermittent catheterization may be used until resolution.

**Respiratory depression**

Though commonly feared, respiratory depression is a rare complication of opioid treatment, particularly with appropriate titration of medications based on patient response to treatment. Patient monitoring should include assessment of vital signs and level of consciousness, as well as pain relief. Breathing may be slowed when adequate pain control is achieved and should not be mistaken for a medication’s side effect. Respiratory depression caused by opioids will also include an unexpected decreased level of consciousness. The use of naloxone to treat respiratory depression should be avoided as it may lead to an increase in pain and possibly even opioid withdrawal. Usually holding or decreasing the opioid dose with close monitoring is effective in reversing respiratory depression in this setting.

**Myoclonus**

Myoclonus can be seen with higher and longer term doses of opioids, due to the build-up of neuroexcitatory metabolic byproducts which can also lead to seizures and personality changes. The appearance of such side effects should prompt consideration of opioid rotation, as described above.

**Adjuvant Medications**

A pain assessment may reveal different types of pain such as nociceptive as well as neuropathic pain; the latter is distinguished by its associated sensations of shooting pain, burning, or allodynia (non-painful stimuli, such as light touch resulting in pain perception). Adjuvant medications, in conjunction with opioids, can be useful for the treatment of neuropathic pain. Some common adjuvant medication classes include: anti-inflammatories; antidepressants (particularly tricyclics); anticonvulsants (commonly gabapentin); steroids; and muscle relaxants.

**Nonpharmacologic Treatments**

Pain management should include an integrated strategy of medications as well as nonpharmacologic therapies or techniques. These strategies may include biofeedback, guided imagery, hypnosis,
massage, acupuncture, herbas, or art therapy. Fifty-nine percent of parents whose children have cancer reported using complementary therapies.21 The evidence for these therapies is still being explored, but appears to have benefit for some patients. Most clinicians encourage the use of complementary techniques unless there is evidence of harm to the patient, to the family’s budget, or in the literature. Their use often enables the parents to feel they are meaningfully contributing to the child’s well-being. Therefore, care plans should be developed based on individual response and in partnership with the family.

In addition, it is important to consider that psychosocial distress or other environmental factors may play a role in pain generation. Recognition and discussion of these factors can result in significant benefit with few side effects. Interdisciplinary care team members such as psychologists, psychiatrists, counselors, spiritual leaders, or social workers may be helpful in this regard.

OTHER SYMPTOMS
Respiratory Symptoms

Dyspnea is one of the most common respiratory symptoms among children with life-limiting conditions, especially at the end of life. The treatment of dyspnea often requires an interdisciplinary approach and the use of relaxation techniques and deep breathing, distraction, or hypnosis. First line medication treatment of nonspecific dyspnea from an irreversible condition includes scheduled opioid medications, with one-quarter to one-half oral starting doses for pain.1,2 Patients with dyspnea who are already receiving opioids for pain control will, of course, need higher doses and should not be reverted to starting doses. Administering opioids for breathing distress often frightens both families and health care providers due to the association of opioids with respiratory depression.

Recent evidence has shown both safety and efficacy for the use of these medications.12 Benzodiazepines can also be considered in the treatment of dyspnea and can be helpful if there is associated anxiety or agitation.18 Oxygen can be considered for patients with hypoxia. A fan blowing on the face is also effective for managing the sensation of breathlessness, based on its stimulation of the V1 branch of the facial nerve. Anticipatory education of families about end-of-life changes in respiratory patterns (apnea, irregular breathing rates, and noisy breathing) can help alleviate their distress.

Secretion Control

Secretions are another common respiratory problem, often presenting well before end of life in children with severe neurologic impairment. Excessive or poorly controlled salivary secretions can be managed chronically with medications such as anticholinergic agents, glycopyrrolate, or the use of a suction machine.1 Management can include educating the family, a reduction of artificial fluid intake, and in long term settings, possibly the use of botulinum toxin in the gland itself.22

Gastrointestinal Symptoms

Nausea, vomiting, anorexia, constipation, and diarrhea are all common symptoms that may be disease-related or a side effect of treatments.23 Management of these symptoms is directly related to the presumed cause, with an effective treatment plan based on a good history, exam, and review of current medications.

Antiemetics are targeted at specific receptors and mechanisms; they should be chosen based on the underlying reason for the nausea. For example, ondansetron, a serotonin receptor antagonist, works well for nausea caused by chemotherapeutic and anesthetic agents. For opioid-induced nausea, dopaminergic (eg, haloperidol), anticholinergic (eg, scopolamine), or prokinetic (eg, metoclopramide) agents may be more effective. Benzodiazepines (eg, lorazepam) are helpful when anxiety is contributing to nausea.23 If the antiemetic medication chosen is ineffective in relieving symptoms, a second antiemetic with a different mechanism of action should be either added or substituted to the current regimen.1

Constipation is another common symptom.1,2,23 Medications used to treat constipation fall into three categories: stool softeners, osmotic agents, and stimulants. Stool softeners, such as docusate, are usually ineffective when used alone for this population; a stool softener plus either an osmotic agent or stimulant is indicated. Osmotic agents include polyethylene glycol 3350, lactulose, and magnesium sulfate. Stimulant medications include senna or bisacodyl.

Appetite Changes

Redirecting the parent to focus on providing companionship and love, rather than food, and offering anticipatory guidance as appetite, physical activity, and metabolic activity typically decrease can be helpful. Earlier in the course of illness, high calorie supplements or pharmacologic therapy may be of benefit. In the case of early satiety, small frequent meals may be appropriate and if the taste of food is altered by the illness or its treatment, soliciting the child’s preferences can lead to improved nutritional intake. It is important to exclude remediable causes of decreased appetite, such as pain, nausea, and depression.23 Many children with profoundly debilitating neurologic conditions are dependent on medically
administered enteral feedings throughout their lives. At the end of life, it is the normal course of most conditions to have loss of appetite and intolerance of feeding. Continuing artificial hydration and nutrition at this point may worsen symptoms. How this is addressed may depend on the family’s beliefs and goals.

**Mood Lability**

Anxiety, depression, insomnia, and agitation are symptoms typically associated with psychosocial or spiritual distress, in addition to underlying physical causes. Their management often benefits from an interdisciplinary approach and nonpharmacologic treatments. Reversible medical causes, such as pain, and medication side effects should be investigated as well. Selective serotonin reuptake inhibitors (SSRIs) can be helpful for depression and anxiety, but must be taken for 4 to 6 weeks (SSRIs) can be helpful for depression and anxiety, but must be taken for 4 to 6 weeks before they reach their full effectiveness.

For children at end of life with only days or weeks remaining, more immediate acting medications should be considered such as benzodiazepines and haloperidol for anxiety and agitation; psychostimulants have been used in adult patients for rapid resolution of depression and asthenia in the palliative setting and may be beneficial in children as well.

**Fatigue Management**

Fatigue can be related to disease process, treatments, medications, nutrition, anemia, pain, depression, anxiety, or other causes. Other than with reversible causes such as anemia, fatigue is very difficult to treat. Structuring activities to include rest time may be helpful.

**CONCLUSION**

The pediatrician is at the front line of symptom assessment and management for children living with life-limiting conditions, starting from time of diagnosis and extending all the way to the end of life. With just a few basic tools, the pediatrician can help prevent and manage many symptoms that may be experienced by these children and families. For symptoms that are difficult to control, consider consulting a physician who specializes in pain or palliative care.

**REFERENCES**