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Pediatric acute pain management

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As defined by the International Association for the Study of Pain, pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. While pain has its roots in a physiologic response to a noxious stimulus, the perception of pain is often a complex, personal experience affected by multiple factors.

Focusing on age, pain can differ in individuals as a function of age for a number of reasons. The nature of disease processes and treatments may differ between children and adults. In addition, children are much less likely to suffer from chronic pain than adults, so the focus of pain management in children often centers on the treatment of acute postoperative and post-traumatic pain. The impact of development is also important. While much of the pain processing system described in adults is functional at birth, the postnatal period is also a time of great structural and functional change in pain pathways. Because of the immaturity of synaptic connections and neural circuits in the newborn, the infant pain experience is more diffuse and less spatially focused than that in adults.

While the experience of pain requires the development of a consciousness, the inability to communicate in no way negates the possibility that an individual is experiencing pain and requires appropriate treatment. In the past, clinicians treating infants and neonates at times provided no analgesia or inadequate analgesia because of their concern that the use of analgesics would produce adverse effects. However, not providing sufficient analgesia can be associated with both immediate and long term problems as well. In 1992 Anand and Hickey published an important study comparing light versus deep anesthesia and analgesia in neonates undergoing cardiac surgery. They demonstrated that neonates who received deep anesthesia had significantly reduced responses of stress hormones, while neonates who received lighter anesthesia had more severe hyperglycemia and lactic acidemia during and after surgery. In addition, the neonates who received deep anesthesia had a decreased incidence of sepsis, metabolic acidosis and fewer postoperative deaths. These results led them to conclude that instead of putting patients at increased risk deep anesthesia might actually be protective for neonates undergoing cardiac surgery.

Furthermore, infants who have been subjected to a painful stimulus can also demonstrate prolonged changes in pain sensitivity following an initial injury. For example, neonatal circumcision is a common procedure that is frequently performed without any analgesia provided to the newborn. However, Taddio and colleagues demonstrated that infants who underwent circumcision without analgesia had an increased behavioral response to immunization several months later that was reduced by the use of local anesthesia at the time of circumcision.

These studies point to the benefits gained by providing appropriate pain management to young children. But to do so requires a coordinated, multistep approach that includes pain assessment and treatment as well as patient empowerment. Considering pain assessment it is important to understand that it is not possible to use the same approach in every patient. Rather, different, developmentally appropriate modalities of pain assessment must be used, including self-report, physiologic and behavioral measures. Once pain is assessed, therapies must be selected and delivered in a logical, coordinated fashion. When treating pain in children, the World Health Organization now recommends a sequential two-step approach, but when treating moderate to severe pain it is often more effective to provide interventions from both steps simultaneously. The goal of this multimodal approach is to improve analgesia, reduce drug induced side effects, and improve recovery and function.

In many respects acute pain management for infants and children parallels the approach taken for adults. Therapies employed include non-steroidal anti-inflammatory drugs, local anesthetics, opioids, alpha-2 adrenergic agonists and neuromodulating agents, but opioids remain a mainstay in the management of moderate to severe pain. Over the past 30 years multiple opioid receptors and subtypes have been identified and classified. These receptors are primarily located in the brain and spinal cord, but also exist peripherally on

peripheral nerve cells, immune cells and other cells. Opioids act by binding membrane-bound G-protein coupled receptors on these cells. Analgesic effects are mediated by decreased neuronal excitability, decreased cyclic-AMP production, increased nitric oxide synthesis and increased production of 12-lipoxygenase metabolites.

Opioids can be administered by multiple routes, often reaching their sites of action in the brain and periphery via the bloodstream. Orally administered opioids, sometimes in combination with acetaminophen or ibuprofen, are frequently prescribed to treat pain in children following outpatient surgery or prior to discharge after more complex surgeries. In the past, when oral dosing of opioids was not a reasonable option, children were administered pain medicine by painful intramuscular injections or nurse administered, as needed intravenous bolus dosing regimens. However, these techniques can be wrought with pain and painful delays. Nowadays, these delays can be minimized by the use of patient controlled analgesia, a technique which allows patients to self-administer small, intermittent doses of opioid. While it was originally felt that this therapy would be appropriate only for teenagers and older children, younger children quickly demonstrated their facility with the technology and many institutions now allow children as young as 7 years of age to use PCA. However, even though many children qualify by age and ability to use PCA, those who are especially young or with developmental disabilities do not. For those children, some institutions, including our own, prescribe parent/nurse controlled analgesia or PCA by proxy. Using this technique the child receives a basal opioid infusion and PCA bolus doses delivered by either a parent or nurse when the child appears to be in pain. While we have provided this modality for many years, in 2004 the JCAHO released a sentinel event warning that serious adverse events can result when family members, caregivers or clinicians who are not authorized become involved in administering analgesia for the patient «by proxy». Subsequent studies have suggested that this technique is generally safe, but it is not without complications especially in the extremely young.

While opioids are an important component of pediatric pain management, all opioids produce unwanted side effects. Hence, we often try to limit opioid consumption and reduce drug induced side effects by utilizing a multimodal approach to pain relief. As a result, a number of classes of adjuvant drugs are now used more and more frequently to limit side effects by decreasing opioid use, including alpha$_2$ adrenoreceptor agonists, such as clonidine and dexmedetomidine, and anticonvulsants such as gabapentin and pregabalin. Although originally used to treat neuropathic pain, over the past several years there have been a number of publications showing enhanced postoperative analgesia and reduced postoperative opioid consumption in patients who receive gabapentin as part of their perioperative pain management, supporting an additional role for gabapentin in the early perioperative period.

One additional way to try to manage opioid-related side effects involves the use of opioid antagonists. In animal models co-administration of morphine with an ultra low-dose of naloxone has been shown to reduce opioid induced hyperalgesia, tolerance and dependence, most likely by altering mu-opioid receptor G-protein coupling and signaling. This approach has also been shown to reduce side effects in some clinical settings as well. One limitation to this approach though is that when naloxone is administered concomitantly with an opioid, the antagonist dose required to block some side effects may be high enough to interfere with the opioid's analgesic effects. However, while most opioid-induced analgesia is a central effect, many opioid induced side effects are mediated at least in part by peripheral opioid receptors. This distinction has led to the development of peripheral opioid antagonists, such as alvimopan and methylnaltrexone which have been shown to improve gut motility postoperatively (alvimopan) and promote laxation and diminish constipation and opioid-induced bowel dysfunction (methylnaltrexone) in adult patients. While neither drug is approved for use in children, anecdotal reports have shown methylnaltrexone to have some efficacy in reducing opioid induced gut hypomotility in select pediatric patients.

In conclusion, patients of all ages experience pain and not treating pain in children can have long-term negative consequences. There are unique considerations when managing pain in children, including how to assess pain and what medications to administer. Considering treatment, it is often multimodal, and may require analgesics as well as therapies to minimize analgesic-related side effects.

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