Pain Management in Children

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Introduction

The prevalence of both acute and chronic pain in children has been increasingly recognized in the past decade, which has led to the need to develop techniques for the management of childhood pain. Pediatric pain management has relied extensively on techniques and medications that have been developed over the past decades for the management of pain in adults.

Epidural Analgesia

Continuous infusion of local anesthetics, opioids, or the two in combination into the epidural space, is an effective method of providing analgesia after injury or surgery of the lower extremities or trunk.

Generally speaking, the catheter tip should be sited as close as possible to the spinal nerves carrying the pain impulses from the surgical area. For example, after ureteral reimplantation with a phantom incision in the T-11 dermatome, one would like the epidural catheter to be within 2 interspaces of the T-11 spine. This would ordinarily be accomplished by inserting the catheter in the L2-L3 interspace and threading the catheter cephalad a pre-measured distance. This will assure maximum analgesia with the least amount of drug. For lower extremity surgery, low lying lumbar or caudal catheters threaded into the lumbar spine are adequate. For thoracic analgesia, maximal analgesia will be obtained with thoracic epidural catheters or with catheters threaded up from below.

Dilute local anesthetic solutions provide analgesia without motor blockade. Ester anesthetics (chloroprocaine, tetracaine) are rapidly metabolized and associated with less toxicity than amide local anesthetics (lidocaine, bupivacaine).

There are no data in children regarding the most effective opioid for epidural administration. It is our strong clinical feeling that hydromorphone (Dilaudid®) is associated with fewer side effects than morphine sulfate. Fentanyl citrate is very lipophilic and spreads poorly in the epidural space. If the catheter tip lies contiguously to the spinal cord (at least at the T12 vertebral body) then fentanyl may be effective. Fentanyl is significantly absorbed into the bloodstream from the epidural space, and much of its efficacy is due to systemic effect rather than selective spinal analgesic effect.

Indications for Use

Postoperative Surgical Patients: Lower extremity and pelvic surgery, urologic surgery, general abdominal and thoracic surgery, cardiac surgery.

Children with Impaired Pulmonary Function: Flail chest, cystic fibrosis with chest pain.

Children with need for Sympathetic Block: Reflex sympathetic dystrophy, microvascular surgery, purpura fulminans.

Medical Pain Poorly Responsive to Conventional Therapy: Sickle cell vaso-occlusive crisis, cancer pain.

Newborns

Almost all cases of epidural opioid induced delayed respiratory depression have been reported in infants less than 6 months of age. For this reason, our practice is not to use opioids in this population, unless the infant is not opioid naïve, or the infant is going to be electronically monitored in an intensive care setting after surgery.

Newborns have low levels of alpha-1-acid glycoprotein, the serum protein that binds to local anesthetics in the blood. For this reason, they may exhibit signs of toxicity at lower serum l.a. levels than would ordinarily produce toxicity in an older child or adult. We use 0.3 mg/kg/hr as the maximum bupivacaine infusion rate and 1 mg/kg/hr as the maximum lidocaine infusion rate in infants < 2months of age.

Infants

Infants > 6 months of age are usually managed with a combined l.a.-opioid infusion. The maximum dose of bupivacaine is 0.6 mg/kg/hr, and the maximum lidocaine dose is 1.5 mg/kg/hr. An infusion of 0.1% bupivacaine or 0.3% lidocaine containing preservative-free hydromorphone 10 µg/ml or morphine 20 µg/ml is infused at a rate of 0.25-0.5 ml/hr.

Children

The maximum dose of bupivacaine is also 0.6 mg/kg/hr, and the maximum lidocaine dose is also 1.5 mg/kg/hr. An infusion of 0.1% bupivacaine containing preservative-free hydromorphone 10 µg/ml of or morphine 20 µg/ml is infused at a rate of 0.25-0.6 ml/hr. Or, an infusion of 0.5% lidocaine containing preservative-free hydromorphone 10 µg/ml or morphine 20 µg/ml is infused at a rate of 0.25-0.3 ml/hr.

Teens

Epidural PCA is an effective method of reducing the overall drug administration rate with epidurals, giving the patient some autonomy and control over their analgesia, and, one hopes, reducing side effects. We typically use hydromorphone 25 µg/ml + bupivacaine 0.1% or lidocaine 0.5%, with a continuous background infusion of 4-5 ml/hr, a PCA dose of 2-3 ml, and a lockout interval of 30 minutes.

Problems

Bupivacaine toxicity with long term infusions may be avoided by limiting the infusion dose to 0.25 mg/kg/hr in children <6 months of age, 0.5 mg/kg/hr in older infants and children, and 0.25-0.3 mg/kg/hr in children with a reduced seizure threshold (e.g. hyponatremia, concomitant drug therapy known to lower seizure threshold or with a history of a seizure disorder).

Side effects

to intraspinal opiates are the most common problem to contend with. Of these the most distressing are nausea and urinary retention. **Nausea** responds well to ondansetron (Zofran®), 0.05-0.15 mg/kg. **Urinary retention** may be subject to benign neglect until the bladder over-distends and overflows, or may be treated with urinary catheterization. The former may lead to considerable discomfort and hypertension, the latter subjects the

child to the risk of UTI. Pruritus responds well to nalbuphine (Nubain®) 0.05 mg/kg, or to a low dose naloxone (Narcan®) infusion at 0.001 mg/kg/hr. The latter may antagonize analgesia, but this usually does not happen. **Respiratory depression** is very uncommon in children over 6 months of age provided that concomitant opiates are not administered, and that the dosage is kept to an acceptable range. We commonly use epidural morphine at 3 µg/kg/hr or hydromorphone (Dilaudid®) at 0.5-1.5 µg/kg/hr mixed with dilute 1/10% bupivacaine. The bupivacaine dilution may be diluted further to reduce motor weakness if it occurs.

Successful application of epidural analgesia in children requires the organization of a pain management service, appropriate nursing protocols and procedures, and the hospital support to provide electronic monitoring of children (e.g. pulse oximetry and perhaps ECG) at other than an ICU setting.

Intravenous Opioids (Continuous and PCA)

Continuous infusion of opioids is an effective method of providing analgesia and is a better alternative in most circumstances to nurse administered prn. analgesia. Each opioid has a unique side effect profile in every patient; some patients may respond better with fewer side effects to one opioid than another. The following table lists opioid dose equivalents; all further discussion will be scaled to morphine doses for the sake of simplicity; you can use this table to calculate how much of other opioids you may use as a substitute for morphine.

Table 1. Opioid Dose Equivalents

DRUG	POTENCY	LOADING DOSE	INFUSION DOSE
Morphine	1	0.05 mg/kg	0.01-0.04 mg/kg/hr
Fentanyl	20	1 µg/kg	0.2-1 µg/kg/hr
Hydromorphone	5	10 µg/kg	0.5-2 µg/kg/hr
Meperidine (not recommended)	0.1	0.5 mg/kg	0.1-0.4 mg/kg/hr

Newborns

Newborns, infants, and children less than about 6 years of age are clearly not candidates for PCA. Continuous opioid infusions are an effective method of providing IV analgesia. Newborns are slow metabolizers of morphine, therefore after establishing analgesia with the usual intravenous bolus doses, the continuous infusion rate should be approximately ½ that seen in Table 1.

Infants, Children

If one calculates opioid requirements in children managed with PCA after surgery, one sees that the morphine requirement after major surgery is 0.2 – 0.4 mg/kg/hr depending on the nature of the surgery and the child's pain threshold. This is therefore a reasonable guideline to use when establishing continuous opioid infusion therapy.

Use bolus doses of opioid to establish an adequate analgesic level.

Institute a continuous opioid infusion starting at the lower end of the 0.2 – 0.4 mg/kg/hr range.

If analgesia becomes inadequate, re-bolus with ½ the original loading dose and increase the infusion by 25%.

Morphine infusions may be conveniently ordered as follows:

1 mg/kg of morphine sulfate in 100 ml D5W.

Run infusion at 1 – 4 ml/hr (equivalent to 0.01 – 0.04 mg/kg/hr).

PCA

Children older than about 6 are usually capable of mastering the concept of PCA. Typical starting doses are in Table 2.

Table 2. PCA Doses.

DRUG	PCA DOSE	CONTINUOUS DOSE
Morphine	10 – 30 µg/kg	5 – 30 µg/kg/hr
Hydromorphone	2-6 µg/kg	1-6 µg/kg/hr
Fentanyl	0.5 – 1 µg/kg	0.25 – 1 µg/kg/hr

Lockout intervals range from 6 – 10 minutes.

The use of continuous background, or basal, infusions is controversial. Several investigators have studied their effects on the quality of analgesia and the incidence of side effects. My interpretation of these studies is that smaller continuous infusion rates (e.g. 5 µg/kg/hr of morphine) improve the quality of analgesia and nighttime sleep, without increasing side effects. Greater infusion rates do not improve the quality of analgesia over smaller rates, but are associated with more frequent side effects (urinary retention, somnolence and desaturation, nausea and vomiting).

In monitoring children on PCA, it is important to score the quality of analgesia by measuring pain, and to examine the pattern of PCA use. Ideally, the PCA infusion and dose selected will result in approximately 1 button activation per hour, and reasonable durations of sleep without awakening in pain.

If analgesia is adequate with few activations of the PCA button, then the continuous infusion is too high. If analgesia is inadequate with few PCA activations, then better patient education is needed or the patient is poorly suited to PCA. PCA demands that exceed 2 per hour indicate an inadequate background infusion rate and/or an inadequate PCA bolus dose.

Adjuvant Drugs

The use of IV PCA or epidural analgesia improves the management of pain, but does not prevent opioid induced side effects, alleviate psychological anxiety related to hospitalization, or eliminate the inflammatory response to stress and surgery. Adjuvant drugs will generally provide augmentation of analgesia without increasing side effects, and usually reduce the quantity of opioids required for analgesia.

NSAIDs

Provide moderate analgesia. Except for acetaminophen, all NSAIDs inhibit platelet activity and should not be used on the first postoperative day following surgery in which hemostasis is incomplete or relies upon platelet function (e.g. craniotomies, spine fusions, tonsillectomy, etc.).

Acetaminophen 30 mg/kg loading dose p.o. or 40 mg/kg p.r., then 10 mg/kg every 4 hours p.o. or 20 mg/kg every 4 hours p.r.

Ketorolac, 0.5 mg/kg every 6 hours IV.

Ibuprofen, 5-10 mg/kg every 6-8 hours p.o.

Naproxen 2.5-5 mg/kg every 8-12 hours p.o.

Benzodiazepines

Anxiety is a universal phenomenon in hospitalized children, and the use of anti-anxiety drugs is important adjuvants to analgesia. They promote a sense of well being, improve the quality of sleep, and reduce opioid consumption or requirement. An extremely important use of benzodiazepines is for the management of muscle spasms and hypnagogic myoclonus. The former is very common in children who have some degree of spasticity, and surgery frequently, indeed always, aggravates the degree of spasticity present, and this in turn accentuates postoperative pain. The latter, hypnagogic myoclonus refers to myoclonic jerks that occur as a person falls asleep. Hypnagogic myoclonus is increased by parenteral opioids, and can also be very painful in post-surgical patients.

Benzo's may, however, potentiate opioid induced respiratory depression.

Midazolam, 0.01 – 0.05 mg/kg/hr (mix as for morphine infusion, above).

Lorazepam, 0.05 mg/kg IV q8 – 12 hr.

Clonidine

Clonidine is an agent rediscovered for its use and application in acute and chronic pain management. Recent studies using clonidine in central and peripheral blockade show that it is co-analgesic when used with either local anesthetics or opioids in epidural, intrathecal, or peripheral blocks.

Clonidine is thought to have applications in the treatment of chronic pain, particularly neuropathic pain. Finally, intrathecal administration of clonidine has been shown to reduce intractable muscle spasms in patients with spinal cord injuries.

Alpha-2 receptors are located on primary afferent terminals (both peripheral and spinal endings) in the superficial laminae of the dorsal horn of the spinal cord, and within several brainstem nuclei. The analgesic effect of clonidine may be at all three sites, with each site's relative contribution to its analgesic effect being unclear. Most studies support a direct and primary spinal analgesic action of clonidine. Supportive data for this conclusion are the facts that the relative potency of epidural clonidine to intravenous clonidine is 2:1, clonidine has a lipophilicity similar to fentanyl, the duration of analgesia of epidural clonidine is 3-5 hours, and that intrathecal administration of clonidine results in a peak effect within 30-60 minutes and has duration of up to 6 hours. Clonidine increases the release of acetylcholine at the dorsal horn.

With regards to the pediatric literature, most studies have been performed using clonidine in combination with a bupivacaine epidural analgesia in the acute pain setting. Motsch studied a group of 40 children undergoing minor surgical procedures. He found that combined caudal analgesia with bupivacaine and clonidine (5 µg/kg) was superior to local anesthetic alone, as determined by both duration and intensity of analgesia. However, children had decreased blood pressure and sedation for the first three postoperative hours . This duration of effect is consistent with the known duration of epidural clonidine in adults.   Other authors have studied caudal analgesia using bupivacaine and clonidine, 1-2 µg/kg, with bupivacaine. This dose of clonidine was seen to decrease mean arterial pressure not to cause bradycardia or respiratory depression.

Techniques of intrathecal or spinal infusions of clonidine are beyond the scope of this review. The experience in adult cancer patients with intractable pain suggests an initial dose of 30-150 µg followed by a continuous infusion of 8-400 µg/day. Extrapolation from experience in adults suggests an initial dose of epidural clonidine of 1-2 µg/kg should also be appropriate either in the subarachnoid or epidural spaces, followed by an infusion of 0.02-0.05 µg/kg/hr, titrating as needed to a maximum of 0.2 µg/kg/hr while observing for undesired hemodynamic effects or sedation.

Chronic Pain Management

General Goals of Therapy

Acute surgical or traumatic pain can generally be expected to last a limited period of time, and this fact influences the therapeutic strategy to manage the pain aggressively with opioids or regional techniques to minimize the pain until healing occurs. Also, short-term duration of pain limits the ability of pain management specialists to develop effective cognitive-behavioral strategies.

However chronic pain is not self-limited, and frequently has no clear anatomic basis. Long term management with opioids is often undesirable in children, and the lack of a clear ability to resolve the underlying mechanism of the pain shifts the focus of the pain management team to increasing coping ability via cognitive-behavioral means while reducing the severity of pain with medical management. The goal is usually not the elimination of pain, but the reduction of pain and the development of coping ability to maximize function. In an adult patient, the goal is to allow the patient to return to gainful employment and function; in a child the goal is to allow the patient to return to school and to maximize socialization with peers.

The majority of our chronic pain complaints are headache, chronic or recurrent nonmalignant abdominal pain, neuropathic limb pain, particularly reflex sympathetic dystrophy, and finally cancer pain. The medical approach to each of these entities is different. All or most patients with chronic pain complaints will benefit from a complete psychological evaluation, identification of personal or family psychopathology, psychotherapy and family therapy, and training in non-pharmacologic behavioral techniques including biofeedback, hypnosis, mental imagery, etc.

Headache in Children

Headache refers to pain felt in or around the cranium including behind the orbits and between the neck and the head. There are several mechanisms for headache, including traction on vascular structures, dilatation and/or inflammation of vascular structures, displacement of cranial contents, increased intracranial pressure, sustained muscle contraction, pressure on cranial nerves, and paracranial pathologic processes including sinusitis, dental infections, etc.

Assuming the clinician has completed a full neurologic history and examination and imaging studies, and has ruled out infection, tumor, vasculitis, and other treatable pathologies that cause secondary headaches, the next task is to classify headache according to the taxonomy of the NIH in 1962:

Table 3. NIH Headache Taxonomy

Vascular Headaches (Migraine)	Classic Migraine Common Migraine Cluster Headaches Hemiplegic And Ophthalmoplegic Migraine Lower-Half Headache
Muscle Contraction Headache	Tension Headaches
Combined Headache	Tension + Migraine
Headache Of Nasal Vasomotor Reaction	Allergic Headaches
Non-Migraine Vascular Headaches	Systemic Infections Hypoxia, CO Poisoning, Nitrate Headache, Caffeine Withdrawal, Postconcussion Syndromes, Hypertension, Hypoglycemia, Hypercapnia, Postictal Headache, "Hangover"
Traction Headache	Neoplasm, Hematoma, Abscess, Post-Lumbar Puncture, Pseudotumor Cerebri
Inflammatory Headache	Meningitis, Encephalitis, etc. Vasculitis

Evaluation

Consists of a detailed diary consisting of a **description of onset and associations** with other illnesses or events including menarche, life stresses, sports, etc.; **time profile** of the headaches including duration, frequency, time of day, etc.; **characteristics** including severity, site, uniformity, and associated symptoms (rhinorrhea, photo- or phonophobia,

nausea, scotomata, etc.); **relief factors** including medications, sleep, time; **associations** including food, activity, beverages, odors, menstrual cycle; **neurologic symptoms** including visual changes, weakness, balance, etc.

Physical examination, EEG, lab evaluation, and imaging studies should of course completely rule out organic disease.

Finally management, having ruled out primary disease, should focus on headache prophylaxis and acute headache management (abortive therapy).

Abortive therapy
NSAIDs:
>Naproxen 5 mg/kg po
>Ibuprofen 10 mg/kg po
>Ketorolac (Toradol®) 0.5 mg/kg IM or IV

Serotonin agonists:
>Sumatriptan (Imitrex®) 0.1 mg/kg s.c., 50 mg p.o., 20 mg nasal spray,
>Naratriptan (Amerge®) 2.5 mg p.o.
>Rizatriptan (Maxalt) 5-10 mg po

Ergotamine:
>Cafergot® 1 mg of ergotamine + 100 mg caffeine q 30 min, max 3 mg

Metoclopramide: 0.1 mg/kg

Butorphanol (Stadol®) nasal spray

Status migraine Treatment

>**Dexamethasone** 0.3 mg/kg IV/IM
>**Dihydroergotamine** (DHE, Migranal®) IV

Prophylactic Treatment
Beta blockade (propranolol 1-2 mg/kg/day, atenolol 1 mg/kg/day, or timolol 0.1-0.5

mg/kg/day)

NSAIDs

Tricyclic antidepressants:

>**Nortriptyline (Pamelor®)** 0.1 mg/kg h.s. advancing to 0.5 mg/kg

>**Amitriptyline (Elavil®)** 0.1 mg/kg h.s. advancing to 0.5 mg/kg

Anticonvulsants:

>**Carbamazepine (Tegretol®)** 10 mg/kg divided doses advancing to 30

mg/kg/day

Gabapentin (Neurontin®) 5 mg/kg divided doses advancing to 40 mg/kg/day

Valproic Acid (Depakote®) 10 mg/kg divided doses advancing to 60 mg/kg/day; especially useful for stabilization of associated mood disorders

Topiramate (Topamax®) 2-4 mg/kg/day at bedtime

Meditation, biofeedback, hypnosis, and other relaxation techniques

Abdominal Pain

Recurrent abdominal pain is pain that occurs at least once a month for at least 3 months. It is an extremely common disorder in children typically between 5 and 12 years of age. Assuming that a complete medical/surgical evaluation and imaging studies have ruled out common and uncommon organic causes of abdominal pain for which specific treatment is available (PUD, Meckel's, malrotation with intermittent volvulus, UTI or obstruction, pancreatic disease, gall bladder disease, hepatic disease, IBD, food allergy, malabsorption syndromes, parasitic disease, neoplasm, pelvic pathology, etc.), then the focus turns to characterizing the disorder, identifying psychosocial features of the disease, and psychiatric management to improve coping and minimizing environmental stress. It is important to remember that while the management of the pain focuses primarily on nonpharmacologic behavioral strategies, many organic causes of pain are difficult to discover. The patient and family must not be labeled as suffering from solely psychiatric disease, because the later identification of organic pathology might undermine the credibility of the practitioner.

Evaluation

The goal is to identify specific characteristics of the pain and unique characteristics of the family and child. The history is parallel to the headache history above.

Pain Management

Opioids are generally avoided because of the chronic and intermittent nature of the disorder and because of the confounding nausea and constipation associated with all opioids. Acetaminophen or NSAIDs may be used liberally, and often recalcitrant cases respond to TCAs. The central focus should be on improving coping skills and reducing family psychopathology.

Neuropathic Pain

Neuropathic pain conditions are associated with injury, dysfunction, or altered excitability of portions of the central or peripheral nervous system. The painful symptoms persist independent of ongoing tissue injury or inflammation, and often intensify over months and years without treatment. This differs from nociceptive pain that typically improves as healing occurs.

Typically neuropathic pain is described as burning, tingling, stabbing pain. It is associated with intense mechanical allodynia even when no skin injury is visible. Drugs that relieve conventional pain (NSAIDs, opioids) are of no value in managing neuropathic pain. On the

other hand, nonconventional analgesics are very effective (antidepressants, anticonvulsants, membrane stabilizing drugs).

Neuropathic pain is more common in children than is frequently recognized, as is one of the most common sources of chronic pain in children. It is often disabling.

Taxonomy

Complex Regional Pain Syndrome Type I: Reflex sympathetic dystrophy, that is, continuous burning pain associated with sympathetic over-activity in an extremity after trauma but without major nerve injury.

Complex Regional Pain Syndrome Type II: Causalgia, that is, sustained burning pain combined with vasomotor, sudomotor, and late trophic changes after traumatic nerve injury.

Differential Diagnosis

Raynaud's disease, septic arthritis, rheumatoid diseases, gout, nerve entrapment syndromes, scleroderma, peripheral neuropathies,

Treatment

Physical therapy. The most important therapeutic modality, it is essential in preserving and restoring limb function.

Ancillary therapy. Several ancillary techniques may be useful, including TENS, acupuncture.

Psychotherapy. Complete psychiatric evaluation is essential to identify family pathology, nonadaptive behavior secondary to the syndrome, secondary gain, etc., and to maximize coping strategies by use of biofeedback, self hypnosis, relaxation therapy, distraction, etc.

Pharmacotherapy. Drug therapy plays an important role in reducing the intensity of pain.

TCAs: Improve sleep and have specific analgesic properties. Through clinical application, antidepressant medications have been found to be effective in treating mood disorders and coincidentally many neuropathic pain states. Most antidepressants take 4-6 weeks to reach full antidepressant effect, but their onset in treating pain states is less clear and usually much shorter. Tricyclic antidepressants are the most studied in treating neuropathic pain. They have multiple mechanisms of action including membrane stabilization, activation of descending inhibitory pain pathways, a local anesthetic effect at the peripheral nerves, as well as having affective input in the limbic system. Most antidepressants take 4-6 weeks to reach full antidepressant effect, but their onset in treating pain states is less clear and usually much shorter. Tricyclic antidepressants are the most studied in treating neuropathic pain. They have multiple mechanisms of action including membrane stabilization, activation of descending inhibitory pain pathways, a local anesthetic effect at the peripheral nerves, as well as having affective input in the limbic system.

Corticosteroids: Empiric trials are sometimes effective in chronic pain states. Dexamethasone produces specific anti-inflammatory effects, but in addition produces antiemesis and mood elevation.

Anticonvulsants: Gabapentin (Neurontin®) is associated with the greatest efficacy and least side effects and toxicity of the anticonvulsants used for analgesia (carbamazepine and valproic acid are the other commonly used anticonvulsants). Gabapentin is an interesting compound that was originally synthesized as a GABA-ergic drug to treat spasticity. It was found to be more effective as a potent anti-convulsants. Animal studies show that gabapentin is effective for treating partial seizures and generalized tonic-clonic seizures. At this time, the mechanism of action of this agent is unclear. Gabapentin may enhance extra-cellular GABA levels by reversing GABA transport in a unique way, by enhanced reversal of GABA transport, and increasing the activity of glutamic acid decarboxylase, a synthetic enzyme necessary for the production of GABA. The compound does not reduce voltage sensitive sodium channels or effect NMDA receptors. On a biochemical level, gabapentin may inhibit a branched chain amino acid transferase ultimately producing a decreased level of glutamate, an excitatory amino acid that may be important in nerve transmission. Increased activity of glutamate dehydrogenase and glutamic acid decarboxylase has also been noted further decreasing levels of glutamate. Finally, gabapentin has been found to act primarily at the alpha-2 dependent delta subunit of L type Ca2+ channels primarily in the hippocampus. Gabapentin has been found to be unequivocally beneficial in treating chronic neuropathic pain syndromes. Mellick reported a series of 4 cases in which adults with complex regional pain syndrome type I (reflex sympathetic dystrophy, RSD) were treated with gabapentin. The authors concluded that gabapentin provided significant pain relief and possible reversal of the disease process.

There is growing experience with topiramate (Topamax), indicating that it will be similarly effective as gabapentin.

Mexiletine may be effective, after the demonstration of a positive IV lidocaine trial. Mexiletine has been used as an oral analog to lidocaine to treat neuropathic pain by decreasing spontaneous neural activity. The original antiarrhythmic studies for lidocaine showed that it was a useful predictor for the antiarrhythmic efficacy of

Table 4. Dosage schedule for adjustment of mexiletine from a starting dose of about 1.6 mg/kg to a final dose of 10 mg/kg, using either 150, 200, or 250 mg tablets

Day of Rx	Rx
Days 1-3:	1 tab h.s.
Days 4-6:	1 tab in morning, 1 tab h.s.
Days 7-9:	1 tab morning, noon, h.s.
Days 10-13:	1 tab morning, noon and 2 tabs h.s.
Days 14-17:	2 tabs morning, 1 tab noon, 2 tabs h.s.
Days 18-:	2 tabs morning, noon, h.s.

End of therapy	Discontinue without weaning

Mexiletine and Tocainide. Tocainide, unfortunately, has significant side effects, blood dyscrasias and interstitial pneumonitis. Mexiletine is much better tolerated, except for its gastrointestinal effects. Moreover, mexiletine is not contraindicated in patients with supraventricular arrhythmias or left ventricular dysfunction.   The table below describes the schedule for initiating mexiletine therapy in a patient.

Repeat sympathetic nerve blocks; placement of an indwelling lumbar sympathetic or stellate ganglion catheter for continuous local anesthetic infusion.

Epidural anesthesia

References

1. Agarwal R, Gutlove DP, Lockhart CH: Seizures occurring in pediatric patients receiving continuous infusion of bupivacaine. Anesth.Analg. 75: 284-286, 1992

2. Berde C: Epidural analgesia in children [editorial; comment]. Can.J.Anaesth. 41: 555-560, 1994

3. Berde CB, Sethna NF, Levin L, Retik A, Millis M, Lillehei C, Micheli L: Regional analgesia on pediatric medical and surgical wards. Intensive Care Med 15 Suppl 1: S40-3, 1989

4. Bray RJ, Woodhams AM, Vallis CJ, Kelly PJ: Morphine consumption and respiratory depression in children receiving postoperative analgesia from continuous morphine infusion or patient controlled analgesia. Paediatr Anaesth 6(2): 129-34, 1996

5. Collins J, Kerner J, Sentivany S, Berde C. Intravenous amitriptyline in pediatrics. Journal of Pain and Symptom Management: 10:471-5, 1995

6. Collins JJ, Geake J, Grier HE, Houck CS, Thaler HT, Weinstein HJ, Twum-Danso NY, Berde CB: Patient-controlled analgesia for mucositis pain in children: a three- period crossover study comparing morphine and hydromorphone. J Pediatr 129(5): 722-8, 1996

7. Doyle E, Harper I, Morton NS: Patient-controlled analgesia with low dose background infusions after lower abdominal surgery in children. Br J Anaesth 71(6): 818-22, 1993

8. Doyle E, Mottart KJ, Marshall C, Morton NS: Comparison of different bolus doses of morphine for patient-controlled analgesia in children. Br J Anaesth 72(2): 160-3, 1994

9. Doyle E, Robinson D, Morton NS: Comparison of patient-controlled analgesia with and without a background infusion after lower abdominal surgery in children. Br J Anaesth 71(5): 670-3, 1993

10. Dunbar PJ, Buckley P, Gavrin JR, Sanders JE, Chapman CR: Use of patient-controlled analgesia for pain control for children receiving bone marrow transplant. J Pain Symptom Manage 10(8): 604-11, 1995

11. Gil KM, Ginsberg B, Muir M, Sullivan F, Williams DA: Patient controlled analgesia: the relation of psychological factors to pain and analgesic use in adolescents with postoperative pain. Clin J Pain 8(3): 215-21, 1992

12. Gunter JB, Eng C: Thoracic epidural anesthesia via the caudal approach in children. Anesthesiology 76: 935-938, 1992

13. Hansen TG, Henneberg SW, Hole P: Age-related postoperative morphine requirements in children following major surgery--an assessment using patient-controlled analgesia (PCA). Eur J Pediatr Surg 6(1): 29-31, 1996

14. Henneberg S W., Hole P, Madsen de Haas I, Jensen PJ: Epidural morphine for postoperative pain relief in children. Acta Anaesthesiol.Scand. 37: 664-667, 1993

15. Krane EJ, Haberkern CM, Jacobson LE: Postoperative apnea, bradycardia, and oxygen desaturation in formerly premature infants: prospective comparison of spinal and general anesthesia. Anesth Analg 80: 7, 1995 Maunuksela EL, Olkkola KT, Korpela R: Does prophylactic intravenous infusion of indomethacin improve the management of postoperative pain in children? Can.J.Anaesth. 35: 123-127, 1988

16. Krane EJ, Jacobson LE, Lynn AM, Parrot C, Tyler DC: Caudal morphine for postoperative analgesia in children: a comparison with caudal bupivacaine and intravenous morphine. Anesth.Analg. 66: 647-653, 1987

17. Krane EJ, Tyler DC, Jacobson LE: The dose response of caudal morphine in children. Anesthesiology 71: 48-52, 1989

18. Krane EJ: Delayed respiratory depression in a child after caudal epidural morphine. Anesth.Analg. 67: 79-82, 1988

19. Max M, Kishore-Kumar R, Schafer S, Meister B, Gracely R, Smoller B, and Dubner R. Efficacy of desipramine in painful diabetic neuropathy: a placebo-controlled trial. Pain: 45:3-9, 1991

20. McCloskey J J., Haun SE, Deshpande JK: Bupivacaine toxicity secondary to continuous caudal epidural infusion in children. Anesth.Analg. 75: 287-290, 1992

21. McCloskey JJ, Haun SE, Deshpande JK: Bupivacaine toxicity secondary to continuous caudal epidural infusion in children [see comments]. Anesth.Analg. 75: 287-290, 1992

22. McNeely JK, Trentadue NC: Comparison of patient-controlled analgesia with and without nighttime morphine infusion following lower extremity surgery in children. J Pain Symptom Manage 13(5): 268-73, 1997

23. McQuay H, Tramer M, Nye B, Carroll D, Wiffen P, Moore R. A systematic review of antidepressant in neuropathic pain. Pain: 68:217-227, 1996

24. Mellick G, Mellick L. Reflex sympathetic dystrophy treated with gabapentin. Arch Phys Med Rehabil: 78:98-105, 1997

25. Mevorach D L., Perkins FM, Isaacson SA: Bupivacaine toxicity secondary to continuous caudal epidural infusion in children. Anesth.Analg. 77: 1305-1306, 1993

26. Millar A J., Rode H, Cywes S: Continuous morphine infusion for postoperative pain in children. S.Afr.Med.J. 72: 396-398, 1987

27. Murrell D., Gibson PR, Cohen RC: Continuous epidural analgesia in newborn infants undergoing major surgery. J.Pediatr.Surg. 28: 548-52; discussion 552-3, 1993

28. Pounder D R., Steward DJ: Postoperative analgesia: opioid infusions in infants and children. Can.J.Anaesth. 39: 969-974, 1992

29. Pullerits J, Holzman RS: Pediatric neuraxial blockade [published erratum appears in J Clin Anesth 1993 Nov-Dec;5(6):529]. J.Clin.Anesth. 5: 342-354, 1993

30. Ready L B., Loper KA, Nessly M, Wild L: Postoperative epidural morphine is safe on surgical wards. Anesthesiology 75: 452-456, 1991

31. Richtsmeier AJ, Barkin RL, Alexander M: Benzodiazepines for acute pain in children. J.Pain Symptom.Manage. 7: 492-495, 1992

32. Schryer NM: Epidural catheters: pain management in the child. Dimens.Crit.Care Nurs. 8: 347-355, 1989

33. Strafford MA, Wilder RT, Berde CB: The risk of infection from epidural analgesia in children: a review of 1620 cases. Anesth.Analg. 80: 234-238, 1995

34. Till H, Lochbuhler H, Lochbuhler H, Kellnar S, Bohm R, Joppich I: Patient controlled analgesia (PCA) in paediatric surgery: a prospective study following laparoscopic and open appendicectomy. Paediatr Anaesth 6(1): 29-32, 1996

35. Tobias J D., Deshpande JK, Wetzel RC, Facker J, Maxwell LG, Solca M: Postoperative analgesia. Use of intrathecal morphine in children. Clin.Pediatr.Phila. 29: 44-48, 1990

36. Tyler DC, Pomietto M, Womack W: Variation in opioid use during PCA in adolescents [see comments]. Paediatr Anaesth 6(1): 33-8, 1996

37. Varley C, McClellan J. Case study: two additional sudden deaths with tricyclic antidepressants. J Am Acad Child Adolesc Psychiatry: 36:390-4, 1997

38. Vetter TR, Heiner EJ: Intravenous ketorolac as an adjuvant to pediatric patient-controlled analgesia with morphine. J Clin Anesth 6(2): 110-3, 1994

39. Vetter TR, Heiner EJ: Intravenous ketorolac as an adjuvant to pediatric patient-controlled analgesia with morphine. J Clin Anesth 6(2): 110-3, 1994

40. Waslick B, Walsh B, and others. Cardiovascular Effects of desipramine in children and adults during exercise testing. J Am Acad Child Adolesc Psychiatry: 38:179-86, 1999

41. Weldon BC, Connor M, White PF: Pediatric PCA: the role of concurrent opioid infusions and nurse- controlled analgesia. Clin J Pain 9(1): 26-33, 1993

42. Wilens T, Biederman J, and others. Cardiovascular effects of therapeutic doses of tricyclic antidepressants in children and adolescents. J Am Acad Child Adolesc Psychiatry: 35:1491-1501, 1996

43. Wolf A R., Hughes D: Pain relief for infants undergoing abdominal surgery: comparison of infusions of i.v. morphine and extradural bupivacaine. Br.J.Anaesth. 70: 10-16, 1993

44. Yaster M, Krane EJ, Kaplan RF, Coté CJ, Lappe DG. Pediatric Pain and Sedation Handbook. Baltimore: Mosby and Co., 1997.

45. Yaster M, Tobin JR, Billett C, Casella JF, Dover G: Epidural analgesia in the management of severe vaso-occlusive sickle cell crisis. Pediatrics 93: 310-5, 1994