

CHAPTER 12

OPIOID ANALGESIA IN THE VERY YOUNG AND THE VERY OLD

The young and the elderly have the most to fear from pain because they are the most defenseless against it.

Liebeskind and Melzack, 1989

The very young and the very old may respond to opioid drugs in a manner different than the typical adult patient. To use these drugs safely in these populations, clinicians should be aware of these differences and appropriately alter the routine approach to prescribing.

Opioids in the very young

In children, long-term opioid therapy is most commonly used to treat cancer-related pain or pain associated with other serious illnesses, such as AIDS or neurodegenerative disorders. Although few studies have evaluated the risk-benefit of long-term opioid use in children, experienced clinicians endorse the need for this treatment in selected patients with other chronic debilitating conditions, such as sickle cell disease, neuropathic pain, and severe headache.

Assessment of pain in children

Assessment is the cornerstone of adequate pain management. The process in children is similar to that in adults but must additionally consider developmental stage and parental knowledge.

The ability of a child to understand and describe pain changes with age. Self-report is the “gold standard” for evaluating pain, and several instruments have been validated to help children describe pain intensity. These include faces in photographs, cartoon faces, colors, and a poker chip tool (ie, child chooses 1 to 4 chips [“pieces of pain”]). Generally, children who are at least 8 years of age can assess their pain using standard numeric or visual analog scales commonly accepted by adults. Beginning at about 3 years of age, children can usually assess their pain if given developmentally appropriate instruments.

Parental attitudes are central to the assessment of pain in children. The reactions of parents strongly influence the child’s expression of pain, and treatment usually depends on the parents’ capacity to evaluate and their willingness to offer therapy. To

ensure adequate treatment, parental attitudes must be understood and an effort must be made to educate. This is particularly important when therapy is unusual or potentially stigmatizing.

Some of the information gleaned from the pain assessment is particularly relevant to children.

This information includes:

- The magnitude of distress for the child and family that is attributed to the pain and the impact of the pain on the child's cognitive functioning, anxiety, depression, and feelings of hopelessness
- The child's and family's perceptions of the cause of the pain and their respective response to it
- The child's perception of what the pain means (eg, punishment, harbinger of more visits to the doctor or hospital)
- A history of pain problems in the child and other family members
- The child's history of birth and early childhood and the family's medical and social history
- Recent stressful events, such as deaths, marital disruption, moves, or other changes in life circumstances

Principles of opioid pharmacotherapy in children

As with adults who have challenging pain syndromes, children with chronic pain appear to respond best to a treatment approach that is multimodal, involving both pharmacologic and nonpharmacologic methods of pain control and a team that is multidisciplinary. Children with complex or refractory problems should be referred to a pediatric pain program, if possible, to ensure that treatment strategies are safe and appropriate and are implemented with a focus on developmental stage and family concerns.

The decision to implement a trial of opioid therapy should be based on the severity of the pain, its associated distress, and other factors elaborated in the pain assessment. Similar to making the decision in adults, clinicians should evaluate the nature of conventional practice and explore the potential risks and benefits of opioid therapy and available alternative treatments. If the decision is made to proceed with opioid therapy, the parents and, if possible, the child should be fully informed about the nature of the therapy, the risk of side effects, the need for communication and adherence, and the issues surrounding abuse and addiction.

Few studies have evaluated opioid pharmacokinetics and pharmacodynamics in children, and dosing recommendations are based primarily on experience in adults (table 30). In the younger or opioid-naïve child, both age and weight influence selection of drug formulation and route of administration.

Table 30. Initial dosing guidelines for opioid analgesics in pediatric patients*

Opioid analgesic	Usual starting intravenous or subcutaneous doses and intervals	
	Child <50 kg	Child ≥50 kg
Codeine	NR	NR
Morphine	Bolus: 0.1 mg/kg q2-4h Infusion: 0.03 mg/kg/hr	Bolus: 5-8 mg q2-4h 0.3 mg/kg q3-4h
Oxycodone	NA	NA
Methadone†	0.1 mg/kg q4-8h	5-8 mg q4-8h
Fentanyl	Bolus: 0.5-1.0 µg/kg q1-2h Infusion: 0.5-2.0 µg/kg/hr	Bolus: 25-50 µg q1-2h Infusion: 25-100 µg/hr
Hydromorphone	Bolus: 0.02 mg q2-4h Infusion: 0.006 mg/kg/hr	Bolus: 1 mg q2-4h Infusion: 0.3 mg/hr
Meperidine‡	Bolus: 0.8-1.0 mg/kg q2-3h	Bolus: 50-75 mg q2-3h

NA, not applicable; NR, not recommended.

* Doses are for patients older than 6 months. In infants younger than 6 months, initial per-kg doses should begin at roughly 25% of the per-kg doses recommended here. Higher doses are often required for patients receiving mechanical ventilation. All doses are approximate and should be adjusted according to clinical circumstances. Recommendations are adapted from summary tables, including those of a consensus statement from the World Health Organization and the International Association for the Study of Pain (World Health Organization, 1998).

† Methadone requires additional vigilance because it can accumulate and produce delayed sedation. If sedation occurs, doses should be withheld until sedation resolves. Thereafter, doses should be substantially reduced or the interval between doses should be extended to 8 to 12 hours, or both.

‡ Use of meperidine should be avoided if other opioids are available, especially for long-term use, because its metabolite can cause seizures.

Adapted, with permission, from Berde CB, Sethna NF. Analgesics for the treatment of pain in children. N Engl J Med 2002;347:1094-103.

For most children, long-term opioid therapy is best implemented using the oral or transdermal routes. Modified-release preparations of opioids must be swallowed whole, which may preclude their use in younger children. If these drugs are prescribed, parents must be educated that crushing or chewing such formulations releases the full dose immediately, potentially leading to overdose. Transdermal fentanyl also must be used cautiously, because the smallest patch

Usual starting oral doses and intervals

Child <50 kg	Child ≥50 kg
0.5-1.0 mg/kg q3-4h	30-60 mg q3-4h
Immediate release: 15-20 mg q3-4h	Immediate release:
Sustained release: 20-35 kg, 10-15 mg q8-12h; 36-50 kg, 15-30 mg q8-12h	Sustained release: 30-45 mg q8-12h
0.1-0.2 mg/kg q3-4h	5-10 mg q3-4h
0.1-0.2 mg/kg q4-8h	5-10 mg q4-8h
NA	NA
0.04-0.08 mg/kg q3-4h	2-4 mg q3-4h
2-3 mg/kg q3-4h	100-150 mg q3-4h

currently available, which delivers 25 µg of fentanyl per hour, provides a dose that is too high for younger, opioid-naïve children. Parents also must be told that the patch cannot be cut into smaller pieces in an attempt to reduce the dose.

Use of painful injections should be avoided in children, because it may lead to the underreporting of pain. Rectal administration also is uncomfortable and should be limited. If short-term parenteral administration is needed, the intravenous route is preferred.

Individualization of the dose is as important in children as it is in adults. This requires repeated assessment of analgesia and side effects. It may be necessary to ask very specifically about side effects, such as constipation or unpleasant dreams, because children may be reluctant to report them. Side effects must be managed aggressively.

Opioids in the very old

Chronic pain is highly prevalent in older patients and has multiple etiologies. Painful osteoarthritis and degenerative spinal disorders are very common in the older US population, and the

prevalence of many painful medical disorders, including cancer, postherpetic neuralgia, and painful diabetic polyneuropathy, increases with age. Large surveys have suggested that, unfortunately, pain in older adults is often undertreated.

Treatment of pain in the geriatric population can be complicated by cognitive impairment and other sources of communication difficulties, gait and balance disturbances, deconditioning, sensory impairments, and comorbidities that increase the risk of therapy (eg, cardiovascular disease, pulmonary disease). As a result, the ill effects of pain, such as mood disorder (especially depression), social isolation, poor sleep, gait disturbance, and inability to perform routine activities of daily living, can be compounded.

Use of analgesics in older patients also may be complicated by concurrent treatment with multiple medications for comorbid disease and symptom management. In this group of patients, drug-drug and drug-disease interactions are a far more significant concern and the consequences of drug-related adverse effects, such as falls, confusion, or obstipation, can have much graver consequences than in younger patients.

Aging and opioid pharmacology

Sensitivity to both the analgesic effects and the side effects of opioids increases with age. Studies in postoperative patients older than 40 years demonstrate a linear age-related increase in the analgesic response to fixed morphine doses. This relationship is explained by both pharmacokinetic and pharmacodynamic factors.

Opioid kinetics change as a result of age-related alteration in drug absorption, distribution, metabolism, and clearance, all of which are influenced by body composition changes (eg, a reduced muscle-to-fat ratio) and reductions in serum protein levels, cardiac output, and organ perfusion. Pharmacodynamic changes relate to poorly understood central nervous system processes that increase sensitivity to both analgesic and adverse effects. The few studies that have evaluated pharmacodynamic effects of analgesic drugs in older patients found that the rate of drug delivery, rather than the absolute dose of drug over time, influences both analgesia and adverse effects, including the risk of respiratory depression.

Assessment in patients who cannot self-report

A significant challenge in geriatric care is the management of symptoms in patients who cannot communicate. Typically, these are patients with advanced dementia, such as Alzheimer's disease or multi-infarct dementia. Patients with dementing diseases

who lack the cognitive capacity to describe their pain have been shown to receive for the same clinical conditions significantly less opioid analgesic than nondemented patients receive.

When self-report is impossible, pain assessment must rely on other measures. Observable behaviors and bodily changes suggesting pain include:

- Facial expressions or body posturing (eg, grimacing, guarding, rigidity)
- New or changed vocalizations
- Change in sleep patterns
- Agitation or restlessness
- Withdrawal from social interaction
- Decreased interest in previous enjoyments (eg, music, feeding, massage, bathing)
- Inconsolability
- Tachycardia, tachypnea, hypertension, diaphoresis

Although the absence of these phenomena does not imply comfort, their presence suggests distress and, in the right context, pain. When other assessments are impossible, an analgesic trial may be appropriate when these observations are made.

Managing the noncommunicative patient

To treat pain in a population that cannot communicate, clinicians must develop the skills necessary to anticipate and recognize nonverbal indicators of distress, treat empirically, and monitor the outcomes of therapy. In some cases, initiating a trial of an opioid may be the best means of testing the hypothesis that a patient who cannot communicate is experiencing pain. Changes in usual behaviors, vocalizations, various forms of agitation, and alterations in eating, sleeping, or interpersonal response patterns may be modifiable by both pharmacologic and nonpharmacologic analgesic therapies. Agitation that responds to analgesics does not require treatment with psychotropics, the effects of which may be to mask the symptoms rather than treat the source of distress. This type of empirical pain management may protect the dignity of these vulnerable patients and provide sensitive and humanistic care.

Principles of pharmacotherapy in older persons

All older patients with functional impairment or diminished quality of life resulting from persistent pain are candidates for pharmacologic therapy. Generally, the same principles applied in younger adults when selecting an opioid trial and implementing therapy may be used in geriatric patients. However, age-related factors must be considered and suggest the following guidelines

and specific dosing recommendations when opioids are used (table 31).

- Slowly and carefully titrate opioids, having specific subjective and objective end points in mind. (ie, 50% of usual adult starting dose).
- Prevent and treat adverse events, particularly constipation, sedation, ataxia (dysmobility and falls), nausea, and cognitive disturbances, including delirium.
- For patients experiencing severely debilitating pain, titrate the opioid rapidly and consider hospital admission for diagnosis, aggressive treatment, and close monitoring.
- Simplify drug regimens as much as possible and adjust regimens to meet individual needs, lifestyle, and care settings.
- Be aware of common economic barriers, including limitations of Medicare reimbursement for outpatient oral medications, limited formularies, and delays from mail-order pharmacies in some managed-care programs. (A noteworthy exception is that the Medicare Hospice Benefit covers the cost of all medications associated with the diagnosis that prompted admittance into the hospice.)
- Do not prescribe propoxyphene or meperidine for older patients; neuroexcitatory side effects may be more likely in this population because of central sensitivity and subclinical renal insufficiency.
- Use methadone very cautiously, because its long and variable half-life makes it especially problematic in older patients. Adverse effects from drug accumulation may arise several days after regular dosing begins.
- If the patient drives, consider restricting driving until doses are stable and cognitive capacity is reassessed.
- For patients with borderline mobility capabilities and a propensity for falls, monitor carefully for increasing gait and balance disturbances.
- Warn patients that chewing or crushing continuous-release tablets destroys their controlled-release properties and causes rapid absorption of the entire dose, which may result in overdose.

Table 31. Recommended opioid analgesic drugs for older patients with moderate to severe pain

Drug	Oral equivalent	Starting dose	Aging effects	Precautions and recommendations
Short-acting drugs			<ul style="list-style-type: none"> • Anticipate increased sensitivity and duration of action with advancing age 	<ul style="list-style-type: none"> • Best for episodic, intermittent, or breakthrough pain • Always commence a bowel stimulant regimen (eg, senna compounds, bisacodyl) when initiating opioid therapy
Morphine	30 mg	5-15 mg q4h	<ul style="list-style-type: none"> • Intermediate half-life 	<ul style="list-style-type: none"> • Start low and titrate to comfort and functional outcomes • Monitor for clinical evidence of toxic metabolite accumulation (sedation, myoclonus, agitation), especially with diminished renal clearance
Codeine	120 mg	15-30 mg q4h	<ul style="list-style-type: none"> • Acetaminophen-NSAID combinations limit dose • Constipation is a major issue 	<ul style="list-style-type: none"> • Anticipate and prevent side effects • Begin bowel program early • Do not exceed recommended maximum dose of fixed-dose combination formulations
Hydrocodone	30 mg	5-10 mg q3-4h	<ul style="list-style-type: none"> • Acetaminophen-NSAID combinations limit dose • Toxicity similar to morphine 	<ul style="list-style-type: none"> • Anticipate and prevent side effects • Begin bowel program early • Do not exceed recommended maximum dose of fixed-dose combination formulations
Oxycodone	20-30 mg	5-10 mg q3-4h	<ul style="list-style-type: none"> • Acetaminophen-NSAID combinations limit dose • Toxicity similar to morphine • Available as a single agent 	<ul style="list-style-type: none"> • Anticipate and prevent side effects • Begin bowel program early • Do not exceed recommended maximum dose of fixed-dose combination formulations
Hydromorphone	7.5 mg	1-2 mg q3-4h	<ul style="list-style-type: none"> • Half-life may be shorter than morphine (3 hr) 	<ul style="list-style-type: none"> • Similar to morphine • Start low and titrate to comfort and functional goals
Long-acting drugs*			<ul style="list-style-type: none"> • Anticipate increased sensitivity and duration of action with advancing age 	<ul style="list-style-type: none"> • Best for continuous pain • Always commence a bowel stimulant regimen (eg, senna compounds, bisacodyl) when initiating opioid therapy
Modified-release morphine	30 mg	15-30 mg q12-24h	<ul style="list-style-type: none"> • Occasionally requires more frequent dosing than recommended on package insert 	<ul style="list-style-type: none"> • Escalate dose slowly because of possible drug accumulation • Short-acting opioid analgesic often necessary for breakthrough pain, especially for patients with pain related to movement or weight-bearing activity (incident pain)
Modified-release oxycodone	20-30 mg	10 mg q12-24h	<ul style="list-style-type: none"> • Similar to sustained-release morphine 	<ul style="list-style-type: none"> • Similar to sustained-release morphine
Transdermal fentanyl	See package insert for recommended dose equivalencies	25-mg patch is lowest available dose	<ul style="list-style-type: none"> • Effective activity may exceed 72-hr usual duration of action 	<ul style="list-style-type: none"> • Not recommended for opioid-naïve patients • Titrate slowly using short-acting analgesics for breakthrough pain • Peak effects of first dose may take 18-24 hr • Responsible caregiver should be available during dose titration

NSAIDs. nonsteroidal anti-inflammatory drugs.

* Some practitioners favor the use of methadone because of its comparatively low cost. However, very careful monitoring and ample clinical experience are needed because of propensity for drug accumulation and the wide variation in apparent relative potency, especially in older patients. A responsible caregiver should be available for monitoring during dose titration and dose escalation phases of treatment.

Adapted, with permission, from Fine PG. Opioid analgesic drugs in older people. *Clin Geriatr Med* 2001;17:479-87, vi.

Suggested readings

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