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Equianalgesic Dosing of Opioids for Pain Management

Lead author: Jennifer Obenrader, Pharm.D.

Equianalgesic doses contained in this chart are approximate, and should be used only as a guideline. Dosing must be titrated to individual response. There is often incomplete cross-tolerance among these drugs. It is, therefore, typically necessary to begin with a dose lower than the equianalgesic dose when changing drugs and then titrate to an effective response. Dosing adjustments for renal or hepatic insufficiency and other conditions that affect drug metabolism and kinetics may also be necessary.[1-4]

Drug	Equianalgesic Doses (mg)		Approximate Equianalgesic 24hr Dose (Assumes Around-the-Clock Dosing)		Usual Starting Dose (Adults >50kg) (Doses NOT Equianalgesic)	
	Parenteral	Oral	Parenteral	Oral/Other	Parenteral	Oral/Other
Morphine (*Roxanol*)	10	30	3-5 mg q 4 h	10 mg q 4 h	2.5-5 mg q 4 h	5-10 mg q 4 h
Controlled-release morphine (*MS Contin, Oramorph SR*)	NA	30	NA	30 mg q 12 h	NA	15 mg q 12 h
Hydromorphone (*Dilaudid*)	1.4	7.5	1mg q 4 h	2-4 mg q 4 h	0.5-1 mg q 4 h	1-2 mg q 4 h
Oxycodone (*Roxicodone, OxyIR*, also in *Percocet, Percodan, Tylox*, others)	NA	20	NA	5-7.5 mg q 4 h	NA	5 mg q 4 h
Controlled-release oxycodone (*Oxycontin*)	NA	20	NA	10-15 mg q 12 h	NA	10 mg q 12 h
Hydrocodone (in *Lorcet, Lortab, Vicodin*, others)	NA	30	NA	30 mg q 3-4 h	NA	10 mg q 3-4 h
Codeine	120	200	130 mg q 3-4 h	180-200 mg q 3-4 h	10-60 mg q 2 h	30-60 mg q 3-4 h
Methadone (*Dolophine*)	1-10	2-20	The conversion ratio of methadone is highly variable depending on factors such as patient tolerance, and length of dosing (short term versus chronic dosing). Because the analgesic duration of action is shorter than the half-life, toxicity due to drug accumulation can occur within 3-5 days.			
Fentanyl (*Sublimaze, Duragesic* (patch))	0.1	NA	Transdermal patch 25 mcg/hr (for chronic pain only) roughly equivalent to oral morphine 50 mg/24hr. Upward titration of patch no more frequently than every 3 days.			
Meperidine (*Demerol*)	75	300	Should be used for acute dosing only (short duration of action (2.5-3.5 hours) and neurotoxic metabolite, normeperidine). Avoid in patients with renal insufficiency, CHF, hepatic insufficiency, and the elderly (potential for toxicity due to accumulation of the metabolite normeperidine). Seizures, confusion, tremors, or mood alterations may occur.			

NA = not available.

Background

Opioids, the mainstay class of analgesics used for treatment of moderate to severe pain, are effective, have a superior benefit-to-risk ratio, and are easily titrated with no ceiling effect. The chosen dose is one that offers the most effective pain relief with the fewest side effects. When patients are not getting sufficient pain relief in spite of increasing the dose or are complaining of side effects, then another opioid agent should be considered. The practice of converting a patient from one opioid to another, as the clinical situation warrants, is often referred to as opioid rotation. Opioid rotation calls for the determination of approximate equianalgesic dosing conversions. Relative analgesic potency,

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or the ratio of doses necessary to produce an opioid equianalgesic dosing table. It is imperative to recognize, however, that a table of this type is to be used only as a conversion guide among these agents. When converting a patient from one opioid to another, an equianalgesic dosing table is one helpful tool for determining an appropriate equianalgesic dose.[1-4]

Opioids can be identified as complete morphine-like agonists, partial agonists, or mixed agonists-antagonists. This classification depends on the receptors to which they bind, as well as their activity at these receptors. The benefits of using opioids and the risks associated with their use vary among individuals. Morphine, hydromorphone, oxycodone, hydrocodone, methadone, codeine, and fentanyl are classified as full agonists. The effectiveness of these drugs is not limited by a ceiling effect with increasing doses. Full agonists also do not antagonize the effects of other full agonists given at the same time. Partial agonists have less of an effect than full agonists at opioid receptors. Partial agonists, such as buprenorphine (*Buprenex*), are also less effective analgesics because they are limited by the dose-related ceiling effect. Mixed agonist-antagonists block or are neutral at one type of opioid receptor, and are active at another opioid receptor. These mixed agonist-antagonists, such as pentazocine (*Talwin*), butorphanol tartrate (*Stadol*), dezocine (*Dalgan*), and nalbuphine hydrochloride (*Nubain*), are contraindicated for use in patients receiving an opioid agonist because they can precipitate withdrawal and increase pain. These mixed agonist-antagonists are also less effective analgesics because they are limited by the dose-related ceiling effect.[1]

Methadone, a synthetic opioid agonist, has been reported to have a number of distinctive properties. These distinctions include superb oral and rectal absorption, a prolonged duration of action, and no known active metabolites. However, because of its unpredictable half-life and somewhat unknown equianalgesic dose, methadone is often used only by pain specialists. The methadone preparation most commonly used in the US is a racemic mix of both the d-isomer and l-isomer of methadone. The d-isomer has antagonist activity at the N-methyl-D-aspartate (NMDA) receptor and appears to be beneficial in controlling neuropathic pain. When switching from an opioid to methadone, the equianalgesic equivalent degree of analgesia, is the basis for the dose ratio of methadone depends on the oral morphine-equivalent daily dose (MEDD) of the preceding opioid. Additional methods of switching to methadone have also been suggested. Some methods count on patient-controlled analgesia with fixed doses and flexible intervals, some require fixed intervals and fixed doses, while others stagger the conversion over a few days. Regardless of the method, this kind of switch requires regular assessments and an understanding of the equianalgesic dose ratio of methadone to morphine in opioid-tolerant patients.[1-3]

Oral MEDD (mg/day)[1-3]	**Initial Dose Ratio (oral morphine: oral methadone)[1-3]**
<30	2:1
30-99	4:1
100-299	8:1
300-499	12:1
500-999	15:1
>1000	20:1 or greater

Meperidine, another opioid option in the treatment of pain, is considered useful only for acute pain. It is not recommended as a long-term treatment option due to its short duration of action and the neurotoxic metabolite, normeperidine. Accumulation of normeperidine, especially when renal function is impaired, causes central nervous system (CNS) stimulation that can progress to seizures. The seizure activity is often preceded by the development of multifocal myoclonus, which clinicians can use as a warning sign.[1]

In general, the first step in switching from one opioid to another is to calculate the total dose of opioids, both short and long acting, used in a 24 hour period. Use an equianalgesic-dose table to estimate the daily dose of the new agent. The dosing interval is then determined by the formulation (immediate versus slow release) used. Because wide ranges in individual responses to the various opioids have been noted, the calculated dose of the new drug should typically be reduced by at least 25% to ensure safety. The

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dose may then be titrated to an appropriate followed closely, reassessed, and dose adjusted according to the intensity of pain and lack or presence of adverse effects. The selection of another opioid is largely subjective because little evidence exists to indicate that one opioid is therapeutically superior over another opioid.[1-4] Long-acting opioids are typically chosen for scheduled dosing, once the effective analgesic therapy has been established, and immediate release opioids are used for rescue dosing. When rescue doses become consistently needed for more than 3 to 5 times per day, the scheduled long-acting opioid may then be increased. Equianalgesic doses may also differ when making a switch from oral to IV or SC forms.[1,3,5] When hydrocodone or codeine is being used, the amount of acetaminophen or ibuprofen in each dose must also be a consideration. A combination of a daily sennoside and stool softener to prevent constipation may also be necessary in patients on chronic opioid therapy.

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