ROUTES OF ADMINISTRATION:

- ORAL
- SUBCUTANEOUS
- INTRAMUSCULAR
- INTRAVENOUS
- EPIDURAL/INTRATHECAL
- RECTAL
- TRANSDERMAL

ORAL:

Oral opioids can be very effective in treating pain. The World Health Organisation (WHO) states that analgesics should be administered by the oral route, whenever possible.

They should be given

"by the clock"

at regular dosing intervals and not on an

"as required"

basis, which tends to result in maximum side effects and minimum analgesia.

Irregular intervals and insufficient dose are likely to lead to the pain returning repeatedly and the patient constantly seeking higher doses.

It must be remembered that only about 40% of the administered dose of some preparations will actually reach the plasma due to "first-pass metabolism."

Opioid analgesic	Oral bioavailability(%)
Oxycodone	60-87
Hydromorphone	60
Morphine	24
Buprenorphine	14

POTENCY: *(relative to effective dose of morphine)

	POTENCY *	DURATION (HOURS)
MORPHINE	1	4-5
HEROIN	2	3-4
HYDROMORPHONE	5	4-5
CODEINE	0.1	4-6
OXYCODONE	0.75	4-5
METHADONE	1	24-48
MEPERIDINE	0.1	2-4
PROPOXYPHENE	0.05	6
FENTANYL	100	1-3
PENTAZOCINE	0.2	2-3

(Based on Jaffe and Martin 1990, and Zacny, 1995, from Drug Use and Misuse, Maisto, Galizio and Connors, 1999, 3rd.Ed.)

Commonly used opioids include morphine, hydromorphone, codeine, oxycodone, hydrocodone, methadone, levorphanol and fentanyl. These opioids are classified as full agonists (see above)

They do not have a ceiling to their analgesic efficacy and will not work against the effects of other opioids within the class when given simultaneously. The term ceiling effect refers to a dose that if increased will produce no change in effect.

There is no maximum recommended dose for full opioid agonists (except in opioid-na?ve patients) so the dose can continue to be titrated up according to pain level and side-effects to very high doses if necessary.

The American Academy of Family Physicians("Treatment of Nonmalignant Chronic Pain" March 1, 2000) has suggested that short-acting opioids should not be given chronically on a daily basis in most cases as there is a higher incidence of side-effects and development of tolerance.

Usually, the milder agents are prescribed first, reserving the stronger ones for more intractable pain, according to the WHO analgesic ladder. The WHO advocates use of non-opioids at Step 1 followed by opioids at Steps 2 and 3 for moderate to severe pain.

Traditionally, weak opioids such as codeine and dihydrocodeine are used at Step 2, stronger agents such as morphine being reserved for Step 3.

Expert opinion([i]) suggests that

"there is no one optimal or maximal dose of a step 3 opioid analgesic drug."

Moderate pain can also be treated with an opioid/ non-opioid combination. However, it may be better to treat with just the opioid so that it can be titrated without having to worry about exceeding maximum daily dosages of non-opioids, for example the maximum daily dose of paracetamol(acetaminophen) = 4000 mg daily. In the case of severe pain, mu agonists are preferred.

Elderly patients or those with major organ failure must be treated carefully with due consideration of changes in metabolism and elimination of drugs. Opioids with short half-lives are recommended (morphine, hydromorphone, oxycodone).

These drugs achieve stable blood concentrations within 24 hours making them simpler to titrate and monitor (Coyle, Cherny, Portenoy, 1995). Drugs with active metabolites (propoxyphene, meperidine) should be avoided in the elderly and in all patients with renal disease.

The patient's age is of much more importance than their weight, in fact, studies have shown there is no correlation between weight and analgesic requirements (Burns, Hodsman, McLintock et al., 1989; White, 1990).

Concurrent medication may affect the way in which the opioid is metabolised and made bioavailable. (see Drug interactions.) If the rate of metabolism is increased , lowered plasma levels of the opioids may result and thus insufficient pain control.

True allergies to opioids are somewhat rare but individual patients may have idiosyncratic reactions to specific drugs. For instance, a lady was taking hydromorphone and developed a persistent cough which was inexplicable despite numerous tests.

On changing the hydromorphone to another drug, the cough completely cleared up.

Zenz et al ([ii]) looked at 100 patients using chronic oral opioids. They found that 51% reported good pain relief, 28% partial pain relief and all patients had improved function.

Generally, when opioid therapy is commenced, the necessary dose is established by titrating up short-acting preparations. However, the majority of patients on long-term opioids are maintained on long-acting preparations such as MS Contin.

These allow a steadier plasma level of the drug to be maintained and also reduce the number of tablets that need to be taken.

As a rule, it is best to begin treatment with a low test dose, to avoid serious or intolerable side-effects. Should these arise, an alternative opioid may be tried. If the initial dose is ineffective, then a second dose 3-4 hours later, say 50-75% higher may be attempted.

If the second dose is ineffective (but tolerated) a further increase of 50% 3-4 hours later is tried. With each dose, the pain level and side-effects should be recorded.

Once pain relief has been achieved, the relevant dose may be repeated at 4-6 hourly intervals. There may be some adjustment necessary depending on effectiveness and side-effects. In general, short-acting opioids reach a steady state (stable plasma level) after about 48 hours.

After becoming accustomed to short-acting opioids, it is possible to move onto longer-acting preparations. If methadone is being used, doses should only be increased every 3 days as it is very slowly metabolised and may otherwise accumulate to dangerous levels.

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[i] Levy MH.. *N Engl J Med* 1996;335:1124-32. Pharmacologic treatment of cancer pain

[ii] Zenz M, Strumpf M, Tryba M, *J Pain Symptom Manage* 1992;7:69-77 Long-term oral opioid therapy in patients with chronic non-malignant pain