PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #53
SUBLINGUAL MORPHINE

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Background The preferred route of administration of analgesics for most patients in pain is oral (PO) considering the longer duration of action and convenience of use in non-hospital settings compared with subcutaneous and intravenous formulations. Soluble tablets of morphine were once commonly used for off-label sublingual (SL) administration in patients who were unable to swallow pills or large quantities of solutions. Although some hospice pharmacies still may be able to compound soluble morphine for sublingual use, the manufacture of soluble tablets of morphine has not been available in the United States since 2007. Instead, most pharmacist experts recommend the use of concentrated oral solution (20 mg/mL) of morphine or oxycodone for this clinical application.

Pharmacology of SL Morphine SL administration of morphine via soluble tablets was used to treat breakthrough pain to hasten analgesic onset and peak; however, available data do not support more rapid absorption of soluble morphine tablets when compared with more traditional oral formulations of morphine (1-3). Indeed, several clinical studies found no substantial advantage to the use of soluble morphine tablets over oral morphine (4-6).

- Mean time to maximum concentration has been shown to be shorter for PO morphine (0.8 + 0.35hr) compared with soluble morphine tablets (1.75 + 1.30 hr), indicating that soluble morphine tablets are likely swallowed and absorbed gastrointestinally rather than through the oral mucosa (3).
- The bioavailability (amount of drug eventually made available to the systemic circulation) of soluble morphine tablets are relatively low: only 9%
- Agents are most readily absorbed through the oral mucosa when they are potent, non-ionized at physiological pH, and lipid soluble (see *Fast Fact* #103). Morphine has a relatively low potency for an opioid, is 90% ionized at the pH of the mouth, and is one of the least lipid soluble opioids. These factors likely explain its poor performance as a SL or buccal medication.

Pharmacology of Concentrated Oral Solutions of Morphine and Oxycodone In lieu of the poor evidence supporting the efficacy of soluble morphine tablets, they are not manufactured in the United States anymore. Instead, the use of concentrated (20 mg/mL) of oral morphine solution has been more commonly utilized for imminently dying patients who are unable to tolerate pills or significant volumes of an opioid solution.

- The bioavailability of the oral solution is 23.8%.
- Concentrated oral morphine solution is considered to be equianalgesic with soluble morphine tablets.
- The amount of SL absorption of the 20 mg/mL concentrated oral morphine solution is estimated to be only 18-20%. Its clinical effect is more likely due to the dose being swallowed with saliva and absorbed gastrointestinally.
- Oxycodone also comes available as a 20 mg/mL solution. The most concentrated oral solution available for methadone is a 10 mg/mL solution. Hydromorphone is not available in a concentrated oral solution.

Formulation and Dosing

- There are several forms of short acting PO morphine available, however, only the soluble tablets or the concentrated oral solution are suitable for SL use. Nonsoluble morphine sulfate immediate release (MSIR) tablets will not be absorbed sublingually, even when crushed, because they will not liquefy under the tongue.
- A usual starting dose for an opioid naïve patient is 5-15 mg PO or every 3 hours. The equianalgesic ratio of IV to PO morphine is 1:3 (10mg of IV morphine is approximately equianalgesic to 30 mg PO/SL morphine).

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