FAST FACTS AND CONCEPTS #53
SUBLINGUAL MORPHINE
Debra Gordon RN, MS, FAAN, Sean Marks MD, Bridget Protus PharmD

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).
References:


Fast Facts and Concepts are edited by Sean Marks MD (Medical College of Wisconsin) and associate editor Drew A Rosielle MD (University of Minnesota Medical School), with the generous support of a volunteer peer-review editorial board, and are made available online by the Palliative Care Network of Wisconsin (PCNOW) and the Center to Advance Palliative Care (www.capc.org). Fast Facts and Concepts are editorially independent of PCNOW and the Center to Advance Palliative Care, and the authors of each individual Fast Fact are solely responsible for that Fast Fact’s content. The full set of Fast Facts are available at http://www.mypcnw.org/#!fast-facts/cb1h or http://www.capc.org/fast-facts/ along with contact information, and how to reference Fast Facts.

Copyright: All Fast Facts and Concepts are published under a Creative Commons Attribution-NonCommercial 4.0 International Copyright (http://creativecommons.org/licenses/by-nc/4.0/). Fast Facts can only be copied and distributed for non-commercial, educational purposes. If you adapt or distribute a Fast Fact, let us know!

Disclaimer: Fast Facts and Concepts provide educational information for health care professionals. This information is not medical advice. Fast Facts are not continually updated, and new safety information may emerge after a Fast Fact is published. Health care providers should always exercise their own independent clinical judgment and consult other relevant and up-to-date experts and resources. Some Fast Facts cite the use of a product in a dosage, for an indication, or in a manner other than that recommended in the product labeling. Accordingly, the official prescribing information should be consulted before any such product is used.