



# Formulary Flash



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## Fentanyl Is Superior To Morphine Fact or Myth ... Revisited

### Background

Selection of an opioid for acute pain management is based upon efficacy, side effect profile, interactions with other central depressants, and duration of action. The likelihood of respiratory depression, apnea, and addiction potential are also of concern. The pharmacodynamics and pharmacokinetics of opioids vary with route and rate of administration.

Reasons cited for inadequate pain management include lack of understanding of opioid pharmacology by physicians and nurses. This is also the major cause of morbidity and mortality associated with the use of opioid analgesics. A brief review of each drug's effects when given as an IV bolus can be found in Table I (reverse side of page).

A request by the Emergency Center resulted in an *ad hoc* subcommittee which recommended revisions to the restrictions.

### Restrictions (revised at November meeting)

Three opioid analgesics commonly used at UHS are morphine, hydromorphone, and fentanyl. Of the three, fentanyl is the least safe and dangerously efficacious when given as an IV bolus.

The P&T Committee restricted the use of IV fentanyl as follows :(*November revisions are italicized & underlined*):

1. IV push fentanyl in the treatment of acute pain to the following services and situations:
  - Any service for patients in the OR, PACU, ICUs, EC and intermediate care where standards of an ICU are met. Standards of ICU care are defined as electrophysiologic monitoring and a nurse at the bedside for the duration of the analgesic effects of Fentanyl.
  - Anesthesiology and Acute Pain Service for patients in any location when ICU standards are not in effect.
2. IV PCA fentanyl for patients on the regular floors, intermediate care, or ICUs managed by the Acute Pain Service. Contact Brenda Perry RN at 756-2270
3. For conscious sedation for invasive procedures per the existing conscious sedation policy, with full non-invasive monitoring and a nurse/physician dedicated to monitoring the patient during the procedure and through recovery after the procedure:
  - Recommended dosing of IV fentanyl is 25-50 mcg q 3-5 minutes (maximum 100 mcg) after other central depressant drugs have been given

There will be **no restriction** on the use of the following:

- Fentanyl patches for chronic pain
- Neuraxial fentanyl-containing infusions managed by the Acute Pain Service
- Fentanyl infusions in the ICUs

### Side Effects

#### Side Effects Common to All These Drugs

- Constipation, nausea, vomiting, dysphoria, sedation, respiratory depression
- Oversedation precedes respiratory depression
- The slower the onset time, the more likely oversedation will be recognized before apnea ensues

#### Fentanyl Side Effects

- High lipophilicity and rapid onset of action make it **highly apneagenic**, especially in the presence of other central depressants
- **Highest emetogenicity**
- Synthetic opioids are associated with **muscle rigidity**
  - Semi-synthetic and naturally occurring opioid alkaloids do not have this property
  - Muscle rigidity can occur with doses as low as 25 mcg in a 70 kg adult
  - Apnea caused by muscle rigidity is often confused for apnea caused by mu-1 receptor agonism
  - Unfortunately, muscle rigidity prevents artificial ventilation by any means until naloxone or a neuromuscular blocking drug is given to reverse the effect
  - Resuscitation while awaiting pharmacological intervention is ineffective
- **Addiction potential is greatest** with highly lipophilic drugs with a rapid onset and short duration of action
  - Addiction potential from least to greatest is morphine, hydromorphone, fentanyl

### Summary

**Myth:** Fentanyl is "better" than morphine

**Facts:** Morphine and hydromorphone are the safest and most efficacious opioids when given by IV bolus. Fentanyl is the least safe of the opioids when given by IV bolus and in combination with other central sedatives.

**Table I.**

	<b>Morphine</b>	<b>Hydromorphone (Dilaudid®)</b>	<b>Fentanyl (Sublimaze®)</b>
<b>Description</b>	Gold standard opioid analgesic; naturally occurring alkaloid derived from opium	Semi-synthetic morphine derivative	100% synthetic
<b>Properties</b>	Highly hydrophilic; strongly lipophobic	Hydrophilic but less so than morphine; moderately lipophilic	Highly lipophilic; strongly hydrophobic
<b>Onset Time (IV push)</b>	5 minutes	3 minutes	< 1 minute
<b>Peak Effect (IV push)</b>	10 minutes	8 minutes	2 – 3 minutes
<b>Duration of Action (IV push)</b>	1 – 4 hours	1 – 4 hours	30 – 45 minutes
<b>Dose (IV push)</b>	0.05 – 0.1 mg/kg, repeat to effect	0.01 – 0.02 mg/kg, repeat to effect	<b>0.25 – 0.5 mcg/kg</b> , repeat to effect
<b>Equianalgesic Dosing for Acute Administration</b>	10 mg	2 mg	100 mcg
<b>Sedation</b>	Moderate	Mild	Minimal to None
<b>Active Metabolites</b>	Morphine-6-glucuronide: more potent analgesic and respiratory depressant than morphine; renal excretion	None	None
<b>Apnea at Therapeutic Doses</b>	Low	Low	High
<b>Chest Wall Rigidity</b>	None	None	High
<b>Addiction Potential</b>	Low	Low to Moderate	High

Reference

"Postoperative Pain Management" editors F. Michael Ferrante and Timothy R. VadeBoncouer; chapter 8, "Opioids" by F. Michael Ferrante, pages 145-209.

Contact Dr. Lynda Wells ([wellsl@uthscsa.edu](mailto:wellsl@uthscsa.edu)) for further information.

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