

## *Hospital Peer Review*

**November 2009**

Hospital Peer Review is a monthly newsletter sponsored by the Rural Healthcare Quality Network to alert Critical Access Hospitals regarding findings from the Peer Review Program. Summarized are a few of the key findings and best practices that would be helpful for other critical access hospitals to be knowledgeable about. This newsletter is edited by Myron Bloom, Medical Director and he can be reached at [drmbloom@msn.com](mailto:drmbloom@msn.com).

### **Caution when Patching Pain**

Fentanyl is approximately 100 times more potent than morphine. While it has a shorter half-life, it is also more lipid-soluble than morphine, which results in a more rapid onset of action, due to improved penetration of the blood-brain barrier. Fentanyl is free of histamine-releasing properties and may therefore be preferred in the presence of hemodynamic instability or bronchospasm. Fentanyl is commonly given as intravenous boluses every 30 to 60 minutes or as a continuous intravenous infusion in an intensive care unit setting, but is also available in a transdermal patch, which is the topic of this paper.

#### **The patch should only be prescribed for patients with moderate to severe pain who have been taking regular doses of oral opioids for a week or more and are therefore opioid-tolerant.**

Fentanyl patches are presently manufactured in five micrograms/hour patch sizes: 12.5 µg/h, 25 µg/h, 50 µg/h, 75 µg/h, and 100 µg/h. Since the transdermal absorption rate is generally constant at a constant skin temperature, the dosage is controlled by the size of the patch. However, the rate of absorption and circulating blood level is also dependent on a number of other factors: skin condition, temperature, amount of body fat, and even the location of the patch. Serum fentanyl concentrations may increase [by ~  $\frac{1}{3}$  in patients with temperature of 104°F (40°C) or use of heating pad] due to temperature-dependent increases in drug released from the transdermal system and an increase in skin permeability; thus, patients with fever should be monitored for adverse opioid effects. Similarly, carbon dioxide retention caused vasodilatation (increased absorption and tissue mobilization) and acidosis (reduces protein binding) increase circulating levels of the drug. Typically, the patch will have analgesic effect under normal circumstances within 8–12 hours, peaking sometime after 24 hours; while the deposition of the drug in adipose tissue results in prolonged opiate effect after removal of the patch (mean elimination half-life of 17 hours!).

***According to the package insert:***

DURAGESIC® should ONLY be used in patients who are already receiving opioid therapy, who have demonstrated opioid tolerance, and who require a total daily dose at least equivalent to DURAGESIC® 25 mcg/h. Patients who are considered opioid-tolerant are those who have been taking, for a week or longer, at least 60 mg of morphine daily, or at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid.

Because serious or life-threatening hypoventilation could occur, DURAGESIC® (fentanyl transdermal system) is contraindicated:

- in patients who are not opioid-tolerant
- in the management of acute pain or in patients who require opioid analgesia for a short period of time
- in the management of post-operative pain, including use after out-patient or day surgeries (e.g., tonsillectomies)
- in the management of mild pain
- in the management of intermittent pain [e.g., use on an as needed basis (prn)]

Since the peak fentanyl levels occur between 24 and 72 hours of treatment, prescribers should be aware that serious or life threatening hypoventilation may occur, even in opioid-tolerant patients, during the initial application period.

Due to the mean elimination half-life of 17 hours of DURAGESIC®, patients who are thought to have had a serious adverse event, including overdose, will require monitoring and treatment for at least 24 hours.

The concomitant use of DURAGESIC® with potent cytochrome P450 3A4 inhibitors (see list below) may result in an increase in fentanyl plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression.

DURAGESIC® is ONLY for use in patients who are already tolerant to opioid therapy of comparable potency. Use in non-opioid tolerant patients may lead to fatal respiratory depression. Overestimating the DURAGESIC® dose when converting patients from another opioid medication can result in fatal overdose with the first dose.

The patches must be properly disposed of as the residual drug after 72 hours of use tempts drug seekers to cut up and eat or smoke the gel from inside the patch. Furthermore, manufacturers of fentanyl patches have come under scrutiny for defective products and have issued recalls because patch malfunction has resulted in life-threatening side effects and even some patient deaths.

Skeletal muscle and ventilation compromising chest wall rigidity (Stiff Man Syndrome) may occur, especially following rapid I.V. administration of fentanyl; transient muscular rigidity has been observed in neonates born to women who were treated with I.V. fentanyl.

## **APPLICATION OF THE PATCH**

Transdermal patch: Apply to non-hairy, clean, dry, non-irritated, intact skin of the flat area of front or back of upper torso, flank area, or upper arm. Apply to upper back in young children or in people with cognitive impairment to decrease the potential of the patient removing the patch. Clip hair prior to application, do not shave area. Prior to application, skin may be cleaned with clear water (do not use soaps, lotions, alcohol, oils, or other substances which may irritate the skin); allow skin to dry thoroughly prior to application. Apply patch immediately after removing from package; firmly press in place and hold for at least 30 seconds. Change patch every 72 hours; remove old patch before applying new patch. Do not apply new patch to same place as old patch. Wash hands after applying patch. Rate of drug delivery may be significantly increased if patch is cut, damaged, or leaking and could result in absorption of a potentially fatal dose. If partial dose is needed, surface area of patch can be blocked proportionally using adhesive bandage (see Lee, 1997). Do not use soap, alcohol, or other solvents to remove transdermal gel if it accidentally touches skin as they may increase transdermal absorption, use copious amounts of water. Avoid exposing application site to external heat sources (eg, electric blanket, heating pad, heat lamp, sauna, heated water bed, hot tub).

## **DRUG INTERACTIONS**

CNS depressants, alcohol, phenothiazines, MAO inhibitors, and tricyclic antidepressants may potentiate fentanyl's adverse effects. When using fentanyl with other CNS depressants, reduce the dose of one or both agents. Use of MAO inhibitors within 14 days of fentanyl is not recommended. Cytochrome P450 inhibitors (eg, amiodarone, clarithromycin, erythromycin, cimetidine, diltiazem, verapamil, fluconazole, itraconazole, ketoconazole, protease inhibitors, etc.) may significantly increase or prolong the clinical or adverse effects of fentanyl - potentially fatal respiratory depression may occur with concomitant use of strong or moderate P450 CYP3A4 inhibitors. Close monitoring and dosage adjustment may be needed. Cytochrome P450 inducers (eg, carbamazepine, phenytoin, rifampin) may decrease the effect of fentanyl; close monitoring and dosage adjustment may be needed. The herbal medicine, St John's wort (*Hypericum perforatum*), may increase the clearance and decrease the effects of fentanyl - its use is not recommended.

**FOOD INTERACTIONS** — Grapefruit juice may significantly increase fentanyl serum concentrations and risk of adverse effects.

## Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain: an educational pilot to improve care and safety with opioid treatment

### Table 1. Summary of Recommendations

Prescribing opioid doses up to 120mg/day MED: (Cumulative daily dose when using one or more opioids. See Table 2 for specific opioid thresholds.)	Before exceeding 120mg/day MED dose threshold: (Cumulative daily dose when using one or more opioids. See Table 2 for specific opioid thresholds.)
<ul style="list-style-type: none"> <li>No pain management consultation needed if the prescriber is documenting sustained improvement in both function and pain.</li> <li>Consider specialty consultation<sup>2</sup> if frequent adverse effects or lack of response is evident in order to address: <ul style="list-style-type: none"> <li>Evidence of undiagnosed conditions;</li> <li>Presence of significant psychological condition affecting treatment; and</li> <li>Potential alternative treatments to reduce or discontinue use of opioids.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Seek pain management consultation<sup>3</sup> to address: <ul style="list-style-type: none"> <li>Potential alternative treatments to opioids;</li> <li>Risk and benefit of a possible trial with opioid dose above 120mg/day MED;</li> <li>Assistance with ongoing documentation of improvement in function and pain; and</li> <li>Schedule for follow up with pain management specialist, if necessary.</li> </ul> </li> </ul>

### Table 2. Dosing Threshold for Selected Opioids\*

Opioid	Recommended dose threshold for pain consult (not equianalgesic)	Recommended starting dose for opioid-naive patients	Considerations
Codeine	800mg per 24 hours	30mg q 4–6 hours	See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. See acetaminophen warning, below.
Fentanyl Transdermal	50mcg/hour (q 72 hr)		Use only in opioid-tolerant patients who have been taking ≥ 60mg MED daily for a week or longer
Hydrocodone	120mg per 24 hours	5-10mg q 4–6 hours	See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. See acetaminophen warning, below.
Hydromorphone	30mg per 24 hours	2mg q 4–6 hours	
Methadone	40mg per 24 hours	2.5-5mg BID – TID	Methadone is difficult to titrate due to its half-life variability. It may take a long time to reach a stable level in the body. Methadone dose should not be increased more frequently than every 7 days. Do not use as PRN or combine with other long-acting (LA) opioids.
Morphine	120mg per 24 hours	Immediate-release: 10mg q 4 hours Sustained-release: 15mg q 12 hours	Adjust dose for renal impairment.
Oxycodone	80mg per 24 hours	Immediate-release: 5mg q 4–6 hours Sustained-release: 10mg q 12 hours	See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. See acetaminophen warning, below.
Oxymorphone	40mg per 24 hours	Immediate-release: 5-10mg q 4–6 hours Sustained-release: 10mg q 12 hours	<b>Use with extreme caution due to potential fatal interaction with alcohol or medications containing alcohol.</b>

\*Meperidine and propoxyphene products should not be prescribed for chronic non-cancer pain.