Transdermal Fentanyl

Fentanyl is a strong opioid that is approximately 75-100 times more potent than morphine. It is available in a transdermal patch that can provide a convenient, non-invasive alternative for managing moderate to severe pain in patients unable to tolerate or comply with administration of oral, long-acting pain medications. However, differences in absorption, dosing/titration considerations, and adverse effects risks may not make it ideal for some patients. The considerations listed below are important to determine whether transdermal fentanyl is the best choice for an individual patient.

Absorption/Timing of Patches[1-3]

- Absorption can vary from patient to patient and within the *same* patient as disease progresses. Transdermal absorption may be affected by things like body temperature, skin permeability, hydration, blood flow, and weight loss/cachexia. Many of these variables are present in hospice patients.
- Onset of analgesia is not immediate, occurring 12 to 24 hours after initial application. Serum fentanyl concentrations gradually increase during this time, and then remain relatively constant for the remainder of the 72-hour application period.
- With sequential use, serum fentanyl concentrations reach steady state by the end of the second 72-hour patch application (i.e., six days after patch initiation).
- The FDA approved and recommended dosing interval is every 72 hours; however, some patients will require dosing every 48 hours (as evidenced by good pain control for 48 hours followed by inadequate pain control during the final 24 hours).
- Absorption is not affected by gastrointestinal status (e.g. malignant intestinal obstruction, gastroparesis, nausea/vomiting) which can make transdermal fentanyl a favorable option in these situations.

Dosing/Titration[2]

- Indicated for patients with chronic, stable pain; not a good choice for patients with escalating or fluctuating pain.
- If adequate analgesia is not achieved, the initial dosage can be titrated upward after 3 days (72 hours); subsequent titrations should be made no more frequently than every 6 days.
- Only indicated for opioid tolerant patients, which is defined as those already taking at least 60 mg oral morphine (or equivalent) for at least one week. Use in opioid-naïve patients can cause dangerous respiratory depression.
- Patches cannot be cut. Therefore, dose titration can be difficult, since each increase in patch strength is the equivalent of 25-50 oral morphine equivalents (OME). These large increments in titration increase the risk of fentanyl overdose or toxicity.
- When patch is removed (and not replaced) serum concentrations fall to 50% of the original value after about 17 hours.
- Use of multiple patches can lead to dosing errors.
- Although studies have shown no clinically significant accumulation in chronic kidney disease,[4] product labeling says to avoid use in severe renal impairment, reduce the initial transdermal dose by 50% in patients with mild to moderate renal impairment, and titrate to desired clinical effect.
- Avoid use in severe hepatic impairment. Reduce the initial transdermal dose by 50% in patients with mild to moderate hepatic impairment and titrate to desired clinical effect.

- Structurally dissimilar to morphine, making it an acceptable alternative for patients with a true allergy to morphine.

Adverse Effects[2]

- Use in opioid-naïve patients can lead to potentially fatal respiratory depression.
- Accidental exposure by children can be fatal, and "used" patches still contain absorbable drug.
- Concomitant use of the fentanyl patch with any cytochrome P450 3A4 inhibitors (such as ketoconazole, erythromycin, diltiazem, or grapefruit juice) may result in an increase in fentanyl plasma concentrations, which may cause potentially fatal respiratory depression.

Hospice Considerations

Fentanyl patches should be considered second-line therapy for long-acting pain management, due to dosing/titration constraints and cost considerations. In general, fentanyl patches should be reserved for opioid-tolerant patients with stable, chronic pain for whom long-acting oral morphine is contraindicated (e.g. true morphine allergy, dysphagia, severe nausea/vomiting, significant hepatic/renal impairment).

Comparative Cost of Long-Acting Opioids

Transdermal Fentanyl	$$$*
Morphine ER (oral)	$$
Oxycodone ER (oral)	$$$$
Methadone (oral)	$

*37.5 mg, 62.5 mg, 87.5 mg patches are significantly higher cost

References

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