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Fentanyl: Abuse Potential and Prevention Strategies for Pharmacists

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Abstract

The abuse of fentanyl is becoming more prevalent, with patients devising new methods of extraction in order to abuse it. Fentanyl patches were originally intended for the opioid tolerant patients still requiring pain relief, but illicit use and drug diversion of this medication continues to grow at an alarming rate. Several cases of abuse have been documented in which patients were chewing patches for oral absorption, distilling the drug into liquid form for injection, or rectally inserting the patches. To discourage and prevent abuse, a keenly aware pharmacist can provide patients with important counseling points on proper use, disposal and education about fentanyl itself.

As an attempt to deter abuse, a novel matrix delivery system was more recently introduced.⁶ The new patch is smaller, with fentanyl-containing dipropylene glycol droplets incorporated into the adhesive rather than the original reservoir system, which is known to leak drug and allows for simple drug extraction. The matrix delivery system has a rate-controlling membrane to improve drug release, which allows the amount of drug loaded in the patch to be reduced by almost 35 percent compared to that contained in the original reservoir system. Since fentanyl is completely dissolved in a semisolid state in the matrix formulation, the risk of incidental drug leakage is decreased. Extraction of drug for abuse was thought to be more difficult, though it has now been shown to be just as commonly abused as the original reservoir patches.⁷

Background

Fentanyl patches are prescribed for the treatment of persistent, moderate-to-severe chronic pain. This drug therapy is reserved for patients who are opioid tolerant; however, due to its euphoria-inducing properties, fentanyl has a high potential for abuse. While fentanyl is less commonly abused than medications such as oxycodone or hydrocodone, abuse has increased in the last decade, with widespread epidemics occurring in cities such as Chicago, Detroit and Philadelphia.²⁻⁴ In 2006, fentanyl was the fifth most common cause of emergency department visits resulting from nonmedical prescription narcotic analgesics.⁵ Due to the prevalence of abuse and severe consequences of misuse, there is a definite need for intervention and patient education on the safe use of transdermal patches.

Fentanyl acts systemically as a mu-opioid receptor agonist (table 1) and has the capability to cross the blood-brain barrier due to its highly lipophilic nature, which results in analgesic effects, mood alterations, euphoria, dysphoria and drowsiness.¹ The high potency of fentanyl allows for a therapeutic dose to be applied to a relatively small area of skin. Chronic opioid users frequently develop tolerance to the analgesic and euphoric effects, but not to the respiratory depressive effects. Toxicity can range from mild, which presents with drowsiness and headache, to severe which may result in respiratory arrest, hypotension and even death. Adverse effects of the transdermal application include nausea, vomiting, confusion, skin irritation and insomnia.

Table 1: Systemic effects of fentanyl by opioid receptor type¹

Opioid receptor	Systemic effects
Mu	Supraspinal and peripheral analgesia, sedation, and euphoria Spinal analgesia, respiratory depression, physical dependence, GI dysmotility, bradycardia, pruritus
Kappa	Spinal analgesia and miosis Dysphoria and psychotomimesis Supraspinal analgesia

Methods of Abuse

Abuse of transdermal fentanyl patches involves unintended routes of administration achieved by altering the delivery system. In situations of abuse, fentanyl may be introduced by transmucosal application, ingestion, intravenous injection of the patch contents, volatilization and inhalation, application of heat to a transdermal patch, or rectal insertion.^{8,9} While the patches are intended for slow, steady drug release, these rapid infusion methods result in uncontrolled quantities of drug delivered.⁸ Moreover, fentanyl is frequently abused in conjunction with alcohol or other illicit drugs, even acting as a substitute for heroin.⁹

The most popular method of abuse involves placement of a transdermal fentanyl patch inside the oral cavity.^{8,9} Oral abusers will affix a patch, or patches, on the buccal membrane, chew on the patch, or boil the patch and consume the liquid. Being thin and lacking keratinization, the buccal membrane allows for rapid absorption, making this an appealing route for abusers. Chewing the patch is particularly dangerous due to the mechanical disruption of the patch, causing release of more than 72 hours worth of drug at one time. Liappas reported a case in which a 36-year-old woman was prescribed 25 mcg/hr fentanyl patches, three times daily.¹⁰ Believing the drug was not appropriately penetrating her skin and providing her with adequate relief, the patient began to apply the patches to the oral cavity. The woman claimed she was able to achieve faster, more effective pain relief using this route. Over the course of several months, the patient increased the dose from 75 mcg/hr daily to 250 mcg/hr daily, totaling 10 patches, which she continued for 15 months. Due to her long-term abuse, the patient developed a high tolerance along with a strong dependence on fentanyl.

Street drug users also have been found misusing fentanyl patches, specifically, the newer matrix formulation.⁷ Users are able to easily retrieve fentanyl by adding vinegar and water to the patch and allowing it to soak or by heating the patch. The resulting solution is placed in a container, from which users load a syringe and inject the drug intravenously. In addition to the increased risk of disease transmission, it is difficult to assess the potency of the drug because the quantity and time-released formulation make it impossible to know the amount of drug being injected. This presents a high risk of accidental overdose.

One of the less frequent, yet more dangerous, routes of administration is rectal insertion of the transdermal patch.⁹ Similar to the buccal membrane, the rectal mucosa is non-keratinized, which, combined with the elevated

temperature, facilitates rapid absorption of fentanyl. In a case reported by Coon, a man was brought into the emergency room, unconscious after rectally inserting three 100 mcg/hr transdermal fentanyl patches. Upon admission, he was given 6 mg of naloxone, to which he did not respond, and was subsequently intubated. An hour after removal of the patches, the patient finally awoke. Acute onset of coma was attributed to elevation of serum fentanyl levels faster than usual, a direct result of the combination of the rapid absorption and number of high-dose patches inserted. The authors suggest that, in such cases, aggressive digital rectal examination, combined with anoscopy or sigmoidoscopy, should be utilized to ensure all internalized patches are recognized and removed.

A number of tactics are employed by potential fentanyl abusers in order to acquire the transdermal patches.^{6,10} Methods include obtaining multiple prescriptions from more than one health care provider, illegal purchase from a drug dealer, theft from a patient who has a legitimate prescription, and removal from the trash or off of a person wearing a patch, including patients in a hospital or morgue.

Prevention and Treatment: The Role of Health Care Professionals

Several methods of monitoring patients who have been prescribed transdermal fentanyl have been proposed.¹⁰ The major focus should be on the initial prevention of abuse, which could include requiring the original prescription and all follow-ups be conducted through specialized pain centers. Anticipation of drug-abuse potential and identification of populations at greater risk of abuse should be considered. Importance is also placed on recognition of abuse behavior and predisposition by thorough examination, including both family and social history of the prospective patient. Any signs of abuse or dependence should be identified and adequately addressed before a prescription is issued. Signs of opiate withdrawal include anxiety, enlarged pupils, excessive sweating, or an increase in blood pressure, pulse and temperature. To monitor for patient compliance and illicit drug use, urine and blood screenings should be encouraged. For those in which abuse of fentanyl has been identified, effective treatment may be most beneficially provided through facilities employing specifically trained psychologists or psychiatrists who can offer psychotherapeutic therapy to complement any required medical treatment. Considerations should be made to taper the patient off the drug in order to avoid withdrawal symptoms. Adding a weak opioid, such as codeine, to the therapy regimen can further facilitate this process.

Pharmacist Counseling Points

Due to its dangerous adverse effects, patients should be fully educated about the abuse potential, life-threatening dangers and proper disposal of fentanyl patches.¹¹ Pharmacists should consider a few points when counseling a patient

- A medication guide must be provided with each dispensing.
- Patches are intended for transdermal use on intact skin only.
- Instruct patients not to use a patch if the package is broken or the patch is cut, damaged or altered.
- Avoid exposure of the application site to any external heating source because drug release may be increased, which could lead to overdose or death.
- Keep patches in a secure location away from pets, children and potential theft of the medication.
- Fentanyl's high potency and significant amount of drug remaining in used patches have resulted in manufacturer and FDA guidelines stating to fold the patch upon itself and immediately flush both used and leftover patches down the toilet.

Pharmacists need to be alerted to drug-seeking behaviors, including urgent refill requests or visits near the end of operating hours, "lost" prescriptions, altered prescriptions, and refusal or reluctance to disclose other medications or current physician(s). A common tactic among abusers is "doctor shopping" to obtain additional prescriptions and "pharmacy hopping" to fill multiple prescriptions for controlled substances.

Conclusion

With recent reports of transdermal fentanyl abuse on the rise, it is critical that pharmacists take an active role in preventing further perpetuation of abuse. This can be accomplished by awareness of the incidence and methods employed by abusers, including altering the patch or use via unintended routes of administration. Patients who have a legitimate need for this medication require proper education and monitoring to avoid abuse or accidental overdose or drug diversion. Health care professionals should be aware of signs and symptoms of abuse and proper treatment methods. Due to the highly potent nature and deadly adverse reactions associated with fentanyl, its misuse should not be taken lightly.

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