

A Multi-Incident Analysis on Fentanyl Transdermal System in the Community

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INTRODUCTION

Fentanyl is a highly potent long-acting opioid and is listed as a high-alert medication in community and ambulatory healthcare settings.¹ In particular, the fentanyl transdermal system (i.e. fentanyl patch) has been a long-standing concern worldwide due to its prescribing and dispensing without proper consideration of patient selection criteria, proper dose adjustments, and safe administration procedures.² Failure to acknowledge these considerations may result in fentanyl overdoses, which can have fatal consequences, especially for opioid naïve users.³ In recent years, there have been a growing number of reported overdoses and deaths in Canada related to misuse and abuse of fentanyl patches; it is becoming a more alarming safety crisis nationwide. Between 2009 and 2014, at least 655 deaths in Canada were associated with fentanyl or fentanyl analogues.⁴ Many stakeholders, including healthcare professionals, regulators, law enforcement, and all levels of government are working closely together to address this concerning issue.^{5,6} Although the Institute for Safe Medication Practices (ISMP) in both the United States and Canada have released several alerts and safety newsletters to address the misuse of fentanyl patches and their potential for serious consequences, fentanyl transdermal system remains an issue of priority with respect to patient/medication safety.^{7,8,9,10}

The Community Pharmacy Incident Reporting (CPhIR) program (available at <http://www.cphir.ca>) is designed for community pharmacies to anonymously report near misses or medication incidents to ISMP Canada for further analysis and dissemination of shared learning from the reported incidents. CPhIR has allowed the collection of invaluable information to help identify system-based vulnerable areas in community pharmacy practice in order to prevent medication incidents. This article provides an overview of a multi-incident analysis of fentanyl patch related medication incidents reported to the CPhIR program.

METHODS

A total of 111 reported medication incidents involving “fentanyl” or “fentanyl patch” or “fentanyl transderm*” or “Duragesic” were extracted from the CPhIR program from January 2010 to January 2016. Fifty-one incidents were excluded from the analysis due to: (1) inadequate information provided in the “Incident Description” field to determine the cause of the incident; (2) other dosage forms that are not related to the transdermal system; and (3) medication

errors that are not related to properties pertaining to fentanyl transdermal system. Two ISMP Canada analysts independently reviewed the medication incidents that met the inclusion criteria to determine the themes and subthemes derived from this multi-incident analysis (Table 1).

MULTI-INCIDENT ANALYSIS ON FENTANYL TRANSDERMAL SYSTEM

Based on the analysis, three main themes were identified: (1) pharmacological properties of fentanyl; (2) opioid-dose conversion and considerations; and (3) product design of fentanyl. These three main themes were further divided into sub-themes (Table 1). Subthemes are elaborated by providing incident examples and a discussion of corresponding potential contributing factors (Tables 2, 3, and 4). Note: The “Incident Examples” provided in Tables 2, 3, and 4 were limited by what was inputted by pharmacy practitioners to the “Incident Description” field of the CPhIR program.

Table 1: Themes and subthemes derived from multi-incident analysis on fentanyl transdermal system

Main Themes	Sub-themes
1) Pharmacological Properties of Fentanyl	Dosing interval
	Drug-drug interaction
	Rate of absorption
	Opioid-naive
2) Opioid-Dose Conversion and Considerations	
3) Product Design of Fentanyl	Supplied in a box of 5 patches
	Dosage availability per patch

Table 2 – Main Theme 1: Pharmacological Properties of Fentanyl

Sub-themes	Incident Example	Commentary
<p>Dosing interval</p>	<p>A resident is prescribed a fentanyl 100 mcg patch to be applied every 48 hours. A medication administration record was received from the pharmacy and checked by three nurses. The next patch should be due on Jan 02/10. On Jan 01/10, medications were received and the fentanyl patch was applied by the registered nurse practitioner. [The nurses were confused about the dosing of fentanyl for this patient.]</p>	<p>There was unclear communication and lack of understanding among patients/caregivers/ other health care professionals in regards to patient-specific dosing interval (e.g. every 72 hours versus every 48 hours) for fentanyl transdermal administration. Although most patients would be adequately maintained with fentanyl patch administered every 72 hours, a small number of patients may require fentanyl patches to be applied every 48 hours instead of every 72 hours in order to achieve adequate pain control.¹¹</p>
	<p>During checking, the pharmacist discovered an error in the prescription directions. She contacted the prescriber who refused to alter prescription because it was suggested by a pain specialist. The specialist indicated that the patch should be applied every day in a consultation note. The pharmacist contacted the specialist who would not alter another prescriber's prescription. After a lengthy explanation, the specialist read his note to the prescriber and realized his error. The specialist agreed that the directions should be every 3 days and not every day.</p>	<p>Complexity of dosing for fentanyl transdermal administration.</p> <p>Lack of knowledge or awareness of the unique dosing interval of fentanyl transdermal patch in pain management.</p> <p>Lack of standardized fentanyl guidelines for prescribers to clearly specify the correct quantity (i.e. number of patches), strength, and dosing interval and to assess patient's opioid-tolerability and contraindications including any concurrent use of other maintenance and/or breakthrough pain medications.¹²</p>
<p>Drug-drug interaction (DDI)</p>	<p>The doctor prescribed Biaxin® 500 mg twice a day to a patient who is on fentanyl; pharmacist called the doctor and suggested to switch it to Zithromax®.</p>	<p>Concomitant use of the fentanyl patch with any cytochrome P450 3A4 inhibitors may result in an increase in fentanyl plasma concentrations, which may cause potentially fatal respiratory depression. Thus, carefully monitor patients who are concomitantly taking CYP 3A4 inhibitors with fentanyl patches for an extended period of time. Adjust the fentanyl dose if necessary.¹¹</p> <p>Lack of a DDI alert system in place to remind the prescriber for potential DDI and/or other contraindications.¹²</p>
<p>Rate of absorption</p>	<p>Prescription directions entered as 1-2 patches when it was supposed to be just 1 patch.</p>	<p>Fentanyl patch is a controlled delivery system designed to release a steady amount of medication at a constant rate of mcg/hour.¹¹ It should not be up to the patient to decide whether to apply 1 or 2 patches. Unlike other "as needed" medications, fentanyl transdermal patch has a strict dosing regimen and direction of use.</p>
<p>Opioid-naïve</p>	<p>The doctor prescribed fentanyl to an opioid-naïve patient. The patient was only taking acetaminophen 650 mg extended release. Administering fentanyl to this patient may have serious effects.</p>	<p>Lack of knowledge or awareness of the indication for the use of fentanyl patches.</p> <p>Contraindicated in the management of postoperative pain, mild pain, or intermittent pain (e.g. use on a "as needed" basis) because of the risk for serious or life-threatening respiratory depression.¹³</p> <p>Only prescribe a fentanyl patch of 25 mcg/hour if the patient has been receiving the equivalent of at least 60 mg of oral morphine per day for an extended period.¹⁰</p>

Table 3 – Main Theme 2: Opioid-Dose Conversion and Considerations

Incident Example	Commentary
<p>The patient’s guardian arrived at the pharmacy to pick-up fentanyl patch expecting a dose increase from 75 mcg to 100 mcg. This dose increase was confirmed by the pharmacy student and dispensed. However, the patient had been using 75 mcg along with ~36 mg morphine equivalents per day for breakthrough. This level of breakthrough use usually only warrants increase in dose by 12 mcg. The doctor should have written for 12 mcg instead of 25 mcg increase. The prescription was processed and prepared without a therapeutic check. As a result, it was released to the patient without having addressed the above issues first. One 100 mcg patch was applied to the patient before this error was discovered.</p>	<p>Incorrect calculation of “morphine equivalents” total daily dose.</p> <p>Over-estimating the dose when doing fentanyl dose adjustment or converting from another opioid analgesic may result in a fatal overdose.¹³</p> <p>Lack of standardized prescribing fentanyl guidelines to include an equianalgesic conversion table as reference for prescribers.¹²</p>

Table 4 – Main Theme 3: Product Design of Fentanyl

Sub-themes	Incident Example	Commentary
<p>Supplied in a box of 5 patches</p>	<p>Two patches were short when trying to fill a fentanyl patch prescription. When checking, the pharmacist discovered that two prescriptions were supposed to be filled for 8 patches but the patient actually received 10.</p>	<p>Confirmation bias with number of boxes versus number of patches.</p>
<p>Dosage availability per patch</p>	<p>Directions for the fentanyl patch was entered as apply 25 mcg along with 100 mcg, but it should have been 25 mcg along with a 50 mcg and 100 mcg.</p>	<p>Requiring multiple patches from the same and/or various strengths to be dispensed at once to meet the total daily dose prescribed.</p> <p>Specify the total dose of fentanyl in the direction of use to ensure all the strengths of fentanyl patches that were prescribed are dispensed appropriately.</p>

RECOMMENDATIONS

The unique properties of fentanyl transdermal patches present many vulnerabilities for medication incidents to occur. It is critical for healthcare professionals to be fully aware of these characteristics in order to successfully incorporate safety measures into their practices. Different harm reduction strategies have been initiated at local, provincial, and national levels (e.g. mandatory patch-for-patch programs, and delisting of high-dose opioids from formularies).^{4,14} However, currently, there is no consistent or standardized approach at the national level. Nonetheless, the following are some suggested recommendations targeting different medication system stages to encourage safer fentanyl patch use in the community (Figure 1).

1. Prescribing

- Standardized fentanyl prescribing guidelines^{4,12,15}
 - Specify the quantity*, strength, dosing interval, and day supply
 - Include an equianalgesic conversion table (e.g. http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b08.html) when making dose adjustments or switching from other opioid medication(s)

* Recommend that no more than 10 fentanyl patches to be dispensed at one time (i.e. one patch every 72 hours x 10 patches = 30 days)

2. Prescription Order Entry

- Adhere to the specific instructions written by the physician in the best interest of the patient⁴
- Directions of use:
 - Include comment "Apply with ___ mcg fentanyl patch (Total fentanyl ___ mcg)" when dispensing multiple strength patches
 - Include comment "Return used patch(es) to pharmacy" at the end of the directions⁴

3. Therapeutic Check

- Assess the following:
 - Contraindications including comorbid medical conditions, drug-drug interactions, and additive effects from other central nervous system medications
 - Opioid-naïve (i.e. patient has no history of opioid use)
 - Other opioid concomitant use (e.g. for breakthrough pain relief) including total equivalent doses in morphine
 - Appropriate indication and dose (e.g. initiating, switching, or discontinuing)

4. Medication Dispensing

- Apply a visible prescription label, with proper brand name, generic name, and specified delivery rate of the fentanyl patches dispensed
- Conduct independent double check on the total number of patches to be dispensed
- Ensure all strengths of fentanyl patches dispensed add up to the total prescribed dose

5. Patient Counselling

- Ensure patients have a comprehensive understanding of the following:
 - Indication of fentanyl patch
 - Administration of fentanyl patch
 - Signs and symptoms of opioid overdose / toxicity
 - Administration of naloxone in case of opioid-associated overdose emergency

6. Monitor / Follow-up

- Initiate a fentanyl patch-for-patch partnership between the physician, pharmacist, and patient to develop a transparent monitoring plan.⁴ The College of Physicians and Surgeons of Ontario (CPSO) and the Ontario College of Pharmacists (OCP) strongly support this; as of October 1st, 2016, the Patch-For-Patch Fentanyl Return Program has been mandatory in Ontario (http://www.ocpinfo.com/regulations-standards/policies-guidelines/Patch_For_Patch_Fentanyl_Return_Fact_Sheet/).
- Provide patients with opioid exchange disposal sheets to help them return used fentanyl patches for safe disposal at the pharmacy⁴
- Initiate provision of naloxone kits to patients and/or family/friends of patients with the following risk factors:¹⁶
 - Concomitant use of benzodiazepine and/or other sedatives
 - Alcohol use
 - High-dose opioid therapy

Safe Use Of FENTANYL PATCHES

IN THE COMMUNITY PRACTICE



PRESCRIBING

- Use a standardized fentanyl prescribing guidelines
- Specify the quantity, strength, dosing interval, and days' supply
- Consult an equianalgesic conversion table when making dose adjustments or switching from other opioid medication(s)



ORDER ENTRY

- Adhere to specific instructions written by the prescriber in the best interest of the patient
- Include comment: "Apply with ___ mcg fentanyl patch (total fentanyl ___ mcg)" when dispensing multiple strength patches
- Include comment: "Return used patch(es) to pharmacy" at the end of the directions



THERAPEUTIC CHECK

Assess the patient on:

- Contraindications
- Opioid-naïve
- Maintenance or breakthrough pain medication use, including total equivalent doses in morphine
- Appropriate indication and dose (e.g. initiating, switching, or discontinuing)



MEDICATION DISPENSING

- Apply a visible prescription label, with proper brand name, generic name, and specified delivery rate
- Conduct independent double check on the total number of patches to be dispensed
- Ensure all strengths of fentanyl patches dispensed add up to the total prescribed dose



PATIENT COUNSELLING

Educate the patient on:

- Indication of fentanyl patch
- Administration of fentanyl patch
- Signs and symptoms of opioid overdose/toxicity
- Accessibility and administration of naloxone in case of opioid-associated overdose emergency



MONITOR/FOLLOW-UP

- Introduce a Patch-For-Patch Fentanyl Return Program to patients (mandatory in Ontario)
- Provide patients with opioid exchange disposal sheets to help them return used fentanyl patches for safe disposal at the pharmacy
- Initiate provision of naloxone kits to patients and/or family/friends of patients with risk factors (e.g. concomitant use of benzodiazepine and/or other sedatives, alcohol use, high-dose opioid therapy, etc.)


Figure 1 - Recommendations for the safe use of fentanyl patch in community pharmacy practice ^{4,12,15,16}

CONCLUSION

The fentanyl patch, when used appropriately, is highly effective in chronic pain management due to its potency. However, it is because of its high potency that fentanyl patch incidents may result in severe harm. Moreover, these incidents occur due to individuals not being familiar with the unique characteristics of the fentanyl transdermal system, and lack of consistent standardization in the medication-use process. Recognizing this, effective March 22nd 2016, naloxone has been removed from Canada's Prescription Drug List (PDL).^{17,18} Increasing accessibility to naloxone (without a prescription) can offer a harm reduction option not only for illicit-drug users, but also for high-dose opioid prescription drug users for emergency use in opioid overdose.^{14,18} Widespread safety concerns continue to arise but it is hoped that the insights from this multi-incident analysis can act as safeguards

to help reduce the medication incidents of fentanyl patches in the community.

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