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WHOLE FENTANYL PATCH INGESTION: A MULTI-CENTER CASE SERIES

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□ **Abstract—Background: Fentanyl is a potent synthetic opioid with large abuse potential. A common preparation of fentanyl is a sustained-release transdermal patch. To our knowledge, there are only two published case reports of whole patch ingestion. A case series of 76 patients with a history of whole patch ingestion is reported. Study Objectives: To characterize whole fentanyl patch ingestion to develop a clinical guideline for management. Methods: This was a retrospective review of all patients who ingested intact fentanyl patches as reported to three regional poison information centers (RPIC) from 2000 to 2008. The three RPIC medical record databases were queried for all exposures with a substance code matching the Micromedex® (Thomson Reuters, New York, NY) fentanyl product codes. Collected data included: age, gender, reason for the exposure, number of patches ingested, dose (μg/h), symptoms, symptom onset and duration, treatment hospital flow (level of care), and outcome. Results: A total of 76 patients met the inclusion criteria. Two patients had both time of onset and symptom duration documented. In both patients, the signs and symptoms developed within 2 h of the exposure, and the patients were asymptomatic at 6½ and 9 h, respectively. Fifty-eight (78.3%) patients were admitted. Of those patients who were admitted, 56 (96.5%) were admitted to a critical care unit. Fourteen patients required intubation, and naloxone infusions were documented in eight cases. Conclusion: Ingestion of whole fentanyl patches may lead to prolonged and significant toxicity based on these poison center data. © 2012 Elsevier Inc.**

□ **Keywords—fentanyl; transdermal; opioid; toxicity; patch; ingestion**

INTRODUCTION

Fentanyl is a potent synthetic opioid with large abuse potential. Fentanyl prescriptions in the United States increased from 0.5 million in 1994 to 7.04 million in 2006 (1). Furthermore, the number of case fatalities from fentanyl overdose in southwestern Virginia increased from three in 2000 to 12 in 2003, and in 2000 the state of North Carolina reported a twofold increase in fentanyl fatalities over the previous 3-year period (2).

A common preparation of fentanyl is a sustained-release transdermal patch. Methods of fentanyl patch abuse include transdermal application, buccal absorption, rectal insertion, removal of the drug from the patch for injection or inhalation, and whole patch ingestion (3). To our knowledge, there are only two published case reports of whole patch ingestion: one of a 38-year-old man who was hospitalized multiple times after ingesting patches and was ultimately found dead in a correctional facility, and another of an accidental ingestion of a used patch by a 1-year-old girl resulting in death (4,5). However, there has not been a clinical case series describing the ingestion of intact patches. A case series of 76 patients with a history of whole patch ingestion is reported.

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Table 1. Number of Patches Reportedly Ingested

Number of Patches	Incidence
1	43/76 (57%)
2	11/76 (15%)
3	2/76 (2.6%)
4	3/76 (3.9%)
5	2/76 (2.6%)
Unknown	15/76 (20%)

MATERIALS AND METHODS

This was an Institutional Review Board-approved retrospective review of all patients who ingested intact fentanyl patches as reported to three regional poison information centers (RPIC) between 2000 and 2008. The three RPIC medical record databases were queried for all exposures with a substance code matching the Micromedex® (Thomson Reuters, New York, NY) fentanyl product codes. The history was reviewed by the investigators, and all cases in which the patient had a history of whole fentanyl patch ingestion were included. Collected data included: age, gender, reason for the exposure, number of patches ingested, dose (μg/h), symptoms, symptom onset and duration, treatment hospital flow (level of care), and outcome (all defined by the American Association of Poison Control Centers National Poison Data System). Symptoms coded as unrelated to the exposure were excluded from the analysis. Descriptive statistics were used to characterize the data.

RESULTS

A total of 76 patients met the inclusion criteria. Ages ranged from 15 to 56 years, with a mean of 32.6 years. Four patients were under the age of 18 years. There were 31 (40.8%) women and 45 (59.2%) men. The number of patches ingested ranged from one to five, with the majority ingesting one patch (Table 1). No patients were reported to have any coingestants. There were 26 different signs and symptoms coded as related to the exposure (Table 2). Fifteen patients had symptoms documented as unknown whether they were related to fentanyl patch ingestion: agitation/irritation occurred in 5/76 (6.6%), and hypertension, vomiting, hyperglycemia, numbness, and other symptoms each occurred in 2/76 (2.6%). Five patients (6.6%) were asymptomatic. The most common related sign was coma. One hundred ninety-eight (198) therapies were administered, the most common of which were naloxone, oxygen, and intravenous fluids (Table 3).

The onset of signs and symptoms compared with the time of exposure was unknown in 66 (86.8%) cases. Two patients had time of onset as well as symptom duration documented. In both patients, the signs and

Table 2. American Association of Poison Control Centers Symptoms, Definitions, and Incidence

Sign/Symptom	AAPCC Definition*	Incidence
Coma	A state of unconsciousness. Include all levels of CNS depression in which the patient cannot be awakened with a stimulus.	35/76 (46%)
Drowsiness/lethargy	Fatigue or sleep or minor levels of CNS depression from which the patient can be awakened with a stimulus. Do not code appropriate sleep (e.g., naps).	30/76 (39%)
Respiratory depression	Diminished tidal volume or rate. Inadequate ventilation. Use this code only if objective information is provided to support the diagnosis of respiratory depression.	13/76 (17%)
Tachycardia	Excessively rapid heart rate (above 100 beats/min in adults). Apply age-related standards for children.	8/76 (11%)
Respiratory arrest	Cessation of spontaneous respirations.	6/76 (7.9%)
Dizzy/vertigo	A disabling sensation in which the affected individual feels that he or his surroundings are in a state of constant movement. Include lightheadedness and other non-vertiginous complaints of dizziness.	5/76 (6.6%)
Bradycardia	Slowing of the heart rate to < 60 beats/min in adults. Apply age-related standards for children.	4/76 (5.2%)
Hypotension	Abnormally low blood pressure; seen in shock but not necessarily indicative of it. In adults, blood pressure < 90 mm Hg systolic or more than 15 mm Hg less than patient's usual systolic blood pressure.	4/76 (5.2%)
Pallor	Abnormal paleness of the skin.	3/76 (3.9%)
CPK elevation	Creatine kinase elevations (including elevation of any isoenzyme) should be coded here. Creatine kinase is the current term for creatine phosphokinase.	3/76 (3.9%)
Cyanosis	Bluish discoloration of the skin and mucous membranes.	3/76 (3.9%)
Dyspnea	Labored or difficult breathing; shortness of breath.	3/76 (3.9%)
Cardiac arrest	Sudden cessation of cardiac function with disappearance of arterial blood pressure.	2/76 (2.6%)
Electrolyte abnormality	An imbalance in any of the electrolytes. Include sodium, potassium, bicarbonate, chloride, calcium, magnesium and phosphate.	2/76 (2.6%)
Chest X-ray positive	Pulmonary V-ray findings other than normal. (Do not code non-pulmonary X-ray findings here.)	2/76 (2.6%)

CNS = central nervous system; CPK = creatine phosphokinase.
* AAPCC (American Association of Poison Control Centers) National Poison Data System Reference Manual, 2007 (6).

Table 3. Therapies Administered to > 2 Patients

Therapies	Incidence
Naloxone	63/76 (83%)
Intravenous fluids	46/76 (61%)
Oxygen	29/76 (38%)
Intubation	14/76 (18%)
Activated charcoal	6/76 (7.9%)
Benzodiazepines	5/76 (6.5%)
Sedation	5/76 (6.5%)
Other therapies not explicitly categorized	4/76 (5.2%)
Vasopressors	3/76 (3.9%)

symptoms developed within 2 h of the exposure, and the patients were asymptomatic at 6½ and 9 h, respectively. Fifty-eight (78.3%) patients were admitted, 12 (15.8%) were treated and released, 4 (5.3%) signed out against medical advice, and 2 (2.6%) were dead on arrival. Of those patients who were admitted, 56 (96.5%) were admitted to a critical care unit and 2 (3.4%) were admitted to a regular unit. There were two (2.6%) fatalities, two (2.6%) unknown outcomes, and two (2.6%) unrelated effects. The dose (μg/h) of the patch was unknown in 55 (72.3%) patients. The known patch doses included: 100 μg/h (n = 8), 75 μg/h (n = 4), 50 μg/h (n = 4), and 25 μg/h (n = 5). In both of the fatalities, the strength of the patch was unknown. Reasons for the exposure included: intentional abuse 59 (77.6%), suspected suicide 13 (17.1%), unknown 3 (3.9%), and misuse 1 (1.4%).

DISCUSSION

Whole patch ingestion represents an important subset of fentanyl misuse. In contrast to other methods of fentanyl misuse, patch ingestion can lead to a longer duration of toxicity for two reasons: the reservoir contains a large amount of fentanyl that can continually be absorbed, and the patches cannot easily be removed from the body. Tissue without stratum corneum, such as mucosa, has a > 30-fold increase in fentanyl absorption, and significant fentanyl absorption has been demonstrated using an in vitro gastrointestinal fluid model with intact patches (7,8). However, extensive first-pass metabolism decreases its oral bioavailability (8).

The primary clinical finding in this case series was that of opioid toxicity. Many patients had severe or prolonged toxicity. Fourteen patients required intubation, and the majority of patients were admitted to a critical care unit. Most required naloxone, and naloxone infusions were documented in eight cases. In the two cases in which the duration of symptoms could be discerned, the patients were asymptomatic 6½ and 9 h after ingestion; this is consistent with a case report describing the ingestion of two 100-μg/h patches in which the patient was admitted to a critical care unit and discharged asymptomatic the following day (5). However, due to the potential for prolonged or delayed toxicity, patients who have ingested fentanyl patches have almost all required naloxone therapy and admission, most often to a critical care unit.

Limitations

The primary limitation of this case series is the utilization of poison center data, which relies wholly upon voluntary reporting from external health care professionals and lacks direct patient and chart access. Additionally, the onset of signs and symptoms compared with the time of exposure was unknown in the majority of cases; this information is critical in terms of developing a concrete management guideline. As such, based solely on these data, guideline development is not possible.

CONCLUSION

Ingestion of whole fentanyl patches may lead to prolonged and significant toxicity based on these poison center data. Further prospective study is necessary to attempt to generate management guidelines.

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ARTICLE SUMMARY

1. Why is this topic important?

Whole patch ingestion represents an important subset of fentanyl deaths. In contrast to other methods of fentanyl misuse, patch ingestion can lead to a longer duration of toxicity.

2. What does this study attempt to show?

This study attempts to characterize whole fentanyl patch ingestions.

3. What are the key findings?

Many patients had severe or prolonged toxicity. Fourteen patients required intubation, and the majority of patients were admitted to a critical care unit. Most required naloxone, and naloxone infusions were documented in eight cases. In the two cases in which the duration of symptoms could be discerned, the patients were asymptomatic after 6½ and 9 h of ingestion.

4. How is patient care impacted?

Patients ingesting intact fentanyl patches are not generally observed in the emergency department and are usually admitted to critical care units due to the likelihood of severe and prolonged opioid toxicity.