

## Fentanyl Dependence Associated with Oral Ingestion

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Fentanyl, a synthetic opioid with a potency 100–200 times that of morphine,<sup>1</sup> has gained widespread acceptance in anesthesia because of its rapid onset, preservation of cardiovascular stability, and relatively short duration of action.<sup>2</sup> Recently, there have been concerns about fentanyl as a drug of abuse, particularly among operating room personnel.

Published reports of fentanyl abuse originate from anesthesia and surgery training programs.<sup>2,3</sup> One suggested that anesthesiology is a specialty at greater risk for drug abuse.<sup>2</sup> A 1983 survey in the *Journal of the American Medical Association* found that of 289 United States anesthesia programs (anesthesia resident and nurse anesthetist programs), 214 (74%) had at least one report of drug abuse or dependence. Meperidine and fentanyl were reported to be the two most frequently used drugs.<sup>2</sup> A 10-yr study of oral and maxillofacial surgery training programs indicated that 51% of the responding programs had at least one incident of drug abuse. As in the anesthesiology programs, meperidine and fentanyl were the most frequently abused substances. Behavior changes and information from coworkers were the usual reasons for investigation.<sup>3</sup>

The following is a case report of an operating room registered nurse who became dependent upon orally ingested fentanyl.

## CASE REPORT

The patient, a 38-yr-old operating room supervisor, was referred to our addictive disease unit by his nursing supervisor, who suspected him of self-administering fentanyl obtained from the operating room. The patient adamantly denied using the drug, but he did admit to symptoms of depression, including decreased appetite, an 18-kg weight loss over the previous 6 months, sleep continuity disturbance, anergia,

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and social isolation. His local physician had treated him with a 6-week trial of amitriptyline, 75 mg twice daily, with very little improvement; this medication was changed to imipramine, 75 mg twice daily, 1 week before his hospitalization. When confronted by his nursing supervisor, the patient submitted to urine drug testing but continued to deny drug use; however, he did believe that his depression needed hospital treatment. The admitting physician decided that the patient would best be treated in the psychiatry unit.

The patient had no past history of psychiatric treatment, although he described a childhood history of sexual and physical abuse. He did admit to taking an occasional Darvocet-N 100 (propoxyphene napsylate) for leg pain secondary to an old injury, but he denied taking more than two tablets per week. A routine admission urine drug screen using thin-layer chromatography was negative, and all other laboratory work was within normal limits. After the drug screen returned as negative, we asked the laboratory to screen specifically for fentanyl. Unfortunately, these results were not available for 10 days because of a laboratory delay in the reporting of results.

During hospitalization, the patient continued to respond to imipramine, 150 mg at bedtime, and showed significant improvement in his mood and affect; his sleep, appetite, and energy began to improve as well. After 10 days of treatment, he requested discharge so that he could return to work and continue treatment as an outpatient.

The day after the patient was discharged from the hospital, the laboratory reported that his urine had tested positive for unchanged fentanyl at 1 ng/ml. The patient believed he had no choice but to return for inpatient treatment on an addictive disease unit lest he lose his job.

On readmission, the patient admitted to long-term use of Darvocet-N 100, which began with his leg injury 5 yr earlier. He had gradually increased his usage to about 20 tablets per day (although the dose had gradually been reduced during the several weeks before his first admission). One year before his admission, he had begun taking fentanyl (Sublimaze) on a sporadic basis. Instead of administering the drug intravenously, he orally ingested the contents of a 500- $\mu$ g ampule once or twice daily. He denied holding the liquid in his mouth, stating that he swallowed it in one quick gulp. He described a mellow feeling with little or no euphoria that would begin within 60 min after ingesting the drug. He continued to take fentanyl by mouth several days per week for the 3 months prior to his admission, amid suspicion and accusations from his coworkers, who noticed behavioral changes and social withdrawal.

After the patient was confronted with the results of the positive urine drug test, he participated actively in the treatment program. His wife was very supportive and attended family sessions to participate in his recovery. His employers, who also were supportive of him, helped facilitate his return to work and encouraged his participation in a continuing program of recovery.

## DISCUSSION

The case report describes involved dependence upon orally ingested fentanyl. Little information involving oral absorption is available because the drug is intended for intravenous use. However, Stanley *et al.* described the use of fentanyl citrate in a lollipop (oral transmucosal fentanyl

citrate) as premedication for surgery procedures.<sup>4</sup> They demonstrated that administration of oral transmucosal fentanyl citrate results in rapid increases in plasma fentanyl concentration, with accompanying dose-related sedation, analgesia, respiratory depression, and common opioid side effects (including pruritus, nausea, vomiting, and difficulty with micturition), but without changes in arterial blood pressure or pulse rate. Smaller doses (0.5–1 mg) of oral transmucosal fentanyl citrate produced analgesia for short periods and produced some sedation, with little respiratory depression, thereby deserving evaluation as premedication in patients. Higher doses of oral transmucosal fentanyl citrate (greater than 2 mg) produced respiratory depression and a higher incidence of side effects.<sup>4</sup>

Stanley *et al.* also reported that two volunteers swallowed an entire 5-mg lollipop; neither experienced sedation, but both experienced 15–20 min of sleepiness approximately 60–80 min after oral ingestion. These observations suggested that, as the lollipop dissolved, some penetrated through the mucosa of the mouth, pharynx, and esophagus, reaching the systemic circulation *via* the venous drainage and right atrium without passage through the liver. In contrast, virtually all venous drainage from the stomach and small intestine passes through the liver *via* the portal circulation. The high hepatic clearance may explain why oral administration of 5 mg fentanyl produced few opioid-related effects, whereas buccal liquefaction produced sedation, analgesia, and respiratory depression.<sup>4</sup> The relative lack of opioid effects in these two volunteers was noted by our patient as well.

Little information is available about gastrointestinal absorption of fentanyl, although *The Extrapharmacopeia* states that absorption does occur from the gastrointestinal tract with rapid onset but short duration of action.<sup>5</sup>

In summary, this case demonstrates oral ingestion of fentanyl as well as the difficulty of detection of fentanyl with the usual comprehensive drug screens. Detection and quantification are now generally performed with gas chromatography/mass spectroscopy (although radioimmunoassays can be used).<sup>6</sup> When fentanyl abuse is suspected, the laboratory should be requested to screen for it specifically. The treating physician should be particularly alert to the possibility of fentanyl abuse when working with anesthesia and operating room personnel.

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### Isolated Masseter Muscle Spasm and Increased Creatine Kinase without Malignant Hyperthermia Susceptibility or Other Myopathies

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There is much controversy about the definition, significance, management, and family counseling of patients

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who develop masseter muscle spasm (MMS) after succinylcholine.<sup>1–4</sup> The clinician must consider whether MMS correlates with malignant hyperthermia susceptibility (MHS) and whether to recommend further investigation such as a muscle biopsy to evaluate the presence of myopathy and/or the halothane–caffeine contracture test to diagnose MHS. Measurement of creatine kinase (CK) within 24 h may show extreme elevations, which may be helpful in the diagnosis of MHS or a myopathy. A previous report<sup>5</sup> documented that CK values of greater than 20,000 IU are highly suggestive of MHS as diagnosed by the halothane–caffeine contracture test. The only patient who did not have MHS had a myopathy that was dem-