Rampant caries from oral transmucosal fentanyl citrate lozenge abuse

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Oral transmucosal fentanyl citrate (OTFC) is a Schedule II controlled narcotic substance that has an analgesic potency substantially greater than that of morphine. The U.S. Food and Drug Administration approved OTFC for use in managing breakthrough pain (BTP) in patients with cancer. BTP is characterized by transient pain flare-ups that are rapid in onset, short in duration and moderate to severe in intensity. BTP occurs if standardized pain treatment offers no relief from an existing persistent painful state. Although OTFC has been approved by the U.S. Food and Drug Administration for BTP only in patients with cancer, it is being used off-label for back pain, bone injuries, migraine and other chronic moderate to severe pain from nonmalignant sources.

OTFC, which is intended for use by opiate-tolerant people, is formulated as a berry-flavored lozenge, containing 2 grams of sucrose, placed at the end of a plastic stick. The patient applies the lollipop to the buccal mucosa and rotates it while sucking and swallowing. The lozenge usually dissolves within 20 to 30 minutes.

ABSTRACT

Background. Oral transmucosal fentanyl citrate lozenges (lollipops) are indicated for the oral management of breakthrough cancer pain. When abused, these sucrose-containing lozenges can cause rampant dental caries.

Case Description. The authors examined a 19-year-old man whose dentist referred him because of his claim that the gross carious destruction of one tooth was caused by the lozenge in his mouth for about 30 minutes. The patient maintained this regimen of eight to 10 lozenges (1,200 µg per lozenge) per day. He took standard analgesic medications and caries. Consequently, his facial pain had become “unbearable.” He had been receiving dental care occasionally. To relieve the pain from the trigeminal neuralgia, BTP, and dental caries, he took standard analgesic medications and caries.

Clinical Implications. Dentists should be aware that oral transmucosal fentanyl citrate lozenges are being prescribed off-label for the control of pain from nonmalignant sources. Fentanyl citrate’s effective analgesic potency can lead to misuse and potential abuse. Early recognition of its misuse could prevent severe dental caries and the need for extensive dental restoration.

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utes. Rapid pain relief is obtained from the portion of OTFC absorbed through the highly vascularized mucosa (25 percent). The remaining 75 percent is swallowed into the gastrointestinal tract, where two-thirds of this amount is either metabolized by the liver or eliminated through the intestines. A prolonged analgesic effect is obtained from the remaining, more slowly absorbed intestinal portion of OTFC.

OTFC is prescribed in multiple formulations, from 200 to 1,600 micrograms, allowing for titration of the dosage to meet individual patient needs. It can be abused and become addictive. Adverse effects and adverse reactions other than addiction include respiratory depression, central nervous system depression, dry mouth, constipation, hypotension, bradycardia and dental caries. Consequently, its recommended use is limited to four lozenges per day, although some reports indicate that one to 10 lozenges (mean, 3.7) of 200 to 1,600 µg per lozenge are being used.

CASE REPORT

In October 2009, a 19-year-old man was referred by his dentist to the Columbia University College of Dental Medicine’s Salivary Gland Center because of total dental coronal destruction.

We conducted an oral examination and found that the patient’s teeth had no crowns (Figure 1). We did see the retained roots of 31 teeth and that the maxillary left lateral incisor was missing. The patient’s oral hygiene was good, and the mucosa appeared to be normally moist. All salivary duct orifices were patent, with normal salivary flows evident when we massaged the respective salivary gland aggressively. A panoramic radiograph showed the roots of 31 teeth, some of which had periapical pathology (Figure 2).

The patient had been diagnosed seven years previously with trigeminal neuralgia that involved the left side of his face and extended from the upper eyelid to the cheek. When we asked the patient about the status of his teeth in previous years, he said that until he was 16 years old his teeth were “decent” and that he had been receiving dental care occasionally. To relieve the pain from the trigeminal neuralgia, he took standard analgesic medications and carbamazepine; however, their use did not result in effective pain relief, and he said his facial pain had become “unbearable.” Consequently, his physician prescribed OTFC (800 µg) lollipops four times a day. After one month, the pain was not totally relieved, and the patient illegally obtained OTFC “off the street” and instituted his own regimen of eight to 10 lozenges (1,200 µg per lozenge) per day. He maintained each lozenge in his mouth for about 30 minutes. The patient was adamant in his claim that the dental problems developed five to six months after he started using the OTFC lozenges. Before coming to the Salivary Gland Center in October 2009, he had already been weaned off of OTFC, and his psychiatrist had prescribed psychotherapeutic medications.

We contacted the referring dentist, and he forwarded dental radiographs that were obtained in January 2006. When we reviewed these radiographs, we saw an intact dentition with coronal caries involving a few teeth (Figure 3). These radiographs substantiated the patient’s claim that the gross carious destruc-

ABBREVIATION KEY. BTP: Breakthrough pain. OTFC: Oral transmucosal fentanyl citrate.
tion of the teeth had developed in the preceding three years. This finding pointed to the use and abuse of the topically applied sucrose-containing OTFC as the key factor in the patient’s dental deterioration.

In view of the condition of the patient’s teeth, we deemed that a restorative approach to treatment was feasible. We performed full-mouth extractions and referred the patient to a prosthodontist for denture construction.

DISCUSSION

Some patients who use addictive drugs may be susceptible to rampant caries. An interplay of factors that include drug-induced hyposalivation, poor oral hygiene and craving for sweets plays a role in the development of dental caries. Although OTFC use is associated with such conditions, its high sucrose content and method of application are unique causes of extensive caries when compared with other addictive agents, particularly when it is abused.

Sucrose is added to OTFC for flavoring, but it also serves as the sole substrate for the synthesis of extracellular glucans. This process is mediated by normally occurring oral Streptococcus mutans and facilitated by the bacteria’s surface enzyme glucosyltransferase. The glucans promote adhesion of S. mutans to tooth surfaces on which the bacteria take part in fermenting the carbohydrate sucrose. The resulting acid overwhelms the protective effect of the thin salivary pellicle on the tooth surface and contributes to enamel demineralization.

Besides promoting adhesion of S. mutans to tooth surfaces, glucans increase the porosity of dental plaque. The increased porosity permits deeper penetration of sucrose into the plaque and results in greater acid production immediately adjacent to the tooth surface. Plaque is a biofilm that adheres to tooth surfaces. It consists of bacterial aggregates (mainly S. mutans), bacterial extracellular products (mainly glucans) and salivary polymers. The biofilm is held together by matrix of extracellular products and protects the contained organized community of bacterial colonies. Because the biofilm has a low concentration of calcium and phosphate ions, it enhances enamel mineral loss and susceptibility to caries.

Stephan first showed that oral bacteria readily metabolize sugars to form the acid that lowers the pH of plaque. However, the Vipeholm dental caries study first demonstrated the linkage of sugar with caries. The study’s results established that the more frequently sugar is consumed, the greater the caries risk. The frequency of sugar ingestion is just as important as the amount, because it causes prolonged acid exposure of the enamel below its critical pH and favors selection of the acid-loving S. mutans. Furthermore, sugar consumed between meals is more cariogenic than that consumed during a meal because masticatory activity promotes sugar clearance.

The initial attachment of plaque to a dental surface begins with pellicle formation. S. mutans attaches to the pellicle, and, with the production of glucans, the stickiness increases and facilitates the close apposition of acid-producing S. mutans to the tooth surface. The presence of acid in the deeper confines of plaque protects the acid from the surface-buffering and lavaging action of saliva.
The inhibitory action all opioid agents—in this case fentanyl—has on salivary production is another factor in the cariogenicity of OTFC. Through several mechanisms, saliva inhibits but does not prevent acid erosion of teeth. Saliva physically dilutes acid and lavages it away when the patient swallows. Saliva is instrumental in the formation of the protective dental pellicle and neutralizes acids. In addition, saliva is supersaturated with calcium and phosphate ions, thus reducing the rate of enamel dissolution while simultaneously helping with remineralization.

Other than a poster presentation at the 2007 meeting of the American Academy of Physical Medicine and Rehabilitation, we were not able to find any reports in the literature regarding OTFC-associated extensive dental breakdown. The manufacturer’s package insert warns of dental decay and advises dental consultations.

When we investigated the patient’s medical history, we found that his caregivers had recognized the presence of an addiction. In our discussions with the patient, it was apparent that he had abused OTFC. The abuse originated from the drug’s off-label use, which is as high as 90 percent. OTFC’s effectiveness can lead to its misuse. The fact that the patient used the sucrose-containing OTFC more frequently than indicated for three years was instrumental in the destruction of his tooth crowns.

CONCLUSION

The topical use and the frequency of application of sucrose-containing OTFC lozenges, combined with the opioid agent’s ability to decrease salivation, are the major causes of carious coronal destruction. Secondary factors usually include poor oral hygiene and a sugar craving.

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