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## CASE REPORT

# Controlling the fluoride dosage in a patient with compromised salivary function

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**T**opical fluoride supplements are a commonly prescribed and valuable treatment to prevent root and enamel caries in patients with head-and-neck cancer. Supplements in the form of tray-applied gels, mouthrinses and high-concentration dentifrices can be used to control caries in patients with compromised salivary function resulting

from irradiation and chemotherapy during and after cancer treatment. However, it is essential that clinicians carefully monitor patients' compliance with the treatment regimen to prevent inadvertent overuse or overingestion of fluoride.

This case report illustrates the potential for adverse side effects when prescribing high doses of patient-applied fluoride, the symptoms clinicians need to recognize and how to eliminate these side effects.

## CASE REPORT

The patient was a 50-year-old man with diagnosed squamous cell carcinoma of the posterior right lateral border of the tongue. Surgical treatment by an oncologist and surgeon at a regional medical center included resection of the right half of the tongue, along with extraction of teeth numbers 29, 30 and 31 and additional resection of the superior ridge of the right posterior mandible. The right mandibular third molar had been extracted previously. The patient's dentist restored all other teeth before surgery, and the patient was in good general oral health.

**Clinicians who prescribe high-concentration at-home fluoride treatment must closely monitor the patient's compliance with the regimen.**

**Background.** High-concentration topical fluorides are used commonly to prevent caries in patients with compromised salivary function due to irradiation and chemotherapy.

### Case Description.

The authors describe a 50-year-old man with previously treated cancer who was using tray-applied topical fluoride gel. He complained of gastric symptoms, difficulty in swallowing, leg muscle soreness and knee joint soreness. A computed tomographic scan revealed thickening of the esophageal walls. An upper endoscopy revealed abnormal motility. The motility test indicated high-amplitude peristalsis and hypertensive lower esophageal sphincter, and urine testing indicated high levels of systemic fluoride. The patient's fluoride regimen was altered, and within a short period his urinary fluoride levels returned to normal and his symptoms resolved.

**Clinical Implications.** Clinicians prescribing home-applied high-concentration fluorides need to be cognizant of the symptoms of fluoride toxicity, carefully monitor the patient's compliance with the treatment regimen, and adjust the dosage or mode of application to control the total ingested dose of fluoride.

**Key Words.** Fluoride; fluoride gel; toxicity; urinary fluoride.

The patient then underwent post-surgical radiation treatment of the tumor area and regional lymph nodes. As a result, salivary function was severely compromised. The patient's dentist advised him to use daily fluoride treatments to prevent the development of caries. The patient also drank water as a salivary supplement throughout the day, and used a dentifrice, a chlorhexidine mouthrinse and a commercial oral lubricating gel as a nighttime moistening agent.

**Fluoride treatment regimen.** The fluoride treatment prescribed by



the patient's dentist consisted of daily use of a 2 percent mass fraction in-office sodium fluoride topical gel applied with custom vacuum-formed maxillary and mandibular thermoplastic trays. The dentist instructed the patient to place approximately 1 milliliter to 2 mL of the gel in each of two trays and wear them for three minutes. The dentist instructed the patient to expectorate all of the excess gel, and not to rinse his teeth or drink for 30 minutes after removing the trays. Because of the patient's concern about the potential for caries, he modified his treatment regimen by using the fluoride twice a day rather than once a day, as he had been instructed. The patient did not inform his dentist of this change and continued with this regimen for about four months before reporting symptoms.

**Symptoms.** The patient visited his physician with complaints of gastric distress, dysphagia, difficulty in swallowing when eating or drinking, soreness of the leg muscles and knee joints, and general malaise. Because difficulty in swallowing and gastric distress were the most bothersome symptoms, the physician performed computed tomography (CT), an upper endoscopy and motility tests.

**Test results.** The CT scan showed thickening of the esophageal walls, and the endoscopy revealed the presence of abnormal motility with normal mucosa. The motility test showed high-amplitude peristalsis and hypertensive lower esophageal sphincter consistent with a spastic motility disorder. Many of these symptoms might have been considered normal sequelae of the head-and-neck cancer treatment if not for the latent onset of joint and muscle pains. After taking a thorough dietary history, the physician hypothesized that perhaps the fluoride treatments were responsible for some of these symptoms and referred the patient back to his dentist for evaluation.

The dentist then made an inquiry to our laboratory to evaluate whether the fluoride treatment could have resulted in the patient's symptoms. One of us (F.E.) conducted an oral examination and took a medical history in our research clinic. The patient was instructed to discontinue the tray treatments and obtain a urine sample at approximately 8:00 a.m.—about 24 hours after the last fluoride treatment—so that the fluoride content could be analyzed.

The patient collected the sample and stored it in a sealed polyethylene laboratory bottle. Within

one hour of collection, he delivered the sample to our laboratory, where it was refrigerated until measured. Two of us (N.E., C.C.) measured fluoride levels using an ion-specific fluoride electrode that was calibrated between 0.1 microgram per gram of fluoride and 10.3  $\mu\text{g/g F}$  and National Institute of Standards and Technology standard solutions. The examiners repeated the calibration before each of three measurements of the sample.

**Urinary fluoride levels.** The urine sample was analyzed and found to be 4 parts per million F ( $\mu\text{g/g F}$ ). (We used parts per million throughout this article because it is the most commonly reported unit of concentration for urinary fluoride.) One of us (F.E.) then instructed the patient to return to the originally prescribed once-daily fluoride treatments while we continued to monitor his urinary fluoride levels. A second urine sample was collected 16 days after the patient returned to using the fluoride trays once per day in the evening (the sample was collected one hour after the nightly treatment).

The results of this analysis show that the sample was 5.63 ppm F. We then hypothesized that perhaps the elevated fluoride level was due to a transient spike occurring within the one-hour period after tray treatment, just before the patient collected the urine. To test this possibility, we decided to collect samples throughout a day, followed by a total daily urine collection for whole-day averaging.

The next week, we instructed the patient to collect urine samples at several times throughout one day (four samples collected at various intervals from one hour to 24 hours after the fluoride treatment) to try to determine any variation in levels throughout the day. The results of this analysis show that the four samples had fluoride concentrations ranging from 1.73 to 7.26 ppm, with a high degree of variability. The highest concentrations—3.40 and 7.26 ppm—were in samples collected one hour after the fluoride treatment and at 8:00 a.m. (nine hours after treatment), respectively. These results indicated that urinary concentrations varied widely throughout the day, and probably were highest in the morning, after the longest period of urinary retention. Sampling repeated the next day confirmed these results.

We then instructed the patient to collect total urine for one day to determine a time-weighted average concentration. The patient was asked to obtain a urine sample just before applying the fluoride (time 0) at approximately 11:00 p.m. and

then to collect the total amount of urine during a 24-hour period in individual containers. We analyzed samples from each of nine containers and from the pooled total of 831 mL. The urine samples ranged in volume from 50 to 200 mL. The figure shows the measured urinary concentrations.

The patient's symptoms persisted, and one of us (F.E.) instructed him to discontinue the tray treatments entirely and switch over to brushing once daily with a mass fraction of 1.1 percent NaF dentifrice, expectorating as much of the dentifrice as possible. After 10 days of dentifrice use, we instructed the patient to collect urine samples at 8.5 hours and 24 hours after brushing. The urinary fluoride concentrations were 1.71 and 0.87 ppm, respectively. The once-daily brushing with a mass fraction of 1.1 percent NaF dentifrice was continued, and all gastric, muscle and joint symptoms resolved during a two-week period.

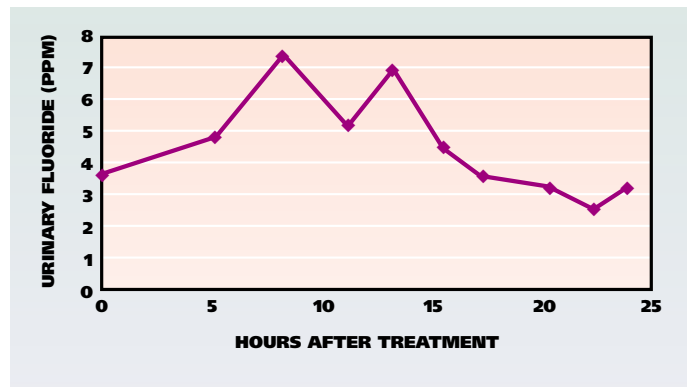
Four years after his radiation treatment, the patient has continued to be symptom-free and caries-free while brushing each night with the 1.1 percent NaF dentifrice. He has not reported any other adverse effects from the fluoride exposure.

**Water fluoride levels.** To determine the ambient exposure, our laboratory measured fluoride levels in tap water from the system supplying the patient's home and in urine samples from one individual residing in the same household as the patient, but not receiving supplemental fluoride. The fluoride concentration in two tap water samples was 1.09 and 0.78 ppm, and in three urine samples collected on different days was 1.23, 1.21 and 1.24 ppm.

## DISCUSSION

If we assume a single-application loading of 2 to 4 mL of NaF gel and ingestion of 50 percent, or 1 to 2 mL of the 2 percent gel (considering that expectorating could not be done properly because of the patient's low salivary level), the daily dose of fluoride from twice-daily use would be 40 milligrams to 80 mg (twice the prescribed dosage). The more commonly prescribed 1.1 percent NaF gel or 1.2 percent acidulated phosphate fluoride gel applied once per day could result in ingestion of approximately 10 to 25 mg of fluoride per day.

A study of long-term fluoride ingestion reported urinary fluoride and endoscopy results from 10 patients with diagnosed osteosclerosis who were receiving 30 mg/day NaF for three



**Figure.** Urinary fluoride levels after treatment with 2 percent mass fraction sodium fluoride topical gel applied with custom trays. The concentrations were approximately 5 parts per million to 7 ppm for the first 13 hours after treatment, and then declined gradually to about 3 ppm. The average concentration for the total amount of urine collected during 24 hours was 3.49 ppm.

months or longer. All 10 patients had upper gastrointestinal dyspeptic symptoms, but those with urinary levels of 2.9 ppm or higher exhibited signs of gastric surface abrasion and loss of epithelium.<sup>1</sup>

### Occupational exposure to fluoride.

Another study found similar urinary levels in people who worked in a sodium aluminum fluoride factory and who were exposed to cryolite dust. Their test results showed that the urinary clearance rate for fluoride was highly variable, but that levels remained elevated three days after exposure.<sup>2</sup> We could consider the exposure of the patient described in this article to be much like an occupational exposure in that the treatment regimen and quantity of fluoride ingested remained relatively constant over a long period.

**High levels of naturally occurring fluoride.** Felsenfeld and Roberts<sup>3</sup> reported a case of a patient exposed for seven years to high levels of fluoride naturally occurring in private well water. The patient's symptoms were stiffness of the knees and hips, and a bone survey showed sclerosis in many skeletal bones. The authors reported elevated urinary levels of fluoride in this patient, as well as in residents of four other local households with similarly high well-water levels of fluoride.<sup>3</sup> This patient may have consumed more water than her neighbors, however, because she was taking three medications (haloperidol, protriptyline hydrochloride and benztropine mesylate) that are known to cause dry mouth.

### Certainly lethal and probably toxic doses.

Whitford<sup>4,5</sup> examined the range of fluoride doses considered to be a certainly lethal dose (defined

as the dose equivalent to the lethal dose [ $LD_{100}$ ] expected to cause death after ingestion by adults) and a probably toxic dose (PTD) (defined as the dose that should trigger immediate intervention because of the likelihood of serious toxic consequences). His review of the literature and death reports of fluoride toxicity concluded that the most reasonable PTD for ingested fluoride is 5 mg/kilogram body mass.<sup>4,5</sup>

The patient in our case report weighed 64 kg, resulting in a PTD of 320 mg, so his ingested exposure (based on the initial estimated ingestion of gel) was one-eighth to one-fourth of the PTD on a daily basis. A 1.1 percent NaF gel or 1.2 percent acidulated phosphate fluoride gel applied once per day still could result in approximately one-tenth the PTD. The PTD, however, is based on a single acute exposure, and little information is available regarding toxicity levels related to long-term exposure.

Normal urinary levels of fluoride can vary considerably, depending on the individual's exposure to fluoridated water and use of fluoride-containing oral hygiene products. The household family member discussed above had a urinary level of 1.2 ppm, which was within the normal range reported by Whitford.<sup>6</sup> Tap water at the household also was within the normal range for fluoridated water. Use of the 2 percent NaF gel within the conditions described in this case report increased the patient's urinary levels by several-fold, and was the likely cause of his gastric anomalies and muscle and joint pain.

## CONCLUSIONS

Topical fluorides have proven to be a valuable tool in battling caries in patients with compromised salivary function. The amount of fluoride in most products designed specifically for this purpose is several times greater than that in standard oral hygiene products. When prescribing fluoride for compromised patients, clinicians should keep in mind both the dosage and method of administration. Lack of saliva could lead to less dilution of the gel or dentifrice, less ability to expectorate efficiently, longer retention in the mouth and a greater proportion of ingested material. Patients also may apply too much fluoride or use it too often in an effort to prevent the development of caries. In addition, the symptoms of fluoride toxicity can be fairly subtle and easily masked by

other local and systemic problems in these patients.

The combination of gastric problems, difficulty in swallowing, leg muscle pain, and pain in the knee and hip joints is a key indicator of fluoride toxicity, and patients using high-concentration home fluoride treatments should be monitored for these symptoms. Fortunately, the symptoms are transient and resolve rapidly once the level of ingested fluoride is reduced. In this case, reducing the amount of fluoride by eliminating the tray treatment and switching to a lower-concentration dentifrice eliminated the symptoms without apparently negating the benefit of treatment.

Clinicians who prescribe high-concentration at-home fluoride treatment must closely monitor the patient's compliance with the treatment regimen, minimize the dosage by using well-fitting custom trays and small quantities of gel or dentifrice, instruct patients to expectorate as much fluoride as possible and advise them to promptly report any gastric problems or joint and muscle pain. ■

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The purpose of this article is to caution practitioners about the risks and symptoms of fluoride toxicity, and offers no comment on the appropriateness of the treatment offered the patient.

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