

# Carbonation dysgeusia associated with topiramate

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**Purpose.** A case of carbonation dysgeusia associated with the use of topiramate is reported in order to bring awareness to a lesser-known adverse effect of the medication so that providers may be able to more effectively counsel patients and provide potential solutions.

**Summary.** A 39-year-old Caucasian woman with longstanding epilepsy was initiated on topiramate therapy after experiencing a generalized seizure (she reported not taking any antiepileptic medication for years). Topiramate was started at a dosage of 25 mg by mouth twice daily and after 3 weeks titrated to a dosage of 100 mg by mouth twice daily for maintenance therapy. After initiation of topiramate therapy, the patient began to experience an immediate change in her carbonation perception when drinking carbonated beverages; all carbonated beverages, including seltzer and beer, tasted “flat.” The patient remained on topiramate for the subsequent 12 months without her carbonation perception returning to normal but noted that drinking carbonated beverages through straws slightly mitigated the adverse effect. Case assessment using the adverse drug reaction probability scale of Naranjo et al indicated that topiramate was the probable cause of the patient’s carbonation taste perversion.

**Conclusion.** A 39-year-old Caucasian woman developed chronic carbonation dysgeusia after initiation of topiramate following a generalized seizure.

**Keywords:** carbonation taste perversion, dysgeusia, topiramate

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Dysgeusia is a medical condition defined as an alteration of the sense of taste.<sup>1</sup> Certain medications can lead to dysgeusia through various mechanisms of action involving chemosensory pathways, such as taste, smell, and salivation.<sup>2</sup> The majority of cases of taste dysfunction due to medication use cited in the literature involved hypogeusia (partially impaired sense of taste) or the more general dysgeusia.<sup>3</sup> Dysgeusia has been reported with use of antibiotics (eg, clindamycin, metronidazole, fluoroquinolones), neurologic medications (eg, central nervous system stimulants, muscle relaxants), and psychotropics (eg, tricyclic antidepressants, anxiolytics, mood stabilizers) as well as antihistamines, antineoplastics, smoking cessation aids, and antifungals, among others.<sup>4</sup>

Metallic taste following medication administration is a commonly reported

medication-induced dysgeusia. In fact, metallic taste is a reported adverse effect of over 300 medications.<sup>5</sup> Medications with sulfhydryl groups, such as acetylcholinesterase inhibitors and antithyroid agents (propylthiouracil and methimazole), can cause metallic tastes. Anticholinergic medications are associated with dry mouth, which can be interpreted as a metallic taste. Metformin has also been associated with metallic taste, which tends to resolve after a few months of metformin use. Angiotensin-converting enzyme inhibitors, especially captopril, are among the drugs most commonly associated with taste disturbances, with strongly metallic, bitter, or sweet tastes having been reported.<sup>6</sup>

Topiramate is a second-generation antiepileptic drug that is used in the treatment of seizure disorders and migraine headaches.<sup>7</sup> Its use has been associated with weight loss; nausea and

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other gastrointestinal adverse effects; paresthesia in the hands, feet, or face; and cognitive and behavioral changes, including memory impairment, confusion, and reduced concentration. Here we describe a case of carbonation dysgeusia potentially related to the initiation and continued use of topiramate following a generalized seizure. The term *carbonation dysgeusia* is used to describe distortions of carbonation taste quality leading to diminished or complete elimination of the pungency or prickly sensation experienced on imbibing carbonated beverages.<sup>8</sup> Other cases of topiramate-induced carbonation dysgeusia have been widely mentioned in various Internet patient forums.<sup>9,10</sup> Although topiramate-induced dysgeusia has been reported in numerous randomized controlled trials, most of the trial reports did not define the specific manifestation of dysgeusia.<sup>11-13</sup> Furthermore, our PubMed search, conducted without date limits using the terms *topiramate* and *carbonation dysgeusia* or *drug-induced taste perversion*, identified no previous reports describing this reaction in detail.

### Case report

A 39-year-old Caucasian woman with epilepsy had a generalized seizure after 12 years without use of antiepileptic medication. Her last generalized seizure had occurred 23 years prior, and her last known partial seizure activity had occurred 15 years prior. Following a brief loss of consciousness, she was brought to the emergency department by ambulance, and levetiracetam was initiated.

The following day, the patient was seen by her primary care physician, who switched from levetiracetam to topiramate 25 mg by mouth twice daily, with titration to topiramate 100 mg by mouth twice daily for maintenance therapy after 3 weeks. The patient reported good adherence to the medication, missing less than 1 dose per month. The serum topiramate concentration was determined 17 days after topiramate initiation, 3 days after a

### KEY POINTS

- A patient lost her ability to taste carbonation in all carbonated beverages immediately following topiramate initiation and found that drinking through a straw mitigated the “flat” taste.
- Carbonation dysgeusia after topiramate initiation has been reported by patients taking the medication but is not well identified in the literature.
- Medication-related changes in taste are important to identify because such changes can negatively affect medication adherence, chronic disease management, and overall quality of life.

dosage increase to 75 mg twice daily, and was considered to be in the therapeutic range, at 6.2 µg/mL (reference range, 5-20 µg/mL). At that time (and also during the initiation and titration of topiramate), the patient was not taking any other medications, vitamins, or supplements.

Promptly after the initiation of topiramate, the patient lost her ability to taste carbonation in all beverages, including soda, seltzer, and beer. The first beverage she tried following initiation of topiramate 25 mg by mouth twice daily was cold seltzer water from a can, and she immediately noted a “flat” taste. Over the course of months she tried multiple carbonated beverages, including soda, seltzer, beer, champagne, and energy drinks. No matter the type of carbonated beverage, each one tasted flat to her since starting topiramate therapy.

The patient looked to online forums for patients with epilepsy and migraine for information on the phenomenon and found numerous reports of similar experiences from others taking topiramate on the websites epilepsy.

org and migraine.org.<sup>9,10</sup> In one such forum, someone suggested using a straw to help mitigate the adverse effect, and our patient found the suggestion helpful. Although the sense of carbonation when drinking with a straw was not as intense as it was prior to topiramate initiation, she noticed considerable improvement; the straw enhanced the carbonation taste sensation enough to make some carbonated beverages “palatable.”

At the time of writing, 12 months had passed since topiramate initiation and the patient’s sense of carbonation had not returned to normal. She was also experiencing mild hand and feet paresthesia, which are commonly reported adverse effects of the medication.<sup>14</sup> Bloodwork performed 10 months after topiramate initiation indicated that all values were within normal limits, with the exception of a low alkaline phosphatase (ALP) level (38 U/L [reference range, 50-136 U/L]) and low creatinine concentration (0.7 mg/dL [reference range, 0.8-1.3 mg/dL]); neither low value was deemed concerning. These results were consistent with results of bloodwork performed years previously; at that time, her bloodwork indicated all evaluated levels were within normal limits except for low concentrations of ALP (40 U/L) and creatinine (0.6 mg/dL). The topiramate level was not rechecked after the first determination 17 days after topiramate initiation.

### Discussion

At the time of dysgeusia development, topiramate was the only medication the patient was taking; thus there seems to have been a clear temporal relationship between topiramate use and the onset of her symptoms. Prior to the administration of topiramate, the patient had never experienced a loss of carbonation sensation while drinking numerous varieties of carbonated beverages throughout her life. Case assessment using the adverse drug reaction probability scale of Naranjo et al<sup>15</sup> indicated a probable relationship between topiramate use and

carbonation-perception loss (ie, a score of 5).

Topiramate is used for migraine headache prophylaxis in adults and for adjunctive or monotherapy treatment of partial onset seizures, primary generalized tonic-clonic seizures, and seizures related to Lennox-Gastaut syndrome.<sup>14</sup> Its antiepileptic properties may be due to several mechanisms of action; topiramate blocks voltage-dependent sodium and calcium channels in addition to inhibiting excitatory glutamate pathways and potentiating inhibitory  $\gamma$ -aminobutyric acid effects.<sup>16</sup> Topiramate also inhibits carbonic anhydrase activity.<sup>17</sup> Its mechanisms of action may underlie both its clinical utility as well as its unique adverse effects.

“Taste perversion” or “taste dysgeusia” in association with topiramate use has been reported in numerous randomized controlled trials; however, most of the trial reports did not define the specific manifestation of dysgeusia as carbonation dysgeusia. Linde et al<sup>11</sup> noted a significant difference in “taste disturbance” adverse effects with topiramate vs placebo use in a meta-analysis of 9 trials involving a total of 1,737 participants. Luykx et al<sup>12</sup> performed a meta-analysis of 10 randomized controlled trials to compare topiramate-related adverse drug reactions in patients taking topiramate for epilepsy and those taking topiramate for migraine disorders. Evaluating data on a total of 2,902 participants in the meta-analysis, the researchers demonstrated that “alteration of taste” as an adverse effect of topiramate was found only among patients taking topiramate for migraine disorders and not in those taking topiramate for epilepsy. Donegan et al<sup>13</sup> performed a systematic review of 90 placebo-controlled trials of topiramate and noted that dysgeusia was reported at a significantly higher rate with topiramate vs placebo use.

Carbonation dysgeusia as a result of topiramate therapy is not well identified in the literature but has been reported by patients in online chat forums.<sup>7</sup> More frequently identified in

the literature as causing carbonation taste alterations is acetazolamide, a carbonic anhydrase inhibitor. Although topiramate has multiple mechanisms of action, its carbonic anhydrase inhibitory effects are similar to those of acetazolamide.<sup>17</sup>

Carbonic anhydrase is a zinc metalloenzyme that reversibly catalyzes the conversion of carbon dioxide ( $\text{CO}_2$ ) and water into carbonic acid ( $\text{H}_2\text{CO}_3$ ), which rapidly dissociates to bicarbonate ( $\text{HCO}_3^-$ ) and a free proton.<sup>18</sup> Carbonic anhydrase inhibitors, such as acetazolamide and dorzolamide, prevent this conversion and have been reported to alter carbonation taste perception.<sup>19</sup> In one reported case, after taking acetazolamide to prevent altitude sickness mountain climbers noted that their beer tasted “like dishwasher.”<sup>20</sup> Another case report described a 31-year-old woman who took acetazolamide to prevent mountain sickness and, within 90 minutes, developed a bitter taste sensation on consuming carbonated soda, tea, and Mexican food.<sup>21</sup> The symptoms resolved within 14 hours after acetazolamide discontinuation.

Mouths are sensitive to the effects of carbon dioxide, the substance that initiates the chemical pathway eliciting a fizzy and tingling sensation upon consumption of carbonated beverages.<sup>19</sup> Results from Dunkel and Hofmann’s<sup>18</sup> study suggested that  $\text{CO}_2$  acts on the sour taste system as well as somatosensory pathways; the fizzy and tingling perception of carbonated beverages is likely due to gustatory and somatosensory inputs leading to multimodal sensation. Dunkel and Hofmann also suggested that carbonic anhydrase 4, specifically, mediates the fizzy sensation experienced on drinking carbonated beverages. In fact, carbonic anhydrase 4 may function as the principle  $\text{CO}_2$  taste sensor for the human body. Therefore, if carbonic anhydrase 4 is inhibited, taste perception of carbonation may be distorted, diminished, or completely eliminated.

Medication-related changes in taste are important to identify because

such changes can lead to poor medication adherence and negatively affect chronic disease management.<sup>2</sup> Taste disturbance can also negatively affect nutritional status; one study found that individuals with taste disturbances consumed 500 fewer calories per day and ate fewer fruits and vegetables than those without taste disturbances.<sup>22</sup> With dysgeusia, one may be more inclined to compensate for the altered taste with added salt or sugar, which can also negatively affect health outcomes. Furthermore, taste disturbances can affect quality of life, as what used to be enjoyable may no longer be so.

The suggestion of drinking carbonated beverages through a straw to mitigate carbonation dysgeusia is an interesting recommendation. It is difficult to ascertain exactly why use of a straw may enhance carbonation perception in the mouth. Perhaps with a straw the carbonated beverage is more concentrated on the tongue, where taste is perceived. Aswini et al<sup>23</sup> noted reduced dental plaque when carbonated beverages were sipped with a straw; the straw concentrated the beverage on the tongue and minimized full-mouth exposure. Patients on topiramate therapy may find carbonation perception enhanced by drinking through a straw, and pharmacists can mention this as a potential counseling point.

Zinc may play a role in taste perception, and zinc deficiencies may contribute to taste disorders.<sup>24</sup> There is evidence to support the use of zinc supplementation in some cases of medication-induced dysgeusia. Najafzade et al<sup>24</sup> demonstrated that zinc supplementation increased perception of all sweet, sour, bitter, and salty tastes among patients with head or neck cancer undergoing radiotherapy.

In theory, because carbonic anhydrase is a zinc metalloenzyme, administration of carbonic anhydrase-inhibiting medications may lead to zinc deficiency and, ultimately, taste distortions. In this line of thought, zinc supplementation may be needed with carbonic anhydrase inhibitor administration to prevent or treat dysgeusia.

However, whether zinc supplementation may be beneficial for carbonation dysgeusia remains to be established.

While treatment plans must be individualized for each person, with careful consideration of anticipated results, the benefits of treatment with topiramate likely outweigh the risks for many patients. However, when considering the addition of topiramate therapy, one should educate the patient regarding potential side effects and methods to mitigate them in order to ensure medication adherence, enhanced chronic disease state management, and improved overall quality of life.

## Conclusion

A 39-year-old Caucasian woman developed chronic carbonation dysgeusia after initiation of topiramate following a generalized seizure.

## Disclosures

The authors have declared no potential conflicts of interest.

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