CASE REPORT

Acetazolamide promotes decreased consumption of carbonated drinks and weight loss

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Abstract

Excessive consumption of carbonated drinks contributes to the dietary surplus of carbohydrates, and is a main driver of the obesity epidemic in the USA. From a public health standpoint, it is therefore crucial to develop strategies that enable individuals to regulate this calorie-rich, but nutrient-poor food intake. However, conservative medical approaches to this end have met with limited success. Using a pharmacological strategy to eliminate the effervescent aspect of carbonated drinks, we report significant weight loss in a patient with long-standing obesity. Administration of low-dose acetazolamide, a carbonic anhydrase inhibitor, resulted in altered taste of carbonation, and in turn a marked reduction in the patient’s carbonated drink intake and the loss of almost 1 kg of body weight per week. The pharmacological intervention also resulted in appetite suppression, which might synergistically contribute to weight loss. These findings point to the use of low-dose acetazolamide as a novel weight reduction strategy.

INTRODUCTION

Obesity is one of the most significant public health issues in our time. It is often compared to an epidemic in terms of its detrimental effects on health and associated long-term morbidity for a significant proportion of individuals in our society [1–4]. It is thought that various dietary and lifestyle changes that have occurred over the past four decades are responsible for this phenomenon [1, 2]. In particular, the consumption of carbonated, sugar-sweetened drinks has more than doubled during the aforementioned time period, mirroring the rising incidence of obesity in the USA [1].

While dietary restriction of carbonated drinks and consumption of sugar-free carbonated beverages are popular approaches to mitigate this epidemic, their degrees of success are modest and transient [5, 6]. In several studies, these approaches have also had counterintuitive effects on body weight [7]. For instance, a significant dose–response relationship has been described between the daily consumption of artificially sweetened carbonated drinks (i.e. net zero calories) and prospective weight gain [7]. These results point to the possibility that carbonated drinks contribute to weight gain and obesity not only via added dietary sugars and calories.

In particular, the carbonation of sweetened drinks is a property that might directly interact with physiological factors underlyng body weight homeostasis and adiposity (Fig. 1) [8–10]. These interactions constitute pathways through which carbonation—via carbon dioxide signaling—might promote obesity. Furthermore, the effervescent aspect of carbonated beverages enhances the perception of sweetness and promotes sugar-seeking behavior in consumers [11–13]. Given these findings, we reasoned that affecting the taste and associated signaling of carbonation in beverages might diminish their appeal to consumers, limiting their intake and effects on energy balance and body weight. Acetazolamide is a carbonic anhydrase inhibitor, which has been shown to eliminate the sparkling or ‘fizzy’ taste of carbonated drinks [14].
of carbonated beverages [14, 15]. Here we tested the effect of administration of low-dose acetazolamide as part of a weight loss strategy in an obese patient with an excessive daily consumption of carbonated, sugar-sweetened beverages.

CASE REPORT

An otherwise healthy 48-year-old Caucasian man with longstanding obesity presented to the clinic with complaints of inability to lose weight, despite regular exercise and attempts at dieting, and with a self-reported addiction to carbonated, sugar-sweetened drinks. He indicated drinking ~6–8 non-diet carbonated beverages daily, often with other snacks (i.e. chips and cookies) while at work. Carbonated drinks represented an estimated 32–42% percentage of his daily caloric intake (average of 2613 kcal/day) to sustain 101.4 kg of body weight and body mass index (BMI) of 31.47 kg/m² (Table 1 and Fig. 2). The patient reported several unsuccessful attempts at decreasing his carbonated drink consumption. At this initial visit, his routine consumption of carbonated drinks (1–3 times/week) and made no other modifications to his diet in an attempt to promote further weight loss. However, the patient reported decreased appetite (a documented side effect of acetazolamide) [16] and reduced consumption of some of the snacks that often accompanied his carbonated sugar-sweetened beverages is associated with stronger correlations between an individual’s genetic predisposition (as assessed by the expression profile of 32 BMI-associated loci) and the severity of their obesity [4]. These findings suggest that interactions between genetic and diet/environmental factors may have synergistic effects in individuals with excessive consumption of carbonated beverages, potentiating their weight gain and other metabolic disturbances.

In fact, behavioral and functional magnetic resonance imaging studies have demonstrated that carbonated drink consumers engage distinct brain perceptual pathways, exhibit diminished salty and sweet taste perception, and have significant biases for sweet foods (Fig. 1) [11–13]. Additionally, studies in animal models and human subjects suggest that carbon dioxide stimulates ghrelin secretion by the stomach and/or small intestine, promoting appetite, deregulating brain reward

**DISCUSSION**

Carbonated drinks are extremely popular throughout the world, and considered the principal contributors of added sugars in the American diet [1–4]. The rise in their consumption has mirrored the increased prevalence of obesity in the USA [1]. While their direct caloric contribution in fueling the obesity epidemic is recognized, the effect of their carbonation is also postulated to be crucial, although the underlying mechanism(s) remain poorly understood [8, 9].

In this line, a dose–response relationship has been reported between the net intake of carbonated drinks and the magnitude of prospective weight gain, irrespective of whether these beverages are sweetened with sugar or artificial substitutes (i.e. with or without the calories) [7]. Moreover, greater consumption of carbonated sugar-sweetened beverages is associated with stronger correlations between an individual’s genetic predisposition (as assessed by the expression profile of 32 BMI-associated loci) and the severity of their obesity [4]. These findings suggest that interactions between genetic and diet/environmental factors may have synergistic effects in individuals with excessive consumption of carbonated beverages, potentiating their weight gain and other metabolic disturbances.
Table 1: Patient’s weight, BMI and other laboratory analyses at baseline and 6 weeks after initiation of administration of low-dose acetazolamide

|                        | Baseline | Six weeks after acetazolamide |
|------------------------|----------|-------------------------------|
| Body weight (kg)       | 101.4    | 97                            |
| BMI (kg/m²)            | 31.47    | 30.14                         |
| White blood cell count (x10³/μL) | 7       | –                             |
| Hemoglobin (g/dL)      | 15.6     | –                             |
| Hematocrit (%)         | 44.5     | –                             |
| Serum sodium (mmol/L)  | 143      | 139                           |
| Serum potassium (mmol/L)| 4.6      | 4.7                           |
| Serum chloride (mmol/L)| 101      | 98                            |
| Serum bicarbonate (mmol/L)| 25   | 22                            |
| Blood urea nitrogen (mg/dL)| 12 | 21                            |
| Creatinine (mg/dL)     | 0.96     | 1.17                          |
| Glucose (mg/dL)        | 101      | 101                           |
| Hemoglobin A1C (%)     | 5.3      | –                             |
| Serum calcium (mg/dL)  | 9.4      | 10.1                          |
| Aspartate transaminase | 25       | 28                            |
| Alanine transaminase   | 40       | 35                            |
| Alkaline phosphatase   | 88       | 90                            |
| Total serum bilirubin  | 0.3      | 0.4                           |
| Total serum protein    | 8        | 9                             |
| Serum albumin          | 4.7      | 5.1                           |

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strategy might help reduce long-term consumption of carbonated drinks by virtue of its effects at multiple levels, such as preventing the sensation or taste of carbonation (effervescence or “fizz”) and rendering carbonated drinks less palatable (Fig. 1). Moreover, acetazolamide might curtail carbon dioxide’s effect(s) on ghrelin signaling that stimulate appetite, and in turn counter its effects on reinforcement learning and addiction, possibly leading to the extinction of deregulated food-seeking behaviors that are not guided by metabolic needs (Fig. 1).

Although our findings are currently limited to a single case (and recently another patient with early promising results as well), the extent of clinical improvement demonstrated here suggests the potential for future longitudinal studies on this strategy for weight loss. This benefit was observed for an administered dose of 125 mg, which is lower than the more typical doses of 250 mg for acute altitude sickness and doses of 500 mg for other indications, suggesting that efficacy may be achieved at even lower-than-typical doses. It would be interesting to postulate and potentially later explore whether there may be a dose-response effect at the more commonly administered doses of this medication.

As a precaution, it is important to consider dose adjustments for patients with renal dysfunction, as impaired acetazolamide clearance and abnormally elevated serum levels have been associated with acid-base derangements [17, 18]. Of note, low doses of acetazolamide (<250 mg once daily), such as the dose employed here, have not been associated with significant serum pH changes (i.e. 0–0.05 unit change in pH) [19, 20], and our daily regimen allows for a sufficient pharmacological clearance window (half-life: 2–4 h) [16]. In fact, our patient exhibited a normal serum bicarbonate level after 6 weeks of daily acetazolamide treatment (Table 1), suggesting a normal acid-base status. As an alternative mode of administration that circumvents potential systemic side effects, acetazolamide could be given as a solution for topical oral rinse, and have been shown effective in attaining a localized inhibition of carbonic anhydrase at taste receptors and eliminating the taste of carbonation in beverages [14]. This mode of administration could also help elucidate the contribution of the role of carbon dioxide in central perceptual versus gastrointestinal neurohormonal effects on appetite and weight gain (Fig. 1).
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CONFLICT OF INTEREST STATEMENT
The authors report no conflicts of interest.

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ETHICAL APPROVAL
None required.

CONSENT
Consent provided by the patient.

GUARANTOR
Steven Lamm.

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