Anosmia Associated with Use

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Introduction
Zinc is an essential mineral. Beneficial zinc absorption takes place via enteral, parenteral, or cutaneous routes. Topical application to the olfactory epithelium, on the other hand, is toxic, producing anosmia. This toxicity is thought to be due to the direct effect of the divalent zinc ions on olfactory receptor cells. Intranasal zinc gluconate \( \text{Zn}^{2+} \) has recently been recommended as a treatment for the common cold. Post-treatment severe hyposmia and anosmia have been observed.

Methods/Observations
Case Report
A 55 y/o man with previously normal taste and smell developed clear rhinitis and congestion and treated himself with OTC zinc gluconate \( \text{Zn}^{2+} \) for a self-diagnosed "cold." On spraying his nose, he noted severe burning. This was followed immediately by loss of smell, which was persistent. His past history included rheumatoid arthritis, GERD, and allergies. He had some indications of lupus and his LFT's were "borderline normal." He took Prilosec\textregistered, Allegra\textregistered, and Flonase\textregistered. He was otherwise in excellent health. He did not smoke.

The olotaryngologic examination was normal. An MRI, with and without contrast was normal. No evidence of sinus disease was seen.

Detailed chemosensory evaluation was done. The threshold results indicated a severely limited detection ability bilaterally. Trigeminal activity was normal. Taste testing was normal except for a persistent salty taste which was partially extinguished by 0.5% Diclofenac\textregistered application.

The severe hyposmia has persisted, unchanged, 10 months post testing and 23 months post incident.

Patient Series Data
Our taste and smell center (Department of Otolaryngology, University of Colorado School of Medicine, Denver, Colorado) comprehensively evaluates patients with chemosensory dysfunction comparing these, a group of patients with hyposmia and anosmia following the use of zinc gluconate \( \text{Zn}^{2+} \) who have been identified.

Seven males and three females, with ages ranging from 31-55 comprised the study series. The distinguishing characteristics were immediate, severe burning of the nose (similar to that reported in the zinc literature of the past [1]) following the use of zinc gluconate \( \text{Zn}^{2+} \) followed by persistent hyposmia or, in complete anosmia, in a patient with previously normal taste and smell and no other causative history to account for the loss. We would assume that additional patients did not contact us and that further cases have not yet been diagnosed, increasing the apparent incidence of associated anosmia.

Clinical Studies

1935-1936: Polo virus was thought to be inhaled into the nose, traveling to the brain via the olfactory nerves. The theory was that protection could be gained by erecting an impenetrable barrier around the olfactory nerves. Protection against the virus could not be gained unless the epithelium was intact. Zinc ions were postulated to "coagulate neural proteins in the olfactory epithelium, forming a protective coating around the nerves which prevented them from absorbing the polo virus." This approach became, "Protect the nose and prevent polio!"

1937: During a polo epidemic in Toronto, 50,000 children received intranasal zinc sulfate. Most of the children suffered some discomfort from the nasal spray. There were a few cases, however, of severe nasal pain which "continued for many hours."[1,3] "It was many months later that Schultz began receiving complaints from physicians that many of their patients had suffered a complete and permanent loss of the sense of smell."[1,3] Zinc sulfate had not protected the children against polo and the toxic effect of the intranasal spray upon human olfactory epithelium was clearly shown. Interindividual variation in drug response and drug toxicity was seen. The use of intranasal zinc was abandoned.

1979: Maltoni observed regeneration and degeneration of the olfactory epithelium in mice receiving intranasal irrigation with 1% aqueous zinc sulfate(4). Progressive manifestations of the degenerative process were seen.

1987: Hearing described immediate and total anosmia in mice irrigated with intranasal 0.17 M ZnSO4(5). This anosmia persisted for 6 weeks in at least 80% of the treated animals and for 4 months in half. Changes were still apparent at 1 year, the limit of the experimental observation.

2000: Corrigan attributed the "neurotic effect" of various metal solutions to the divorce of zinc cation in irritation experiments upon the ciliated olfactory mucosa(6).

2003: Mayer and Rosenblatt reported that spray application of ZnSO4 to the olfactory mucosa in rats produced anosmia in 80% of treated animals(9).

Basic Investigations

1987: Maltoni observed regeneration and degeneration of the olfactory epithelium in mice receiving intranasal irrigation with 1% aqueous zinc sulfate(4). Progressive manifestations of the degenerative process were seen.

1992: Burd reported histopathologic changes of the olfactory epithelium of mice irrigated with intranasal zinc sulfate as early as 1 day with complete destruction of the olfactory epithelium and replacement with cuboidal cells within 2-4 days(8).

2007: Meyer and Rosenblatt reported that spray application of ZnSO4 to the olfactory mucosa in rats produced anosmia in 80% of treated animals(10).

Conclusion
Since patients use the intranasal zinc for colds, postviral anosmia could be considered a cause of this chemosensory loss. Three factors argue against this conclusion. First, the admittedly modest study population had a mean preponderance of more than 2:1, as opposed to the 2:1 female ratio seen in postviral anosmia; the patients in the postviral group were also younger than typical post-viral patients (17). Second, postviral anosmia typically occurs with "the worst URI I've ever had." Our study population typically took medication illegally in the course of a mild URI. Most convincing was the immediate, acute, "burning" pain with the use of the zinc gluconate followed immediately by persistent hyposmia or anosmia.

Recent advertisements for zinc have added a pediatric applicant. This extension of its use to the pediatric age group is of particular concern since this group is less likely to describe the loss of smell, resulting in an increased total dosage of the drug. The effect appears to be dose-related.

It should be noted that the brand name \( \text{Zincum Gluconum} \) has been extended by the manufacturer to several products. This communication concerns only the association of hyposmia and anosmia with the use of the product containing zinc gluconate and all references are so intended.

In conclusion, zinc ions are reported to be toxic to olfactory epithelium. The temporal association of the use of intranasal zinc gluconate \( \text{Zn}^{2+} \) with development of severe partial or total loss of the sense of smell raises significant concern regarding its safety for intranasal application. The general public may assume that since zinc is an over-the-counter (OTC) "patented, homeopathic" preparation, containing a "natural," or even "essential" element, that it is safe. This study raises important questions about that generalization. Since the effects appear to be somewhat dose-related, use of this drug in the pediatric age group would be expected to generate an even larger incidence of anosmia in this population and is especially concerning.

References