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A possible correlation between vitamin D deficiency and loss of smell: 2 case reports

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Abstract

Objective: The purpose of this report is to present 2 cases of diminished olfaction that improved with increasing serum levels of vitamin D3.

Clinical Features: Both patients were under the care of medical and chiropractic physicians for various complaints. A 47-year-old hyposmic woman was diagnosed with vitamin D deficiency who incidentally noticed a progressive return of her sense of smell while taking vitamin D supplements as prescribed by her medical doctor. A 34-year-old anosmic woman noticed a direct relationship with her ability to smell and vitamin D3 supplementation.

Intervention and Outcome: Treatment for the first patient consisted of vitamin D supplementation of 10 000 IU a day. Her serum D3 levels increased substantially over a period of 8 months, at which time she reported a marked improvement in her sense of smell. The second patient was prescribed 50 000 IU of vitamin D a week; and she reported an increased ability to smell, although only the strongest of odors.

Conclusion: A link between hypovitaminosis D and a diminished sense of smell was noted in these 2 individuals.

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Introduction

Vitamin deficiencies occur in both industrialized and developing countries. To prevent such deficiencies, some clinicians suggest daily recommended values of each nutrient. Determination of the nutrient reference

intake values can be challenging, such as with vitamin D where there are several suggested values.¹ Therefore, when suggested intake of a supplement is in question, individual patient needs should be based on current serum levels rather than recommended intake levels. Serum 25-hydroxyvitamin D (25[OH]D) is commonly accepted as a robust and reliable marker of vitamin D status and is frequently used as the marker for vitamin D levels.² *Vitamin D deficiency* is defined as a serum 25(OH) D level less than 17.5 nmol/L (6.8 ng/mL); and *vitamin D insufficiency*, less than 62.5 nmol/L (25 ng/mL).³

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Based on one study, vitamin D deficiency in the United States increased from 2% to 6% between data collection ranges of 1988-1994 to 2001-2004; and vitamin D insufficiency increased from 55% to 77% during the same periods.⁴ Another study found that an overwhelming majority of US patients (87%) were mildly to severely deficient.⁵ In yet another recent study, the US population was divided by higher and lower latitudes. Both subpopulations were found to have a less than 1% vitamin D deficiency. However, the lower-latitude population was found to have a higher vitamin D insufficiency rate than the higher-latitude population (up to 57% and 49%, respectively).³ A nationally representative sample of US children also demonstrated that 9% were found to be 25(OH)D deficient and 61% were found to be insufficient.⁶

Vitamin D is gaining more attention in recent years, with low levels of 25(OH)D being correlated with many common diseases. For example, low levels of serum 25(OH)D were associated with increased cardiovascular mortality in a nationally representative US sample.⁷ Vitamin D deficiency was also found to be an independent risk factor for cardiovascular disease,⁸⁻¹⁰ with supplementation leading to a reduction in blood pressure^{11,12} and prevention of cardiovascular events.¹³

Vitamin D supplementation has been shown to reduce the risk of certain cancers, such as colorectal cancer,¹⁴⁻¹⁶ breast cancer,¹⁷ and pancreatic cancer.¹⁸ Two recent systematic reviews have also found that vitamin D supplementation reduced the risk of falling in older adults^{19,20} and prevented fractures in elderly women.²¹

Unfortunately, little evidence guides clinicians on when to screen for vitamin D deficiency.²²

There are some possible symptoms associated with vitamin D deficiency for a clinician to assess, but no specific guidelines have been developed. This is unfortunate considering that vitamin D deficiency is associated with a variety of potentially serious conditions. If an association is determined, anosmia or hyposmia may be a potential screening test for vitamin D deficiency. The purpose of this study is to describe 2 cases in which the loss of smell was improved by vitamin D supplementation.

Case report

Both patients gave consent to have personal health information published without divulging personal identifiers.

Case 1

Case 1 is a 47-year-old woman measuring 5'7" and weighing 141 lb. She is a nonsmoking female homemaker who presented to her primary care (allopathic) physician with complaints of fatigue, depression, moodiness, headaches, anxiousness, memory problems, and muscle aches. Her musculoskeletal complaints prompted her to also seek care at a chiropractic physician's office. She also had a long-term loss of smell, but did not disclose this to her allopathic physician during the initial visit. Extensive laboratory studies were performed with no definitive etiology for her complaints. She was prescribed an antidepressant by her medical doctor; however, she reported muscular rigidity as an adverse effect and therefore discontinued use. The allopathic physician ordered additional laboratory work, including a serum 25(OH)D level. Her initial vitamin D level was low at 23 ng/mL, with the reference range indicated as 30 to 100 ng/mL. She was prescribed 10 000 IU of vitamin D a day; and after approximately 8 months of supplementation, her serum 25(OH)D level was 96 ng/mL. At that time, she reported a decrease in her symptoms including that her depression was resolved and that she "no longer dreaded getting out of bed in the morning." She had an increase in her ability to perform her usual activities of daily living including having the energy and desire to paint the interior of her house. She also reported improvement in her memory.

Along with these benefits from her supplementation of vitamin D, this patient also experienced a return of her sense of smell. Before her course of supplementation, she could only smell the strongest of odors and only if the item was held close to her nose. She was unable to smell smoke or spoiled food in her refrigerator. After approximately 1 month of supplementation, she noticed a slight increase in her ability to smell; and after 2 months, there was a progressive and noticeable increase in her sense of smell. She stated that, over the 8 months, she was progressively able to smell more subtle odors and that she was also able to enjoy the taste of food again.

Once this patient's sense of smell returned, she disclosed that she believed her lack of smell was a safety issue. Before supplementation, she was unable to smell food burning on the stove or in the oven. Her family members would tell her if something was burning and were concerned that she would be unable to tell if there was a fire in the house. She was also concerned that she may be serving her family spoiled milk or food.

Case 2

A 34-year-old nonsmoking woman presented to her primary care (allopathic) physician for evaluation of complaints of depression, headaches, fatigue, and a loss of desire to perform her usual activities of daily living. She was also under periodic chiropractic care for neck and back complaints. During the course of her chiropractic care, she indicated a history of diminished olfaction for years; however, she had not discussed this with her allopathic physician. Laboratory studies included a thyroid panel and general metabolic blood work along with a computerized axial tomographic scan of her brain, and all results were within normal limits. The allopathic physician then ordered serum 25(OH)D levels that demonstrated extremely low results of 8.4 ng/mL, with normal limits listed as 30 to 100 ng/mL. She was prescribed an antidepressant and 50 000 IU of vitamin D3 once per week for 8 weeks. She decided not to take the antidepressant and only filled the vitamin D supplement prescription.

One day after taking her first dose, the patient was surprised that she was able to smell curry spice on a person who had used it while cooking that day. She continued taking the 50 000-IU supplement every Sunday for 8 weeks, during which time she consistently and progressively noticed more odors, with the strongest odors noticed on Mondays and with olfaction diminishing as the week progressed. She reported initially only being able to smell the most noxious of smells such as dog feces, garlic, curry, and her son's guinea pig cage. After 8 weeks of supplementation, her serum 25(OH)D level was 29.0 ng/mL; and she was consistently able to smell additional and different odors. However, she still could not sense subtle odors such as flowers.

This patient noticed a decrease in the original symptoms for which she originally presented to her allopathic physician, including a reduction in depression, fatigue, complacency, and headaches. After the 8 weeks of vitamin D3 treatment, she did not return to her physician for over a month, during which time she stated she again lost all sense of smell. Her physician prescribed another 8 weeks of D3 supplementation; and she noticed the same pattern of a progressive return of olfaction, most marked the 2 days after taking the vitamin D. She again stopped supplementation after the end of the 8-week prescription; and she reported another complete loss of olfaction, at which time her blood level was 18.0 ng/mL.

Discussion

Loss of smell is a relatively common occurrence as people progress through adulthood. In one large epidemiological study of US adults, 25% had a measurable olfactory impairment.^{23,24} Similarly, 19% of Swedes were found to have hyposmia or anosmia.²⁵ Many times, the ability to smell diminishes gradually over time, making self-reported olfactory impairment substantially underestimated.²³ Patients frequently do not discuss their olfaction difficulties; however, the loss of smell can lead to depression and a lower quality of life.²⁶⁻²⁹ Loss of smell can also lead to safety issues and severely altered eating habits and nutritional intake.³⁰ Resolution of anosmia is unlikely in most cases because the majority of patients with olfaction problems receive from their physician no, unclear, or unsatisfactory information about their diagnosis and prognosis.³¹ This is not surprising considering that few validated tests exist for physicians to use in the assessment of smell function.³²

The most common known etiologies for anosmia are nasal/sinus congestion, upper respiratory tract infection, current smoking, head trauma, stroke, and epilepsy.^{23,33-35} Some investigators theorize that olfactory declines may be a consequence of autoimmune mechanisms³⁶ or neurodegenerative diseases.³⁷

The prognosis of olfactory dysfunction is influenced by certain demographic and clinical factors. Over time, regaining the sense of smell is more likely in females,³⁸ younger persons,^{38,39} those with lesser severity of initial olfactory loss,³⁹ and those with shorter duration of dysfunction.³⁹ However, there is no clear understanding of why olfaction issues come and go over time.

Two cases are presented in which the sense of smell was substantially diminished but was regained, presumably through the supplementation of vitamin D3. Both cases presented with similar complaints of depression,^{10,40-42} fatigue,⁴³⁻⁴⁵ and muscle aches,^{44,46-48} all of which have been previously associated with vitamin D deficiency. However, there are no current studies correlating a loss of smell with vitamin D deficiency.

There are different hypotheses for the possible interaction between vitamin D and hyposmia. Vitamin D is thought to have immunomodulating effects that may explain the reported epidemiological associations between vitamin D status and a large number of autoimmune and inflammatory diseases, such as rheumatoid arthritis, systemic lupus erythematosus,

type 1 diabetes, multiple sclerosis, inflammatory bowel disease, asthma, and cardiovascular disease.^{22,49,50} Because vitamin D supplementation is beneficial to many diseases characterized by inflammation, perhaps vitamin D also improves sinus congestion, allowing for improved olfaction.

Vitamin D is a secosteroid hormone and has been shown to have biological targets mediated by the vitamin D receptor in many cells.⁵¹ A review of studies published over a 20-year period was performed to describe the relationship between vitamin D and the nervous system.⁵² This review found an increasing amount of support in favor of the role of vitamin D on the central nervous system,⁵² and a deficiency in vitamin D was shown to be associated with neurologic dysfunction.^{51,53} The central nervous system contains the enzymes required to metabolize its own vitamin D, thus supporting the role of vitamin D in brain homeostasis.⁵⁴ Vitamin D acts like a neurosteroid hormone that binds to vitamin D receptors in the brain, spinal cord, and olfactory network.^{55,56} As a possible example of vitamin D deficiency leading to symptoms within the central nervous system, hypoacusis has been documented in rodents deprived of functional vitamin D receptors.⁵⁷

Although the mechanism is unclear, vitamin D appears to have a neuroprotective effect on the nervous system⁵⁸ promoting an increase in the synthesis of neurotropic agents,⁵⁹ an acceleration of neuronal growth,⁵⁹ and a protection of neurons against the direct effects of superoxide ions and hydrogen peroxide.⁶⁰ Vitamin D also seems to be associated with conduction speeds in the peripheral nervous system.^{61,62} Therefore, perhaps a lack of vitamin D leads to neurological decline of the central and peripheral nervous system, including the cranial nerves, leading to reduced olfaction.

The issue of reduced olfaction with vitamin D deficiency is not just an issue of mechanistic interest. Lack of smell can lead to a substantial reduction in an individual's quality of life. This issue may have public health consequences as well. If larger studies demonstrate this association, anosmia or hyposmia may be an easy screening test for vitamin D deficiency.

Limitations

There are several limitations in the report of these cases. First, both cases provide anecdotal evidence without objective measures of reduced olfaction. Future studies should include more substantial

methods of determining change in smell perception, rather than subjectively reported changes such as occurred in these cases.

Second, the incidental finding of reduced olfaction was not the primary complaint of either patient attending the chiropractic clinic. Rather, both patients attended the chiropractic clinic because of a musculoskeletal complaint. Likewise, neither patient approached their primary care physician with the symptom of hyposmia. Therefore, we might deduce that the severity of the hyposmia had minimal impact on the patients' quality of life. Again, more research is needed to determine the level of anosmia and the personal impact of such a finding.

Third, the improvement in these patients' ability to smell may have occurred because of other factors in the patients' lives. For example, if the patients were able to overcome previously perpetual sinus congestion, their sense of smell might have improved. In addition, there are other nutritional deficiencies that might have led to a loss of smell; and improving their nutritional status may have helped their sense of smell.

Finally, just as most case reports, we cannot be sure if what was experienced by these 2 individuals is generalizable to other patients. We caution readers about the anecdotal nature of this article and encourage researchers to follow up with a larger study to verify these results.

Conclusion

Two cases are presented in which reduced olfaction appeared to improve after supplementation with vitamin D. Larger studies are needed to confirm these results; and, if confirmed, this symptom may be an effective screening tool used to determine the need to assess serum 25(OH)D levels.

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