

Severe Symptomatic Vitamin D Deficiency During COVID-19 “Stay-at-Home-Orders” in New York City

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Introduction

The majority of circulating vitamin D originates from sunlight exposure. Cholecalciferol (vitamin D3) is made from UVB radiation of 7-dehydrocholesterol or ingestion of animal-based foods. Ergocalciferol (vitamin D2) is typically found in plant-based foods. Both types are inactive prior to hydroxylation in the liver to 25-hydroxy vitamin D (25OHD) and in the kidney to 1,25-dihydroxy vitamin D (1,25OH2D), which acts in the kidney and intestines to increase calcium absorption. In hypocalcemia, there is a rise in parathyroid hormone (PTH) in order to maintain normal serum calcium. PTH increases renal calcium absorption, decreases renal phosphorous absorption, and enhances production of 1,25OH2D.¹ 25OHD levels are used clinically to measure vitamin D status due to the relatively long half-life. There is a lack of consensus on what value constitutes 25OHD deficiency, though levels under 30 ng/ml are considered insufficient. Non-white race, obesity, and living at higher latitudes have been associated with increased prevalence of vitamin D deficiency.² 25OHD levels have also been shown to be lower at the end of the winter and in individuals spending more time indoor.³

Severe vitamin D deficiency can result in hypocalcemia and nutritional rickets. Appropriate calcium levels are important for myocyte contractility and neuronal stability. Hypocalcemia can result in tetany, seizures, prolonged QTc intervals, and sudden cardiac arrest.¹ Vitamin D has also shown to be related to immune function, with recent studies evaluating the role of vitamin D supplementation and deficiency in patients with COVID-19.⁴ National Health and Nutrition Examination Survey (NHANES) data from 2001 to 2004 (n=6275) showed 61% of children had 25OHD insufficiency.⁵ It is unclear how many cases of severe hypocalcemia result from 25OHD deficiency or what 25OHD level places patients at risk for hypocalcemia. Although executive

order “New York State on Pause” was only in effect from March 22nd through June 8th 2020, organized sports and outdoor play were avoided during the summer and fall of 2020 resulting in decreased sun exposure for many children.⁶ We present three children who presented with severe vitamin D deficiency and symptomatic hypocalcemia, which was hypothesized to be an unintended consequence of “stay-at-home orders” during the COVID-19 pandemic.

Case Presentations

Case 1 is a 13-year 5-month male of Hispanic descent, with a past medical history of transient hypoglycemia and poor oral feeding, requiring gastrostomy feeds until 12 months of age, presenting to the emergency department with a first time generalized tonic-clonic seizure. He reported lower back pain, diffuse muscle pain, and bilateral hand cramping for 1 month. His diet consisted primarily of bagels, cheese pizza, chicken, and sandwiches. He had negative Chvostek and Trousseau signs. He was in mid-puberty with a BMI in the 93rd percentile. Laboratory studies revealed hypocalcemia in the setting of severe vitamin D deficiency, as shown in Table 1. He had normal cortisol and thyroid levels and a negative celiac screen. He had low vitamin A, vitamin E, and zinc levels, with normal inflammatory markers and fecal elastase. Electrocardiogram (ECG) showed sinus tachycardia and borderline prolonged QTc. Thoracic spine radiograph revealed mild loss of height in several

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midthoracic vertebral bodies, indicative of compression fractures. He was treated with seven IV calcium gluconate boluses of 30 mg/kg each, followed by 100 mg/kg/day elemental calcium, calcitriol 0.25 mcg daily, and 2 doses of ergocalciferol 50 000 international units (IU) during the first week. He was discharged on hospital day 3 on 120 mg/kg/day elemental calcium, calcitriol 0.25 mg daily, and cholecalciferol 10 000 IU daily, with a calcium level of 9.4 mg/dl and ionized calcium of 1.13 mmol/l. Calcitriol was discontinued after 11 days, and current medications include cholecalciferol 50 000 IU weekly and 100 mg/kg/day elemental calcium.

Case 2 is an 11-year 9-month female of Yemeni descent with no relevant medical history presenting to the emergency department with right-sided knee pain of 1 year. She reported a diet of predominantly French fries and rice with minimal dairy and vegetable intake. She had tenderness to palpation of the anterior and lateral aspects of the right knee with normal gait and range of motion. Knee and femur radiographs were normal. She was post-menarchal with a BMI in the 15th percentile. Initial laboratory studies demonstrated hypocalcemia and vitamin D deficiency, as shown in Table 1. ECG showed a borderline prolonged QTc. She was treated with 2 IV calcium gluconate boluses (doses of 30 and 40 mg/kg) and a dose of 50 000 IU of ergocalciferol, and then started on enteral replacement of 100 mg/kg/day elemental calcium. She was discharged on hospital day

4 on ergocalciferol 50 000 IU twice a week and 100 mg/kg/day elemental calcium, with a calcium level of 9.1 mg/d. Her doses have been decreased to ergocalciferol 50 000 IU every 2 weeks and 25 mg/kg/day elemental calcium.

Case 3 is a 10-year 9-month Black male with a past medical history of autism, eczema, asthma, and food allergies, who was followed in rheumatology clinic for 1-year of bilateral knee pain. He was referred to the hospital for hypocalcemia on outpatient labs. He had a limited diet with minimal dairy products. Exam was notable for generalized musculoskeletal tenderness and hyperreflexia with a positive Chvostek sign. He was prepubertal with a BMI in the 75th percentile. Initial laboratory studies are shown in Table 1. ECG displayed a borderline prolonged QTc. Left wrist radiograph showed osteopenia and thinning cortices with subperiosteal reactions and fraying of the distal radial and ulnar metaphyses, consistent with rickets. He received two IV calcium gluconate boluses (60 mg/kg each), 1 g magnesium sulfate IV, and 50 000 IU of ergocalciferol. He was then placed on 90 mg/kg/day elemental calcium enterally. He was discharged on hospital day 5 on ergocalciferol 10 000 IU daily and 90 mg/kg/day elemental calcium, with a stable ionized calcium level of 1.09 mmol/l. Doses were decreased to ergocalciferol 8 000 IU daily and 30 mg/kg/day elemental calcium with improvement in his laboratory parameters.

Table 1. Laboratory Values at Presentation of Each Patient in Case Series.

| Laboratory values at time of diagnosis of hypocalcemia | | | |
|--|-----------|-----------|-----------|
| | Patient 1 | Patient 2 | Patient 3 |
| Vitamin D 25-OH (Range 20.0–50.0 ng/ml) | <3.4 | 4.1 | <5.0 |
| Total Calcium (Range 8.8–10.3 mg/dL) | 6.3 | 6.3 | 4.9 |
| Intact Parathyroid Hormone (Range 15.1–85.7 pg/mL) | 89.0* | 455.3 | 197.0 |
| Magnesium (Range 1.7–2.1 mg/dL) | 2.2 | 2.0 | 1.6 |
| Phosphorus (Range 3.3–5.3 mg/dL) | 7.2 | 4.9 | 4.7 |
| Alkaline Phosphatase (Range 116–468 U/L) | 501.0 | 502.0 | 1,052.0 |
| Urine Calcium-to-Creatinine Ratio (Range <0.2) | <0.02 | <0.02 | <0.02 |

*The intact Parathyroid Hormone in Patient 1 was obtained following repeated IV boluses of Calcium Gluconate.

Discussion/Conclusion

This case series suggests that the “stay-at-home orders” and pandemic-related decrease in seasonal sun exposure may have exacerbated vitamin D deficiency and symptomatic hypocalcemia in children who were at increased risk due to winter season, high latitude residence, and darker complexion. All 3 patients had limited dietary calcium intake, were not on vitamin D supplementation, and presented at the end of winter 2021, with severe

vitamin D deficiency, symptomatic hypocalcemia, appropriately elevated parathyroid hormone, and urinary retention of calcium. The elevated phosphorus in patient 1 was attributed to muscle breakdown from his seizure. Although patient 1 had other nutritional deficiencies, no evidence of malabsorption was found.

While it is well-known that vitamin D deficiency can lead to hypocalcemia, there are few studies and case reports implicating primary vitamin D deficiency as the cause of hypocalcemia, and it is hypothesized

that this hypocalcemia occurs in times of greater growth and increased metabolic demand for bone.⁷ In the NHANES data, there was a statistically, but not clinically, significant decrease in calcium in the vitamin D deficient (25OHD < 15 ng/ml) and insufficient groups (25OHD < 30 ng/ml).⁵ Furthermore, in a study of 51 subjects aged 10 to 13 in India with nutritional rickets, 55% had asymptomatic hypocalcemia.⁸ Other studies have found that symptomatic hypocalcemia from vitamin D deficiency primarily occurs in infants, especially in Black infants or in the setting of maternal vitamin D deficiency or exclusive breastfeeding.^{7,9-12} Symptomatic hypocalcemia in children has been attributed to covered clothing, dark skin, and/or decreased sun exposure.^{7,13,14}

Children in New York City (NYC) live in higher-population density areas with increased risk of COVID-19 spread, limiting their ability to safely spend time outside.¹⁵ The COVID-19 pandemic in NYC also disproportionately affected racial and ethnic minorities, as well as those residing in lower socioeconomic status (SES) neighborhoods.¹⁶ Due to public school closures, children participated in virtual school throughout the spring and fall of 2020, without the usual summer sun-exposure. Lower SES and minority populations have been shown to have access to fewer parks with more congestion.¹⁷ We hypothesize that a combination of “stay-at-home orders,” virtual schooling, and limited green space may have exacerbated or contributed to symptomatic vitamin D deficiency in the presented patients.

A recent systematic review on vitamin D deficiency found that there is an overall recommendation for screening, as well as a daily preventive dose, in children at risk for vitamin D deficiency, such as those with chronic medical conditions, dark skin, or minimal sun exposure.¹⁸ Although none of our patients had obesity, weight gain has been documented as an unintended consequence of “stay-at-home orders” and is associated with an increased risk of vitamin D deficiency.^{5,19} While larger studies are needed to evaluate the prevalence of vitamin D deficiency and subsequent complications in children affected by “stay-at-home orders,” this report aims to bring our attention to severe symptomatic vitamin D deficiency. Given the severity of hypocalcemia in the described patients and the cost of admissions, we recommend that pediatricians reinforce preventative vitamin D supplementation and actively screen and treat vitamin D deficiency in at-risk patients.

Author Contributions

Drs. Weiner, Nichols, Rahming, and Gopalakrishnamoorthy conceptualized the case report, drafted the manuscript, and

reviewed the manuscript. Drs. Oberfield, and Fennoy contributed to the design of the case report and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Consent

Written informed consent for patient information to be published was provided by the patients’ legally authorized representatives.

Declaration of Conflicting Interests

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