

## Hypervitaminosis D, a note of caution. Is the increase associated to pandemic Covid19? Report of 5 cases

### Hipervitaminosis D, alerta de precaución. ¿Incremento asociado a pandemia Covid 19?. Reporte de 5 casos

María Loreto Reyes G.<sup>a</sup>, Cristian Seiltgens S.<sup>a</sup>

<sup>a</sup>Red salud UC. Santiago, Chile

Received: November 23, 2020; Approved: November 30, 2020

*Mr. Editor,*

The objective of this letter is to alert about hypervitaminosis D (HD) in children in Chile, by reporting five cases diagnosed between August and October 2020. HD is defined as values of 25 OH vitamin D (25OHD) > 100 ng/ml. Its incidence is rare, and there are only anecdotal cases documented in the literature. Table 1 shows demographic and clinical data.

We presented five cases aged 4, 8, 10 months, and 6 and 11 years whose 25 OH vitamin D levels were >100 ng/ml. Two were males and three were females. Three patients received vitamin D as treatment and two as prophylaxis. The average cumulative dose in children under 1-year-old was 138,000 IU, in the 6-year-old patient was 1,200,000 IU, and in the 11-year-old patient was 600,000 IU. Three children presented with hypercalcemia and all of them hypercalciuria. Other manifestations were acute pyelonephritis, nephrocalcinosis, vomiting, stable weight, and low weight. Two patients were asymptomatic.

Through the first publication in Chile, in 2002, we warned about the high prevalence of vitamin D defi-

ciency (VDD) in children with chronic diseases. Subsequently, we reported that 33% and 8% of healthy children in the Metropolitan region presented levels of 25OHD < 30 ng/ml and < 10 ng/ml, respectively. Eight years later, the pediatric community has a high suspicion level of VDD, improving the frequency of diagnosis, prevention, and treatment. In a study of 250 healthy children in the Metropolitan region, we found no values > 72 ng/dl.

The onset of HD cases in a short-term period may be associated with formal and informal information on the possible protective role of vitamin D against Covid-19 infection. In two of our five cases, the mothers increased the indicated dose as prophylaxis and the other three were treated due to VDD. During the Covid-19 pandemic, severe VDD has increased (25OHD < 10 ng/dL), which may be associated with less sun exposure and higher suspicion of VDD.

Recommendations for the prophylactic use of vitamin D in children reported by various academic bodies differ, and there is no consistent, well-evidenced recommendation for the treatment of VDD. Several reports show that 25OHD values at diagnosis of hyper-

Correspondence:  
María Loreto Reyes G.  
mlreyes@med.puc.cl

Table 1

	Case 1	Case 2	Case 3	Case 4	Case 5
Age/Sex	8 meses/F	10 meses/F	6 años /M	4 meses/M	11 a 5 M/F
Associated pathology	Prematurity Cow's milk protein allergy	Cerebral Palsy Mother increases indicated dose	Low height	Healthy Mother increases indicated dose	Healthy Puberty follow-up
Vitamin D source	IF (400 UI/l) + daily drops 1,200 UI	IF (400 UI/l) + daily drops 1,200 UI	Drops 100,000 UI per week	IF (400 UI/l)+ daily drops 1,000 UI	Over 50,000 UI per week
Cumulative dose of the last 3 months (UI)	144,000	144,000	1,200,000	126,000	600,000
Baseline 25OHD level	Not measured	8 ng/ml	12 ng/ml	Not measured	19 ng/mL
25OHD level at diagnosis	102 ng/ml	125 ng/ml	134 ng/ml	145 ng/ml	113000
Condition at diagnosis	Acute pyelonephritis	Stable weight	No symptoms	Vomiting Weight loss	No symptoms
Calcemia/ Calciuria	Normal/High	High/High	High/High	High/High	Normal/High
PTH pg/mL	22 pg/mL	21 pg/mL	17 pg/mL	12 pg/mL	18 pg/mL
Kidney ultrasound	Normal	Grade I nephrocalcinosis	Normal	Normal	Normal

M: Male; F: Female; PTH: Parathormona; ECO: Echotomography, IF, Infanto Formula

vitaminosis correlate with cumulative dose and time of treatment, but not with baseline 25OHD levels. Loading doses are used in cases of severe VDD and have proved to be effective in increasing 25OHD levels rapidly. However, although the literature is limited, there is some consensus that doses greater than 300 IU total are associated with hypercalciuria in 40 to 60% of cases and hypercalcemia in 7 to 14% of cases.

Given the occurrence of HD in children and the lack of consensus, we propose a VDD treatment scheme based on the experience of the Pediatric Metabolic Bone Clinic of the Pontifical Catholic University of Chile. In severe VDD, the proposed loading doses are lower than those reported in the literature, being closer to 50,000 IU in children under 2 years of age. In children over 2 years of age we recommend 100,000 IU

and in children with BMI > 90, 200,000 IU.

It is necessary to administer elemental calcium at 50 to 100 mg/kg, in addition to the recommended vitamin D dose for the age. Loads can be repeated after 2 to 4 weeks, if values remain < 15 ng/ml. In the case of values > 15 and < 30 ng/ml, we recommend using daily or weekly doses and not exceeding twice the recommended preventive dose. This scheme is more conservative and therefore has a lower risk of hypervitaminosis.

Hypercalcemia can be a life-threatening condition, so we consider, as does the Drugs and Therapeutics Committee of the Pediatric Endocrine Society, that in any child receiving doses higher than those recommended and for a prolonged period, 25OHD values should be monitored.

## References

1. Reyes ML, Hernández MI, Palissson F, Talesnick E. Deficiencia de vitamina D en niños con enfermedades crónicas evaluados por osteopenia. Revisión de la literatura. *Rev Med Chile* 2002;130:645-50.
2. Reyes ML, Cattani A, Gajardo H, García C, McGrath JA, Palissson F. Bone metabolism in children with epidermolysis bullosa. *J Pediatr*. 2002;140:467-9.
3. Reyes ML, Hernández MI, Urrejola P, et al. Normal values of biochemical and densitometric test on bone metabolism in Chilean children 2-18 year-old. *Bone* 2005;36:S70-1.
4. Benskin LL. A Basic Review of the Preliminary Evidence That COVID-19 Risk and Severity Is Increased in Vitamin D Deficiency. *Front Public Health*. 2020;8:513. doi: 10.3389/fpubh.2020.00513. PMID: 33014983; PMCID: PMC7513835.
5. Vogiatzi MG, Jacobson-Dickman E, DeBoer MD; Drugs, and Therapeutics Committee of The Pediatric Endocrine Society. Vitamin D supplementation and risk of toxicity in pediatrics: a review of current literature. *J Clin Endocrinol Metab*. 2014;99(4):1132-41. doi: 10.1210/jc.2013-3655. Epub 2014 Jan 23. PMID: 24456284.
6. McNally JD, Iliriani K, Pojsupap S, et al. Rapid normalization of vitamin D levels: a meta-analysis. *Pediatrics*. 2015;135(1):e152-66. doi: 10.1542/peds.2014-1703. Epub 2014 Dec 15. PMID: 25511115.