Vitamin D macro dosing in pregnancy: a case report of D hypervitaminosis in pregnancy according to non-conventional Coimbra protocol and perinatal toxicity

[1]Cecilia Lanzi*, [1]Andrea Missanelli, [1]Alessandra Ieri, [1]Brunella Occupati, [1]Arianna Totti, [1]Francesco Gambassi, [3]Gilda Belli, [1,2] Guido Mannaioni, [1]Alessandra Pistelli.

[1]Toxicology Unit and Poison Control Centre, Teratology Information Service, Careggi University Hospital, Florence, Italy.

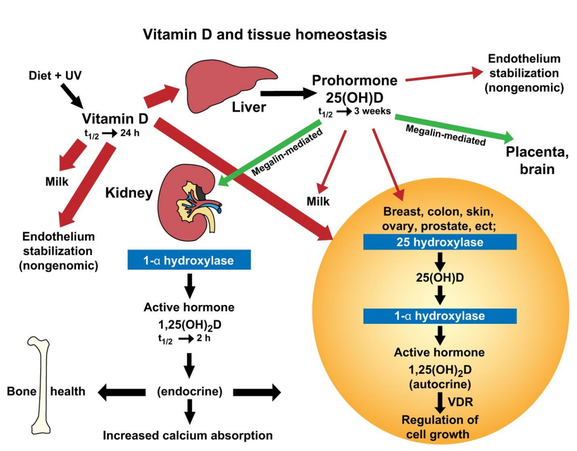
[2]Department of Neurosciences, Psychology, Drug Research and Child Health, University of Florence, Florence, Italy.

[3] Neonatal intensive care unit (NICU), Nuovo Ospedale san Giovanni di Dio Florence, Italy

INTRODUCTION

Vitamin D3 (cholecalciferol) is a secosteroid and prohormone metabolized in various tissues to the biologically most active vitamin D hormone 1,25(OH)2D3 (calcitriol). Vitamin D has a modulating role in the immune system via interaction with the vitamin D receptor (VDR) (Charoenngam et al 2020).

Vitamin D is increasingly utilized not only within prophylaxis, but also within therapy of various diseases.

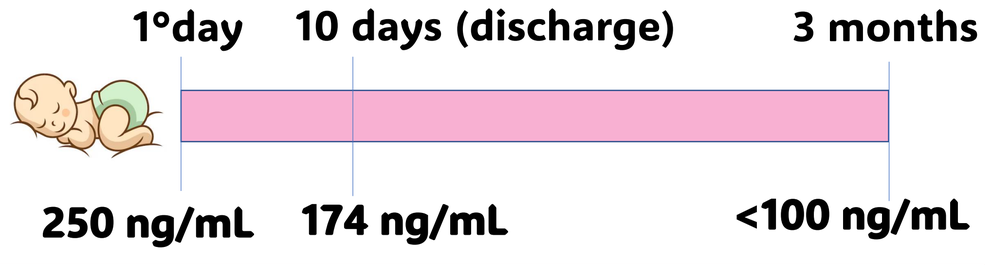


In 2013, the group of Cicero Coimbra reported the clinical efficacy, the so-called "Coimbra protocol" (CP), of high doses of vitamin D3 in patients suffering from autoimmune skin disorders. A very small cohort received vitamin D3 35,000 IU daily for six months in association with a low-calcium diet and sufficient hydration. The necessity of high doses of vitamin D3 for treatment success can be explained by the concept of an acquired form of vitamin D resistance (Lemke et al 2021).There is no clinical evidence on the efficacy of Vitamin D macro doses on ulcerative colitis even though the gut microbiota could be positively influenced by it it (Battistini et al 2020). In experimental animals, vit-D megadoses was linked to oxification defects (Zusman et al, 1981; Lieben et al, 2013) and an increased risk for supravalvular aortic stenosis (Chan et al, 1979; Friedman et al, 1966; Friedman et al, 1969).

CASE REPORT

A 31-year-old pregnant woman affected by ulcerative colitis treated with the CP: **cholecalciferol 100.000 UI/die**; magnesium 200 mg/day; vitamin B2 150 mg/day; vitamin K 100 mcg/day; Omega 3 500 mg/day; low-calcium diet (500-600 mg/day), 2.5 liters of low-calcium water per day and daily exercise. She was 8 weeks pregnant when referred to the Florence TIS reporting a good clinical control of the ulcerative colitis. The patient was informed on the lack of evidence of such treatment and the **potential dangers of D hypervitaminosis during pregnancy** according to data on animal in utero exposures. Vitamin D in serum was far above toxicity.
Despite the indication to stop such treatment she continued it through pregnancy and gave birth to a baby girl of 3.410 kg, with 9 and 10 apgar score at week 40+3. At birth the maternal 25OH vit D was still very high. The baby showed a high values of 25-OH-vitamin D, phosphorus and creatinine (in table above).

At birth (baby)	D VITAMIN	CALCIUM	PHOSPHORUS	CREATININE
value	250 ng/ml	10.3 mg/dl	7.4 mg/dl	1.23 mg/dl
Normal range	30-100	8.5 -10.3	2.5-4.5	0.44-0.95



Vitamin D level in breast milk was 2fold the normal for human milk. Therefore, a human milk-based diet from the Children's Hospital milk bank was provided to the baby, while IV fluid therapy was carried out with diuretic therapy in order to promote adequate hydration and avoid a further increase in calcium and vitamin D levels. Renal and cerebral echography showed no anomalies while echocardiography showed microcalcifications at the papillary muscles of the left ventricle, not confirmed on a second examination. The baby was discharged on day 10. A neonatal endocrinology day hospital was performed during the first month. The growth was regular during the first 3 months and vitamin D slowly decreased to levels <100 ng/mL.

As far as we know this is the first well documented case of a baby born by a mother on Vit-D megadose treatment and the first documented mother's milk D hypervitaminosis. We can conclude that despite a long afterbirth hospitalization and the need for human milk from donors **the baby showed no congenital defects** and only mild and transient alterations of phosphorus and creatinine. Vitamin D macro-dosing should be avoided in precoceptional period and pregnancy as its elimination and the consequent reduction of the blood level requires extremely long times both in mother and baby.

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