24,25(OH)2D AS A MARKER OF VITAMIN D DEFICIENCY IN CHILDREN: A RETROSPECTIVE ANALYSIS ON 1200 CASES

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Introduction:

Vitamin D deficiency definition is a matter of intense debate. CYP24A1, the enzyme responsible for 25(OH)D degradation metabolite of 25(OH)D, has been shown to be induced when 25(OH)D levels started to reach sufficiency levels. The simultaneous measurement of 25(OH)D and 24,25(OH)2D is now proposed as a novel approach for predicting vitamin D deficiency and allows distinguishing CYP24A1 lack of function from hypervitaminosis D during vitamin D intoxication. In this study, we retrospectively measured 25(OH)D and 24.25(OH)2D, the metabolite of CYP24A1, in a population of 1200 children to evaluate the 25(OH)D threshold above which the enzyme was induced.

Material and Methods:

Serum samples from 1200 children (from 5 months to 20 years old, mean age: 12±5.5 years old) who underwent a blood sampling for allergy exploration were used to simultaneously quantify 25-hyfroxy-Vitamin D (25(OH)D) and 24,25-dihydroxy-Vitamin D (24,25(OH)2D) with our previously described LCMS/MS method. The limits of quantification of 24,25(OH)2D and 25(OH)D were 0.5 and 2 ng/mL, respectively.

Results:

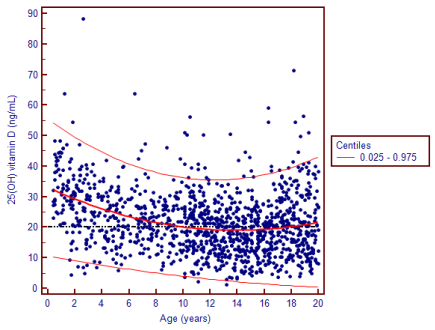

Fig 1. **Repartition of 25(OH)-vitamin D values according to age in a population of 1200 children.:** 25(OH)D values ranged from 1.3 to 88.4 ng/mL, with one subject presenting value below the LOQ. 562 subjects (46.8%) presented 25(OH)D concentrations <20 ng/mL and 217 of them (18.1%) were above 30 ng/mL. Of note, 195 children (16.2%) were strictly below 12 ng/mL, the threshold generally considered as corresponding to severe vitamin D deficiency. 25(OH)D values were higher in the 0-2 years old group, decreased over time to reach a nadir around the puberty period (in the 10-14 years old group) and then slightly increased in older children.

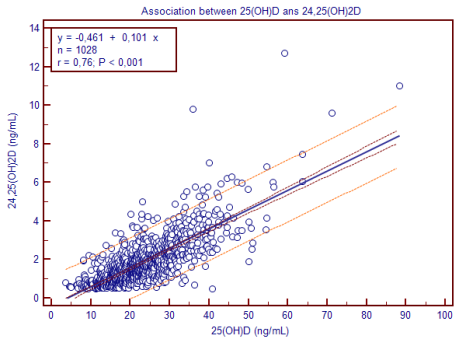

Fig 2. **25(OH)D and 24.25(OH)2D expression in a population of 1200 children**: Median levels were 20.6 ng/mL (Inter-Quartile Range: 14.4; 27.2 ng/mL) for 25(OH)D and 1.40 (IQR: 0.78; 2.20) ng/mL for 24,25(OH)2D. None of the children presented a 25(OH)D/24.25(OH)2D ratio higher than 50, the threshold generally used to detect Idiopathic Infantile Hypercalcemia. There was a very good correlation between 25 and 24,25(OH)2D concentrations (Spearman's rho = 0.740, p<0.0001).

25(OH)D concentration	Total number of children	Number of children presenting detectable 24,25(OH)2D concentrations	Percentage of children presenting detectable 24,25(OH)2D concentrations	Percentage of children presenting undetectable 24,25(OH)2D concentrations
Between LOQ and 11 ng/mL	195	72	36.9%	63.1%
Between 12 and 15 ng/mL	188	151	80.3%	19.7%
Between 16 and 20 ng/mL	235	223	94.9%	5.1%
>21 ng/mL	586	582	99.3%	0.7%

Fig 3. **Children presenting undetectable 24,25(OH)2D concentrations:** One hundred and seventy-two subjects (14.3%) presented 24,25(OH)2D values below the LOQ. The percentage of 24,25(OH)2D exponentially correlates to 25(OH)D concentration (rho = 0.9917).

Conclusions:

Total or partial loss of function of CYP24A1 can lead to various diseases, including severe hypercalcemia. Laboratory evaluation consists in the simultaneous determination of 25(OH)D and 24,25(OH)2D by LCMS/MS. Our results show that, physiologically, a large percentage of children presenting low 25(OH)D values will have undetectable 24,25(OH)D ones. This percentage will decrease with increasing 25(OH)D and will become marginal when 25(OH)D concentrations are higher than 21 ng/mL.