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Diet as a risk factor for hypovitaminosis D in the Spanish pediatric population

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Summary

Objetives: It is not clear whether diet in the Spanish general population is also a relevant determinant of hypovitaminosis D. The objective of the study was to analyze the impact of diet on the prevalence of hypovitaminosis D in healthy children.
Methods: Demographic, anthropometric, nutritional, analytical data and vitamin D (25 (OH) D) level were studied using an enzyme-immuno-analysis using an observational design in a sample of the pediatric population between 4 and 14 years old. The 24-hour reminder diet survey was evaluated with the DietSource 3.0 software. The probability of hypovitaminosis was analyzed using logistic regression.
Results: 280 healthy children with a mean age of 9.0 years were recruited. The prevalence of hypovitaminosis D (<20 ng/ml) was 18.15% and that of severe deficit (<10 ng/ml) 1.4%. Ethnicity, seasonality, skin phototype, and time of sun exposure were significantly associated with the presence of hypovitaminosis D. The distribution of nutrients did not show differences between the groups with and without hypovitaminosis except for Pyridoxine B6 and saturated fatty acids.
Conclusions: Diet plays a reduced role as a risk factor for hypovitaminosis D in healthy children and the relevant factors are those related to sun exposure. An adequate outdoor lifestyle, sun exposure free of sunscreens and dietary patterns that ensure a correct intake of vitamin D and calcium remain the ideal recommendations for the general population. Supplementation should be limited to risk groups.

Key words: Gipuzkoa, hypovitaminosis D, healthy population, risk factors, diet, sun exposure.

Introduction

Vitamin D is an essential micronutrient in bone and non-bone metabolism[1]. The high prevalence of its deficit has been documented in multiple studies[2-5]. However, the definition of its reference values continues to be controversial and consequently doubts are raised about its diagnosis and treatment[6]. Although rickets was eradicated in the mid 20th century with sun exposure and the enrichment of milk with vitamin D, in recent years there have been reports of rickets in different parts of the planet, the mainly affected black-skinned and exclusively breastfed babies[7-9]. While rickets is the most serious consequence of vitamin D deficiency, mere deficiency also has important health consequences[6].

Studies that measure the level of vitamin D show great geographic variability due to the great regional differences in climate, sun exposure and diet. For this reason, there is a need to specifically investigate the role of the different determinants of hypovitaminosis D[10] in each country. The diet meets only 10% of the human body's vitamin D requirements, the remaining 90% being obtained through the photosynthesis process that occurs in the skin by the direct action of the sun's rays[11]. Risk factors repeatedly identified in the literature as causes of hypovitaminosis (dark skin phototype, low sun exposure, lack of physical exercise, latitude >40º north, and winter and spring seasons) act by interfering in the second mechanism[2,12]. Other factors associated with hypovitaminosis such as maternal deficit, obesity or advanced age could be related to both mechanisms of obtaining vitamin D[12-14].

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In Spain there are numerous studies that measure hypovitaminosis D prevalence in children[2-4,15,16]. However, most focus on the risk factors related to sun exposure. Rodríguez-Sangrador et al. include dietary measurement of vitamin D intake[16]. Recently, the debate on the need to supplement with vitamin D was described as a puzzle in which the pieces begin to fit together and it was recommended to give vitamin D in adults to those who need it to maintain serum levels of 25 (OH) D above 20 ng/ml[17,18]. Clarifying whether schoolchildren with hypovitaminosis D have a deficit of intake in the diet would help to fit this piece to also supplement the child population. For this, it is necessary to jointly address both the factors associated with the exposure and synthesis and with the intake of vitamin D.

In this study, we analyze the impact of diet on the prevalence of hypovitaminosis D in healthy children in the Goierri-Alto Urola region to provide recommendations for the prevention of hypovitaminosis D in the school population.

Methods

A cross-sectional observational design was used, with cluster sampling during a calendar year (September 1, 2012 to September 30, 2013). The study was carried out with the financing of a Research Grant from the Department of Health of the Basque Government (Project No. 2011111107) and was approved by the Ethics Committee of Gipuzkoa. The children participated after signing the informed consent form by their parents. The reference population was the one served by the Integrated Health Organization (OSI) Goierri-Alto Urola in Gipuzkoa and the sample was recruited among girls, boys and adolescents between 4 and 14 years old, who attended Primary Care Services, being their The main populations Beasain, with latitude 43.05 N, and Zumárraga, with latitude 43.11 N. During the study period they had an average solar irradiation of 10.4–11.8 MJ/m^2 (Euskalmet, Basque Meteorology Agency)[19]. It was estimated that a sample of 298 schoolchildren would be sufficient to achieve a precision of 4% in a universe of 891, with a 95% significance, losses of 10% and an estimated prevalence of 20%. The schoolchildren were recruited successively, coinciding with the reviews carried out by the Primary Care pediatricians on healthy children until the sample provided for each month was completed in order to collect measurements throughout the year. The study exclusion criteria were: lack of informed consent, nephrotic syndrome, chronic renal failure, cancer patients, prolonged use of ketoconazole or anticonvulsants (phenobarbital-phenytoin), treatment for tuberculosis, and severe liver injury.

The variables collected were: age, sex, ethnicity (Caucasian and non-Caucasian), weight, height, BMI, skin phototype with the Fitzpatrick scale (1: least pigmentation to 6: maximum pigmentation)[20], sports activity in the last month (in three categories: less time than school sports, only school sports and two days more than school sports), time of sun exposure in the last month (nothing, less than 30 minutes a day, more than 30 minutes a day, more than 1 hour daily), use of sunscreen and vitamin supplements in the last 3 months. The phospho-calcium metabolism (calcium, phosphorus, magnesium, alkaline phosphatase, parathyroid hormone (PTH) and 25(OH) D).

An individual survey on feeding was conducted using a 24-hour recall survey (ER24hs). After conducting the analysis, the Primary Care pediatrician who recruited the student was in charge of reviewing and re-interviewing the parents on the standardized and self-completed questionnaire with the food eaten in the previous 24 hours. For the conversion of food into nutrients, the DietSource 3.0 program was used, which has a food composition table from Nestlé Healthcare Nutrition S. A. (A. Jiménez, P. Cervera and M. Bacardi). By managing the dishes and food eaten, this program breaks down the daily menu by estimating the amounts of immediate principles, nutrients and caloric distribution in each child's diet. Although the method applied is less valid than records based on the weight of food consumed for three or more days, the literature that has compared them supports its use[21,22].

Analytical determinations of phosphocalcic metabolism (calcium, phosphorus, magnesium, alkaline phosphatase, PTH, 25 (OH) D) were carried out in the OSI Goierri-Alto Urola laboratory. To measure the level of 25 (OH) D in serum, the Elecsys-Chemiluminescent Immunoanalysis kit was used. The cut-off point of 20 ng/ml was used to determine the levels of vitamin D that are considered deficient and 10 ng/ml for the cases with severe deficiency. The results were presented according to whether the values were within the normal reference ranges that were 10-65 pg/ml for PTH, 8.8-10.8 mg/dl for calcium, 3.0-6.5 mg/dl for phosphorus, 1.5-2.6 mg/dl for magnesium and for alkaline phosphatase <269 IU/L from 4 to 6 years and <300 IU/L from 7 to 12 years.

Statistic analysis

Univariate analysis was carried out using the Chi-square statistic or Fisher's exact statistic for categorical variables and the Student's t-test or the non-parametric Mann-Whitney U test was applied in the case of continuous variables as a function of its distribution. The level of significance used throughout the study was 5% and the analyzes were performed with the statistical software Stata version 13.0. Multivariate analyzes were carried out using logistic regression models in which the dependent variable was the probability of having hypovitaminosis and the independent variables were risk factors associated with exposure and intake of vitamin D. Variables to be included in the model were selected based on clinical interest and the level of significance in the univariate analysis. The goodness of fit of the models was evaluated using the well classified percentage, the area under the ROC curve and the Hosmer and Lemeshow test.

Results

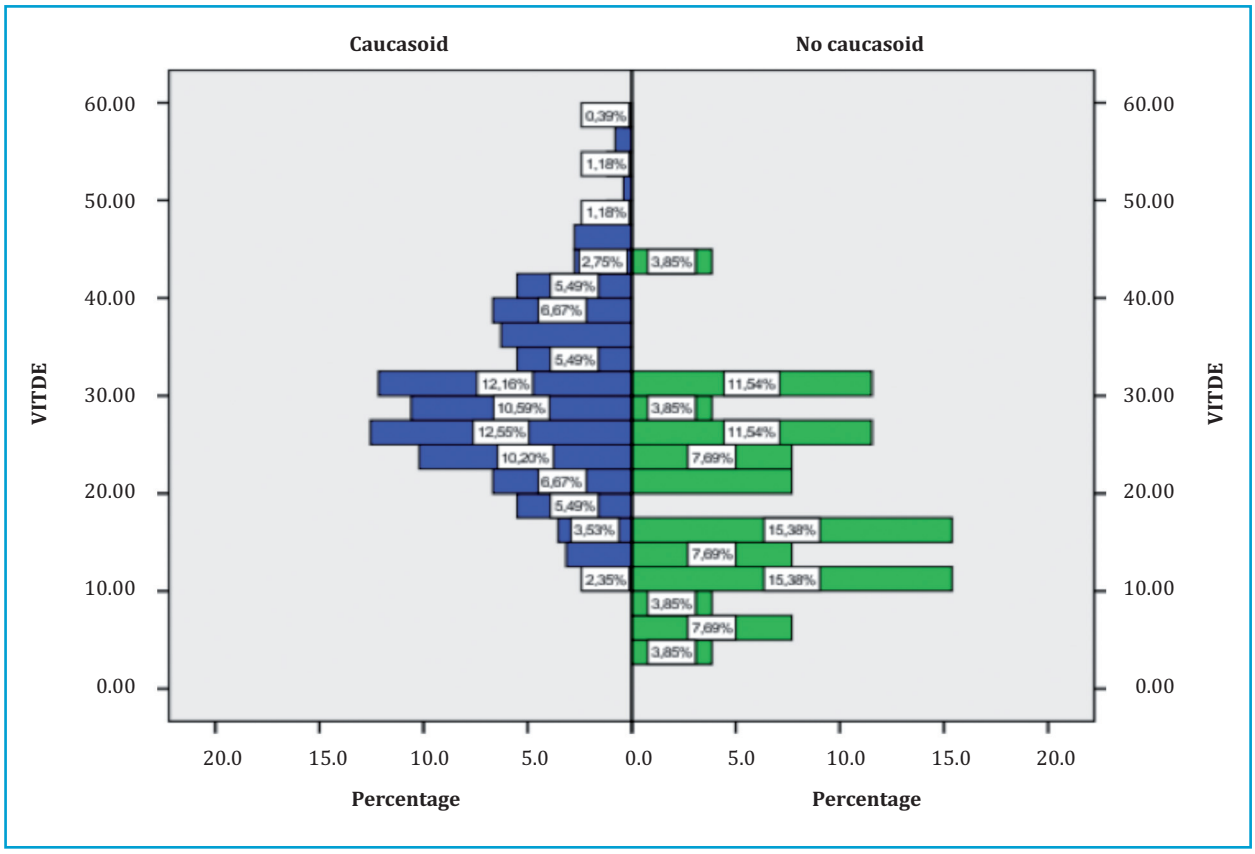
281 schoolchildren (140 boys and 141 girls) were recruited for the study. The global prevalence of hypovitaminosis D in this population, understood as serum 25 (OH) D values lower than 20 ng/ml, was 18.1%. Cases of severe deficiency (25 (OH) D <10ng / ml) represented 1.4%.

Table 1 shows the distribution of demographic data and other previously known risk factors in the sample, classifying schoolchildren according to a higher or lower vitamin D level (hypovitaminosis) of 20 ng/ml. Statistically significant associations were observed for season of the year, ethnicity, skin phototype, time of exposure to the sun, and age of the child. The mean vitamin D level in schoolchildren of Caucasian ethnicity was 29.83 ± 9.45 ng/ml, while among non-Caucasians it was 19.25 ± 9.71 ng/ml.

Table 1. Description of categorical variables of the sample according to vitamin D levels

		Vitamin D deficiency		Normal vitamin D		
Total		**n 51**	**% 18.1%**	**n 230**	**% 81.9%**	**p-value**
Season						
	Winter	20	29.4%	48	70.6%	
	Spring	17	31.5%	37	68.5%	
	Summer	6	9.1%	60	90.9%	
	Autumn	8	8.3%	88	91.7%	<0.001
Sex						
	Man	22	15.7%	118	84.3%	
	Woman	29	20.6%	112	79.4%	0.353
Age						
	<10 years	21	14.3%	126	85.7%	
	>=10 years	30	22.4%	104	77.6%	0.089
Ethnicity						
	Caucasian	37	14.5%	218	85.5%	
	Other	14	53.8%	12	46.2%	<0.001
Tanner						
	Prepubertal	27	14.8%	156	85.2%	
	Puberalanner	24	24.5%	74	75.5%	0.052
Personal history						
	Yes	6	17.1%	29	82.9%	
	No	45	18.3%	201	81.7%	1.000
Sport						
	Less than school	2	6.9%	27	93.1%	
	School only	29	23.2%	96	76.8%	
	School + two days	20	15.7%	107	84.3%	0.078
Skin phototype						
	Red/blond/brown	33	14.5%	195	85.5%	
	Brown/black	18	34.0%	35	66.0%	0.002
Exhibithion time						
	<30 minutes	34	28.3%	86	71.7%	
	>30 minutes	17	10.6%	144	89.4%	<0.001
Sunscreen	No	38	21.7%	137	78.3%	
	Yes	13	12.3%	93	87.7%	0.055
Use of filter	No	41	20.6%	158	79.4%	
	Yes	10	12.2%	72	87.8%	0.125
Medication	No	41	17.5%	193	82.5%	
	Yes	10	21.3%	37	78.7%	0.537
Supplementation	No	50	18.5%	221	81.5%	
	Yes	1	10.0%	9	90.0%	0.696

Figure 1. Distribution of the percentages of the vitamin D level according to the ethnic group of the schoolchild



Correspondingly, only 14.5% of Caucasians were in the group with vitamin D deficiency, compared to 53.8% of non-Caucasians, with the difference in the distribution by groups also significant (p <0.001). Figure 1 shows the frequency of the percentages of vitamin D levels between children of Caucasian origin and those of non-Caucasian origin. The resulting distributions are clearly different. Laboratory tests were within normal ranges in all cases except PTH, which in 5 cases was above the cut-off point of 65 pg/ml.

Table 2 shows the comparison of the means for each of the micronutrients in the diet in the subsamples with levels greater or less than 20 ng/ml in vitamin D measured in serum. Statistically significant differences were observed in pyridoxine B6, saturated and monounsaturated fatty acids. The mean mg of vitamin D ingested was not statistically significant despite the fact that individuals with hypovitaminosis reported a 40% lower vitamin D intake.

The results of the logistic regression adjusted for season, sex, age (older or younger than 10 years), ethnicity and time of exposure to the sun show a statistically significant effect of pyridoxine B6 and saturated fatty acids (table 3). Increasing the intake of pyridoxine B6 by one milligram decreases 1.85 times the possibility of presenting vitamin D deficiency in our sample. Similarly, the intake of 1 gram more of saturated fatty acids the possibility decreases 1.04 times.

Discussion

The main contribution of our work is that diet plays a reduced role as a risk factor for hypovitaminosis D in healthy children. On the contrary, and according to the literature[2,3,5,23], factors related to sun exposure are the determinants of the presence of insufficient levels of vitamin D. From a clinical point of view, it has two consequences. The first is that a correct diet should not be a reason not to assess the possible risk of hypovitaminosis in a schoolchild. Second, it highlights that known risk factors such as non-Caucasian ethnicity and seasons with less sun exposure continue to be factors that determine a vitamin D assessment in schoolchildren. The strengths of our study should be highlighted as the size of the sample, its representativeness of the healthy population, and the obtaining of 25 (OH) D determinations throughout a year. A limitation of our work is the type of nutritional survey used since the diet with a 24-hour ER at a single moment is a method with limited precision. In addition, ER24hs requires adequate recent memory, it is not recommended for children under 12 years of age and in these cases the contribution of the parents was recorded. However, the work of Rodríguez Sangrador et al. that conducts a survey on the frequency of food consumption in 2 months of the year and measures the level of vitamin D but does so in a population of only 47 adolescents[16]. The difficulty of applying methods based on the weight of the food consumed over several days is the cause of the low number of published works. In the case of ER24hs we had trained interviewers, but we recognize the weakness of this type of survey in relation to recent memory and the low estimate of a person's nutritional and energy contributions. Despite its limitations, the literature that has compared the methods for measuring nutrient intake indicates that the ER24hs provides valid, although less precise, information[21,22].

Table 2. Nutrient content of the 24-hour intake

	Vitamin D deficiency		Normal vitamin D		
Total	**n 43**	**% 84.3%**	**n 205**	**% 89.1%**	
	Mean	**SD**	**Mean**	**SD**	**p-value**
Protein (g)	87.41	25.01	93.51	25.10	0.149
Lipids (g)	86.86	25.50	96.06	29.26	0.057
Carbohydrates (g)	227.19	62.15	232.29	59.07	0.611
Energy (kcal)	2040.16	437.83	2169.47	472.11	0.100
Proteins %	17.21	4.11	17.34	3.35	0.844
Lipids %	38,09	7.43	39.44	6.70	0.239
Carbohydrates %	44.63	8.00	43.15	7.48	0.545
Phosphorus (mg)	1294.27	347.95	1341.90	377.92	0.447
Magnesium (mg)	235.31	77.57	238.44	73.60	0.802
Calcium (mg)	1002.79	338.96	1054.87	359.35	0.384
Iron (mg)	13.04	4.31	13.44	4.54	0.590
Zinc (mg)	10.37	4.32	11.00	4.07	0.366
Sodium (mg)	1691.45	763.64	1806.33	677.01	0.324
Potassium (mg)	2590.07	828.46	2591.71	843.90	0.991
Iodine (mg)	44.90	30.04	48.06	33.50	0.569
Selenium (mg)	65.80	33.69	70.41	59.32	0.623
Copper (mg)	958.35	620.54	975.99	741.93	0.884
Fluorine (mg)	403.93	278.13	364.40	214.89	0.300
Chlorine (mg)	0.00	0.00	1.56	15.75	0.517
Manganese (mg)	0.00	0.00	0.01	0.05	0.517
Chromium (mg)	0.00	0.00	0.49	4.95	0.517
Molybdenum (mg)	0.29	2.98	0.00	0.00	0.517
Vitamin C mg	104.56	92.29	109.91	109.46	0.739
Thiamine B1 mg	1.50	0.67	1.32	0.59	0.098
Riboflavin B2 mg	1,80	0.61	1.70	0.51	0,330
Nicotinic Ac mg	20.19	9.43	19.45	9.50	0.640
Pyridoxine B6 mg	1.92	0.97	1.63	0.68	**0.018**
Vitamin A µg	1568.10	1443.63	1692.35	1444.86	0.608
Vitamin D µg	3.92	9.49	6.52	15.20	0.286
Vitamin E mg	9.22	3.83	8.36	4.55	0.192
Free folic acid µg	84.34	50.44	91.30	69.81	0.445
Total folic acid µg	203.41	110.43	200.85	109.06	0.890
Cyanocobalamin B12 µg	4.99	8.83	4.71	3.81	0.839
Biotin µg	0.34	3.62	0.00	0.00	0.538
Saturated AG g	29.22	11.59	24.87	8.45	**0.021**
Monounsaturated FA g	41.40	13.83	36.84	13.35	**0.049**
Polyunsaturated FA g	8.52	4.87	7.83	4.45	0.393
EPA g	0.06	0.16	0.08	0.28	0.408
DHA g	0.09	0.29	0.16	0.54	0.419
Cholesterol mg	412.54	229.78	407.56	254.68	0.899
MCT g	0.01	0.13	0.00	0.00	0.517
Dietary fiber g	14.77	6.69	14.90	6.47	0.904

SD: standard deviation; g: grams; FA: fatty acids; EPA: icosapentaenoic acid; DHA: docosahexaenoic acid; MCT: medium chain triglycerides.

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Table 3. Multivariate analysis of the probability of hypovitaminosis D, according to risk factors

	95% CI for AOR			
	AOR	**Lower**	**Higher**	**Sig.**
Summer-autumn season	0.17	0.06	0.42	0.000
Sex female	1.45	0.61	3.44	0.404
Age >= 10 years	1.21	0.40	3.62	0.736
Non-Caucasoid ethnic group	17.67	4.77	65.46	0.000
Exposure time >30 min	0.45	0.19	1.06	0.067
Pyridoxine B6 (mg)	0.54	0.31	0.95	0.031
Saturated AG (gr)	0.96	0.92	1.00	0.048
Vitamin D (µg)	1.02	0.99	1.06	0.126
Fluorine (mg)	1.00	1.00	1.00	0.106
Constant	0.38			0.312
Well ranked percentage	85.9%			
Area under the ROC curve	0.87	0.82	0.93	
Hosmer and Lemeshow test				0.382

AOR: adjusted Odds Ratio; AG: fatty acids; min: minutes.

Upon analyzing the different dietary micronutrients, statistically significant associations with hypovitaminosis D only appeared for pyridoxine B6 and saturated fatty acids in both the univariate and multivariate analyzes, with no pathophysiological explanation for this finding. Among the micronutrients, the frequencies of magnesium, calcium and potassium intakes were deficient regarding the recommendations for each sex and age. Regarding vitamins, the same happened with folic acid and vitamins C, A, D and E. The 2005 Basque Country Nutritional Survey showed similar nutritional habits to ours[24].

Our results indicate that hypovitaminosis D is associated with the same factors as in the literature[25,26]. The percentage with severe deficiency (<10 ng/ml of 25 (OH) D) was small (1.4%), as corresponds to a healthy population. Using 20 ng/ml as a cut-off point, the deficiency reached 18.15% prevalence. According to the American Institute of Medicine (USA), the level of 20 ng/ml covers the needs related to phosphocalcic metabolism of 97% of the population[25]. However, with a cut-off point of ≤30 ng/ml, as established by other studies[6], the level of hypovitaminosis D would reach 56.3%. Hypovitaminosis D was focused on risk groups such as the non-Caucasian population in which it was greater than 50%. In fact, a case of rickets in a non-Caucasian, Pakistani child was the trigger for this study. Other variables such as seasonality and weight were also relevant[3,5,23]. For this reason, the outdoor lifestyle, sun exposure free of sunscreen and dietary patterns that ensure a correct intake of vitamin D and calcium continue to be the recommendations to be followed by the general population. It is important to highlight that the population studied was healthy and that only 5 schoolchildren found elevated levels of PTH (>65 pg/ml). In no case were there clinical manifestations or alterations in calcium, phosphorus and magnesium levels were found. The five children underwent a subsequent clinical evaluation and analysis of phosphocalcic metabolism (alkaline phosphatase, calcium, phosphorus, magnesium, PTH and vitamin D), with normal examination and analysis. For this reason, it was considered that the alterations in PTH levels corresponded more to physiological variations of adaptation than to a response to a vitamin deficiency[26].

Exposure to the sun for more than 30 minutes was statistically significant in the univariate analysis, but this relationship disappeared in the multivariate analysis with a significance level of 5% since the p was 0.67. This "anomaly" may be due to the sample size since, although the adjusted Odds Ratio was 0.45, its upper confidence interval exceeded one.

According to our results, population screening for vitamin D deficiency should not be performed and supplementing with it should be limited exclusively to risk groups[6,27]. The criteria for carrying out an analytical determination of 25 (OH) D and supplementing it, according to its results, have been described by expert committees[28-30]. However, these indications vary between different scientific societies. Thus, the American Pediatric Association (AAP)[30] and the European Association of Pediatrics (EAP)[29] reserve this indication for risk groups. A study by Saggese et al.[28] in a global consensus in Italy proposes supplementing with vitamin D in children and adolescents with the following risk factors for vitamin D deficiency: non-Caucasian ethnicity with dark skin pigmentation, reduced exposure to sunlight (due to lifestyle factors, chronic illness or hospitalization, institutionalization, complex disability, covering with clothing for religious or cultural reasons) or constant use of sunscreen, international adoption, obesity, chronic diseases (kidney, liver, Malabsorption syndromes, chronic therapies (anticonvulsants-antiretrovirals-glucocorticoids-systemic antifungals). In all these situations it is necessary to monitor vitamin D status at least once a year.

The vitamin D needs are covered by 90% with sun exposure and the remaining 10% is achieved through the diet, so both factors should be specifically valued in the Primary Care programs of the child and adolescent population, both for its prevention, diagnosis and treatment. Currently the best option to increase the dietary intake of vitamin D is food fortification. In the European Union, countries are divided into 3 categories; those with a policy of mandatory fortification (Norway, United Kingdom), voluntary (Spain, Portugal) or that there is no fortification. In Spain, there are exceptions to some products used for a long time as the sole source of nutrients by some population groups (infant formulas for

initiation, continuation and cereals – enteral and parenteral nutrition products for hospital use and low-energy diets for reduction of weight, whose fortification is mandatory for all member states of the European Union)[31]. In our country there is a tendency to fortify skimmed and semi-skimmed milk until reaching the vitamin D level of whole milk that is lost with the skimming process. In addition, there are other products on the market that are also fortified, such as cookies, yogurt, margarines, cheese, breakfast cereals, juices and beverages[32].

Children require less exposure to sunlight than adults to produce sufficient amounts of vitamin D, both because of their higher body surface area to volume ratio and because of the greater capacity of their metabolism to produce vitamin D[33]. In relation to sun exposure, it is known that the effective dose of UV radiation to produce 1000 IU of vitamin D, which guarantees sufficient levels of it in the blood, is achieved with 25% of the minimum erythromatogenic dose (MED), which is equivalent to 10-15 minutes in 25% of the body surface (face, arms, hands), without sunscreen and in the central hours of the day, from 10 to 15 hours[34].

A varied, balanced diet adapted to the needs of the different stages of its evolution is key for adequate physical and psychological growth, to prevent diseases and to obtain an optimal state of health. Their vigilance makes the risk of a short- and long-term nutritional deficit generally unlikely. Despite this, it should not be a reason to rule out vitamin D deficiency risk.

Promoting adequate levels of vitamin D in schoolchildren and adolescents is important because nutritional rickets can develop throughout the pediatric age and because its deficiency negatively affects bone health[35]. The comparison of the numerous studies that assess supplementing with vitamin D is very complex given the heterogeneity in the administration of vitamin D (interval, dose, duration) and the recruited population (sex, age, ethnicity, BMI, latitude of the country of residence, season of the year, baseline vitamin D status). In our region, an unfavorable latitude, there is little synthesis of vitamin D in late autumn, during the winter months and early spring. During this period, an adequate level of vitamin D is only maintained by endogenous stores accumulated during the previous summer or by exogenous supplements. The presence of hypovitaminosis D due to risk factors, the recommended doses are between 600 IU/day (reduced sun exposure) up to 1000 IU/day (multiple risk factors for vitamin D deficiency). The way to supplement is with intermittent doses (weekly-monthly) from 5-6 years and especially during adolescence; continuous doses should be reserved for children with permanent risk factors for hypovitaminosis D[28].

This work recognizes the importance of vitamin D during the pediatric stage and the challenge posed by an individualized assessment according to age, seasonality, skin phototype, adequate outdoor lifestyle, the controlled and prudent use of sunscreens and patterns nutrients that ensure a correct intake of vitamin D and calcium. The study of vitamin D also implies an effort to reduce health inequalities since it focuses on a social group with a low socioeconomic level and associated with immigration. Thus, pediatric control of hypovitaminosis D in schoolchildren is at the same time an exercise in the implementation of public health strategies aimed at promoting children's health.

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