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Vitamin D Status and the Effect of Oral Vitamin D Treatment in Children with Alopecia Areata

Karaguzel G[1*], Sakarya NP[2], Bahadır S[3], Beyhun E[4] and Yaman S[5]

[1]*Department of Pediatric Endocrinology, School of Medicine, Karadeniz Technical University, Trabzon, Turkey*

[2]*Department of Pediatrics, School of Medicine, Karadeniz Technical University, Trabzon, Turkey*

[3]*Department of Dermatology, School of Medicine, Karadeniz Technical University, Trabzon, Turkey*

[4]*Department of Public Health, School of Medicine, Karadeniz Technical University, Trabzon, Turkey*

[5]*Department of Biochemistry, School of Medicine, Karadeniz Technical University, Trabzon, Turkey*

[*]**Corresponding author:** Karaguzel G, Department of Pediatric Endocrinology, School of Medicine, Karadeniz Technical University, Trabzon, Turkey, Tel: +90 462 3775924; E-mail: gkaraguzel@ktu.edu.tr

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Abstract

Objectives: Little is known about the association of vitamin D and alopecia areata (AA). Our objectives were to search a relation between 25-hydroxyvitamin D [25(OH)D] levels and the development of AA and the efficacy of oral vitamin D treatment in children with AA and vitamin D deficiency.

Methods: Thirty newly diagnosed AA patients and 30 sex- and age-matched controls were included in the study. Levels of 25(OH)D, parathormone, calcium, inorganic phosphate, alkaline phosphatase were measured at baseline and sixth month. Both patients and controls who diagnosed vitamin D deficiency were treated with oral vitamin D for six months.

Results: Serum 25(OH) D levels of the patients and controls were 25.3 ± 19.4 ng/ml and 21.3 ± 12.5 ng/ml, respectively ($p>0.05$). The frequency of vitamin D deficiency was similar in patients and controls. Serum levels of 25(OH)D and calcium were increased significantly after six months of the treatment in both patients and controls with vitamin D deficiency ($p<0.05$). A higher frequency (47%) of complete improvement was observed in patients with AA and vitamin D deficiency during oral vitamin D treatment.

Conclusions: There was no statistically significant difference in 25(OH)D levels between the patients with AA and controls. However, we observed a higher frequency of complete improvement in these patients with an improved vitamin D status. Thus, oral vitamin D treatment can be given only to selected AA patients who are also deficient in vitamin D.

Keywords Vitamin D; Alopecia areata; 25-Hydroxyvitamin D; Vitamin D deficiency

Introduction

Alopecia areata (AA) is a common immune-mediated non-scarring hair loss disorder that can involve any hair-bearing area. Loss of the growing hair shaft has been related to lymphocytic infiltration on which CD4+ T-cells constitute the majority of lymphocytes in the hair follicule site. A predominant Th1 cytokine profile has also been found at the site of AA lesions [1-5].

AA associated with an increased overall risk of autoimmune disorder such as autoimmune thyroiditis, vitiligo, pernisiyoz anemia, type 1 diabetes, lupus erythematosus, myastenia gravis, celiac disease, and polyendocrinopathy syndrome type 1 [1,3,4]. Environmental and genetic factors have also been suspected as contribute to the disease [1,3,6].

It has been reported that vitamin D plays an important role in cutaneous immune modulation [7-9]. The active form of vitamin D (1,25-dihydroxyvitamin D) acts as an immunomodulator targeting various immune cells such as macrophages, monocytes, dendritic cells as well as T lymphocytes and B lymphocytes [9-11]. Vitamin D receptors (VDR) are expressed in dermal papilla cells and in the epidermis of the hair follicles. 1,25-dihydroxyvitamin D plays an important role in the development of hair follicle via VDR expression [12]. Furthermore, total or partial alopecia is an important finding of the patients with vitamin D-dependent rickets type II [13].

There are a few studies in adults regarding the role of vitamin D in the pathogenesis of AA and there is only one pediatric study assessing vitamin D level in 20 children with AA [14-16]. The objective of the present study was to search a possible relation between the serum levels of 25-hydroxyvitamin D [25(OH)D] and the development of AA in childhood. We also evaluated prospectively the efficacy of oral vitamin D treatment on vitamin D status in children with AA and vitamin D deficiency.

Materials and Methods

This study was carried out in Trabzon (latitude 41˚N), northeastern Turkey. Thirty patients (20 girls) aged 6 to 17 years with newly-diagnosed AA from our outpatient Pediatric Endocrinology and

Dermatology clinics were included consecutively in the study. The participants were excluded if they had any other autoimmune or chronic illness, if they were obese or had been using medication in previous six months that could alter outcome of the study. Controls were 30 sex- and age-matched apparently healthy children (20 girls) with no family history of AA or systemic autoimmune diseases in their first-degree relatives were recruited on the same day as the patients to avoid the effects of the seasonal variation in vitamin D levels.

Topical therapy was started all patients with AA at the beginning of the study (Figure 1). The questionnaire covering general nutrition attitude, time spent outside, and clothing preference was applied and socio-demographic data were obtained.

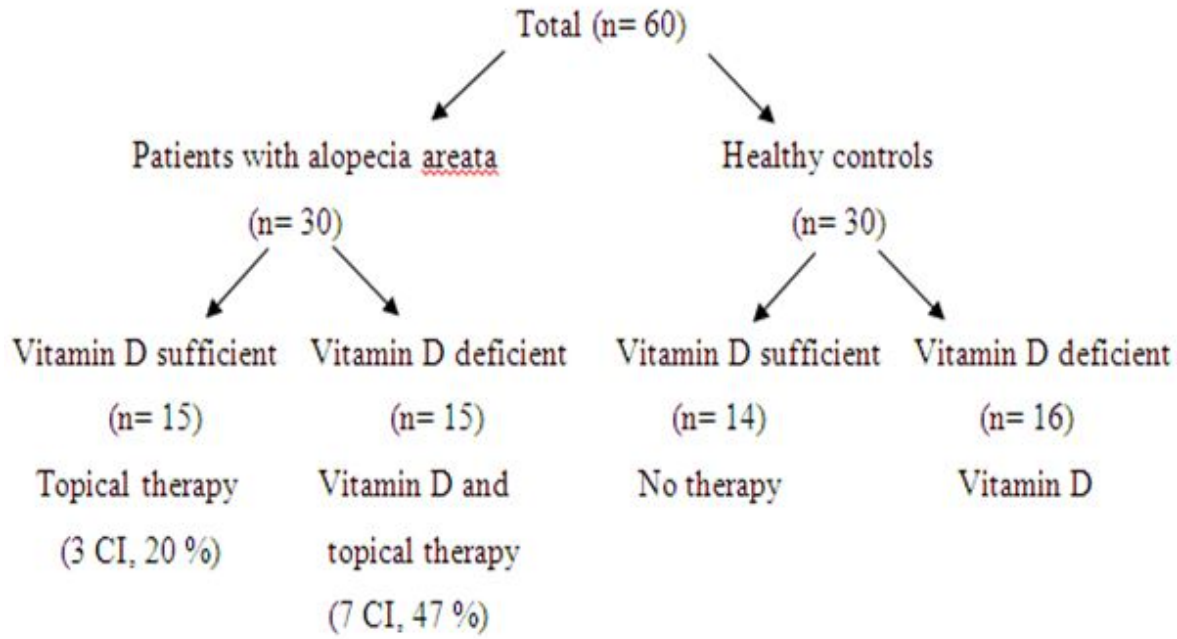

Figure 1: Distribution of the patients and controls (CI: complete improvement).

Blood samples were obtained in the morning for serum 25(OH)D, calcium, inorganic phosphate, alkaline phosphatase (AP), and parathormone (PTH) measurements at baseline and sixth month for whom vitamin D deficient. The samples were separated within half an hour and stored at -80˚C until analysis. Height and weight of participants were measured and recorded. Body mass index (BMI) was calculated using the formula: weight(kg)/height(m)^2. Vitamin D deficiency was defined as serum 25(OH)D levels of <20 ng/ml. Both patients and controls who were diagnosed vitamin D deficient were treated with vitamin D for six months with a dose of 1500 IU/day vitamin D was given if the serum 25(OH)D level<20 ng/ml and 3000 IU/day if the level<10 ng/ml. Informed written consent was obtained from the parents. The study was approved by our Institutional Ethics Committee (No: 2011/110).

Laboratory measurements

Serum 25(OH)D levels were assessed by high-performance liquid chromotography (HPLC with reversed phase column, IC3401rp, Thermo Seperator Products, Immuchrom GmBH, Germany). The intr-aassay coefficient of variations (CVs) were 2.6% at 22.6 ng/ml and 1.5% at 41.9 ng/ml, the inter-assay CVs were 4% at 21.6 ng/ml and 3.6% at 42.2 ng/ml. Intact PTH was measured using a 2-site chemiluminescence enzyme-labeled immunometric assay (Immulite 2000 Siemens, LA, USA) with the upper limit of normal was 65 pg/ml. Serum calcium, inorganic phosphate, and AP were measured using colorimetric methods (Cobas 8000, Roche Diagnostic, Manheim, Germany). Secondary hyperparathyroidism was defined as a serum PTH>65 pg/ml and a serum calcium<10.5 mg/dl.

Statistical analyses

Data were analyzed by using SPSS for Windows (SPSS, Inc, Chicago, IL). Results were expressed as mean ± standard deviation or percentages. The normality of the distribution of each variable was determined using the Kolmogorov-Simirnov test. Data comparisons of means between two groups were performed with student's t-tests after testing for normality. Paired-sample t-test was used to compare the dependent variables after testing for normality. The chi-square analysis was used to compare categorical data. Pearson's correlation was used in correlation analyses of the variables. Statistically significance was set at $p<0.05$.

Results

Twenty (66%) of the patients with AA in the study were girls and 34% of them were boys. Serum 25(OH)D levels were not significantly different between the patients and controls. The baseline clinical and biochemical characteristics of the patients and controls were similar (Table 1).

Parameters	Patients (n= 30)	Controls (n=30)	P*
Girls/Boys (n)	20/10	20/10	NS
Age (years)	10.5 ± 2.9	10.5 ± 2.8	NS
Body mass index (kg/m^2)	17.9 ± 2.2	17.4 ± 2.1	NS
25(OH)D (ng/ml)	25.3 ± 19.4	21.3 ± 12.5	NS
Calcium (mg/dl)	9.6 ± 0.3	9.7 ± 0.4	NS
Phosphorus (mg/dl)	4.6 ± 0.4	4.5 ± 0.7	NS
Alkaline phosphatase (U/l)	212 ± 81	202 ± 64	NS
Parathormone (pg/ml)	51.0 ± 29.6	42.2 ± 29.9	NS

Table 1: Clinical and laboratory characteristics of the patients with alopecia areata and Controls at baseline (mean ± SD).

The frequency of vitamin D deficiency was similar in patients (50%) and controls (53%). Hyperparathyroidism was found only 27% (n=4) of AA patients with vitamin D deficiency at baseline. Serum 25(OH)D levels were increased and PTH levels were decreased significantly after six months of treatment with oral vitamin D in AA patients. In controls, 25(OH)D levels were increased significantly at sixth month.

None of the children had hyperparathyroidism or hypercalcemia at the end of the study. Any new lesion did not develop during the treatment in the patients who were vitamin D deficient. We observed complete improvement in 10 patients with AA, seven of whom were vitamin D deficient and received combination treatment with oral vitamin D and topical treatment in Figure 1. There was no statistically significant relation between serum levels of 25(OH)D and the general nutrition attitude, time spent outside or clothing preference (data not shown). We did also did not find any correlation between BMI and 25(OH)D levels (p>0.05) (Table 2).

Parameters	Baseline	6th Month	P*
25(OH)D3 (ng/ml)			
Patients$^{\theta}$	10.5 ± 2.9	25.5 ± 12.4	<0.001
Controls	11.5 ± 5.1	30.4 ± 16.4	<0.001
Parathormone (pg/ml)			
Patients$^{\theta}$	68.0 ± 31.0	47.0 ± 15.0	<0.05
Controls	52.4 ± 35.9	48.2 ± 32.9	NS
Calcium(mg/dl)			
Patients$^{\theta}$	9.6 ± 0.3	9.8 ± 0.2	<0.001
Controls	9.8 ± 0.4	9.6 ± 0.4	<0.005
*P values of <0.05 statistically significant; θ *vs.* controls, all of the comparison p>0.05; NS: non-significant			

Table 2: Serum levels of 25-hydroxyvitamin D, parathormone, and calcium in patients (n=15) and controls (n=16) who were vitamin D deficient.

Discussion

The study results showed that serum 25(OH)D levels were not significantly different between the children with AA and the sex- and age-matched healthy controls both at the time of diagnosis and sixth month. Oral vitamin D treatment improved vitamin D status in both patients and controls with vitamin D deficiency. It is well known that low 25(OH)D levels are associated with increased PTH levels. At the end of the present study, none of the patients had hyperparathyroidism supporting that the doses of vitamin D treatment for vitamin D deficient children were adequate. To our knowledge, this is the first prospective study to compare serum 25(OH)D levels in patients with AA and healthy controls in childhood. It was reported only in a seven year-old patient with AA treated with topical calcipotriol [17]. There are also a few studies regarding the relationship between serum 25(OH)D levels and AA [14-16,18].

We determined that vitamin D deficiency is a frequent problem among the patients with AA as well as healthy controls. This finding was not surprising for us because the prevalence of vitamin D deficiency was found 93% in spring and 71% in autumn in healthy school-children in our previous study [19]. Studies investigating the association between hypovitaminosis D and AA have yielded conflicting results [14,15,18]. In a cross-sectional study from Turkey, 42 adults with AA and healthy controls were analyzed in terms of 25(OH)D levels and found that 25(OH)D levels were significantly lower in patients than that of controls [14]. There is no national vitamin D fortification program in Turkey and the difference could be related to the extent of sunlight exposure during outdoor physical activities in their study area which geographically located at south of Turkey (latitude 36˚N). As a similar finding to ours, d'Ovidio et al. reported that the frequency of vitamin D deficiency in patients with AA was not significantly different from controls [15]. They also reported that decreased level of 25(OH)D was not correlated with extent of hair loss. In a recent study from Israel, 25(OH)D levels were evaluated in 23 adult patients with AA and controls (n=20) [18]. The authors reported that vitamin D levels were significantly lower in patients than those controls and suggested vitamin D deficiency could be a risk factor for AA occurrence. However, their study group was relatively small and they did not exclude obese patients or the patients who treated with vitamin D that could have influence upon 25(OH)D levels.

The active form of vitamin D mediates its action by binding to specific VDR located in the nucleus of target cells. It has been demonstrated that VDR is strongly expressed in the key structures of human and murine hair follicles [9,20]. A lack of VDR could be associated with reduced epidermal differentiation and hair follicle growth [21]. We did not find any difference between the patients with AA and controls in terms of 25(OH)D levels during six months suggesting that vitamin D deficiency is not a significant risk factor for AA occurrence. Further trials with a large number of patients are needed to confirm these results.

In this study, no statistically significant difference was observed in the serum 25(OH)D levels between the patients with AA and the controls however, we observed that the oral vitamin D treatment improves hair regrowth with the higher frequency of complete improvement in patients with AA and vitamin D deficiency. The finding support the thought that oral vitamin D treatment can be given only to selected AA patients who are also deficient in vitamin D.

Author Contributions

Karaguzel G contributed to the study design, study conduct, data collection, data analysis and interpretation and manuscript preparation. Sakarya NP, Beyhun E, Bahadır S and Yaman S contributed to the study design, data collection and analysis.

Conflict Of Interest

All authors declare no conflict of interest.

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