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by Abdul Qadar Punagi

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The Role of Vitamin D Suplementation in Allergic Rhinitis Management

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ABSTRACT

Background: In recent years the increase in the incidence of allergic diseases worldwide is often associated with vitamin D deficiency. This study aimed to see the effect of additional therapy of vitamin D on the specific immunoglobulin E (IgE) levels of allergic rhinitis patients.

Materials and Method: It was an experimental research with pre and post test design group control design. This study involved 40 patients with allergic rhinitis that positive for Der p allergen in skin prick test, divided into 2 groups. Group I was 20 patients receiving intranasal fluticasone spray and vitamin D 2x400IU/day for 21 days. Group II is 20 patients who only get fluticasone intranasal spray therapy for 21 days. Both groups of patients examined the levels of 25(OH)D and specific IgE Der p pre and post therapy.

Results: Examination of 25(OH)D and specific IgE Der p was done by enzyme-linked immunosorbent assay (ELISA) method. From the analysis of demographic characteristics of the subjects in each group showed no significant difference ($p > 0.05$) between the two groups based on sex and age of the patient. The results of the Mann-Whitney test showed significant difference ($p < 0.05$) between the two groups, where the specific IgE level decreased more in the vitamin D group than in the non-vitamin D group.

Conclusion: There is a significant correlation between changes in levels of 25(OH)D and specific IgE Der p levels of patients with allergic rhinitis, where the increasing levels of 25(OH)D caused decreasing of specific IgE Der p levels.

Keywords: *Allergic Rhinitis, Vitamin D, 25(OH)D, Specific IgE Der p*

INTRODUCTION

Today, allergic rhinitis is a global health problem that affecting 10-25% of the population worldwide where its prevalence continues to increase.[1,2] In recent years, an increased incidence of allergic diseases worldwide is often associated with vitamin D deficiency.[3] Vitamin D is an essential nutrient that humans acquire through sun exposure, diet and dietary supplements. Ultraviolet B radiation (UVB) photolysis 7-dehydrocholesterol in the skin to previtamin D3, which is then converted to vitamin D3 (cholecalciferol). Cholecalciferol from the skin and diet will experience hydroxylation in the liver into 25-hydroxyvitamin D3 (25(OH)D) and stored in the liver. Vitamin D levels are known by measuring serum or plasma levels of 25(OH)D, which is the most widely obtained form in the circulation. The half-life of 25-hydroxyvitamin D is about 3 weeks in circulation. Levels of 1,25-hydroxyvitamin D can be normal or even elevated in vitamin D deficiency states so it can not be used to measure the patient's calciferol status.[5,6]

Vitamin D works by binding to its high affinity receptor. This receptor is known as the Vitamin D Receptor (VDR). The association between calciferol and VDR will stimulate interaction with Retinoic acid X Receptors (RXR) to form heterodimer complex (VDR-

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RXR). This complex bond will then bind to the specific DNA located in the target gene and known as VDRE. The VDR-RXR and VDRE bonding complex will caused gene transcription through the release of co-repressor (SMRT, NCOR) which subsequently withdraws the nuclear receptor co-activation protein.[6,7]

IgE is an antibody that plays a major role in the type I hypersensitivity reaction. Regulatory resistance of IgE occurs through transcriptional mechanism of ε germline transcription. This process begins with the 25(OH)D binding to its receptor VDR, which then binds to RXR and VDRE on the target genes and forms a heterodimer complex. The target of the gene known as Iε is the area where transcription ε germline took place. The heterodimer bond complex will then draw the SMRT co-repressors, then draw HDAC1 and HDAC3 to join on Iε. It is now known that the role of HDAC in the body's immune system. HDAC has a role in maintaining the balance of Th1 and Th2. The complex of VDR-RXR-VDRE-co-repressor SMRT-HDAC1 and HDAC3 formed causes DNA chromatin condensation and transcription process ε germline is inhibited until CSE IgE process does not occur.[8,14]

This study aims to examine the effect of additional therapy of vitamin D on specific IgE Der p levels of patients with allergic rhinitis.

METHOD

Research Site: This research was conducted in the outpatient unit of ENT department Dr. Wahidin Sudirohusodo hHospital Makassar starting from August 2017 until October 2017. Processing of research result is done at laboratory of Education Hospital of Hasanuddin University Makassar.

Design and Research Variables: The design of this study is experimental study with pre test design and post test control group design. The independent variable in this study was vitamin D, while the dependent variable was specific IgE Der p levels.

Samples: The sampling technique was performed randomly. In this study patients that positive with Der p allergen in Skin Prick Test were divided into 2 groups with the number of patients each group was 20 patients, thus total patients as many as 40 people. Patients included in the first group received fluticasone nasal spray and vitamin D 2x400IU oral therapy per day for 21 days, while the second group received only fluticasone nasal spray without vitamin D for 21 days. Patients from both groups were examined for 25(OH)D and specific IgE Der p pre and post therapy.

Exclusion Criteria: Having a history of kidney disease, liver, rickets, colorectal carcinoma and mamae, as well as autoimmune diseases such as systemic lupus erythematous, taking immunomodulators, history of immunotherapy, history of vitamin D consumption in the past 1 month.

Drugs: The drug that we used is vitamin D ® GNC VITAMIN D-3 400, with a given dose of 2x400 IU (total of 800 IU/oral/day), given for 21 days (3 weeks).

Statistical Analysis: Data were analyzed using Statistical Package for Social Sciences (SPSS) software (version 23.0 for Windows; SPSS Inc, Chicago, IL).

Research Ethics Aspect: The study was obtained from Biomedical Research Ethics Committee on Human Faculty of Medicine Universitas Hasanuddin (Register No. 600/H4.8.4.5.31/PP36-KOMETIK/2017).

RESULTS

Characteristics of Population: Characteristics of the study population were shown in Table 1. The results of the analysis showed no significant difference (p> 0.05) between the two groups based on gender and age of the patient.

Table 1: Demographic Characteristics of Research Subjects in Each Group

Characteristics	Groups		p
	With Vitamin D (n = 20)	Without Vitamin D (n = 20)	
Age (years)	34,8 ± 10,2	30,8 ± 8,5	0,182*
Gender (M/F)	9/11	10/10	1,000**

**independent t test; **chi-square test*

Levels of 25(OH)D: The summary of the analysis of results in Table 2 showed a significant increase of 25(OH)D levels (p <0.05) in the serum group of vitamin D by 13.7%, while in the group without vitamin D actually decreased 5.1% p <0.05). The results of the Mann-Whitney test showed significant difference between the two groups. Levels of 25(OH) D increased significantly in the group given vitamin D.

Table 2: Comparison of Changes in 25(OH)D Serum Between the Two Groups

Groups	Changes of 25(OH)D Serum Levels (ng/mL)				p*
	Pre (Median?)	Post	Changes	Median % of Increasing	
With Vitamin D	14,92 ± 3,40	17,37 ± 2,64	2,46 ± 1,91	13,7%[b]	<0,001
Without Vitamin D	15,26 ± 3,23	14,56 ± 3,63	0,70 ± 0,92	-5,1%[a]	0,005

**Wilcoxon test; **Mann-Whitney U test if superscript on the median % changes column is the same, it means that Mann Whitney U test results not significantly changes (p>0,05); if different it means significantly difference (p<0,05).*

Immunoglobulin E Specific Der p: Table 3 shows a significant decrease (p <0.05) at specific IgE Der p levels of serum group vitamin D by 48.7%, while in the group without vitamin D only decreased by 0.81% and not significant (p> 0.05). The results of the Mann-Whitney test showed significant difference (p <0.05) between the two groups. Specific IgE levels of Der p decreased more in the vitamin D group than in the non-vitamin D group.

Table 3: Comparison of changes in specific IgE levels Der p between the two groups

Groups	The Changes of Spesific IgE Der p levels (kU/l)				p*
	Pre	Post	Changes	Median % of Decreasing	
With Vitamin D	21,95 ± 15,68	10,72 ± 6,89	-(11,23 ± 12,80)	48,7%[b]	<0,001
Without Vitamin D	17,97 ± 10,07	17,41 ± 9,78	-(0,56 ± 1,17)	0,81%[a]	0,078

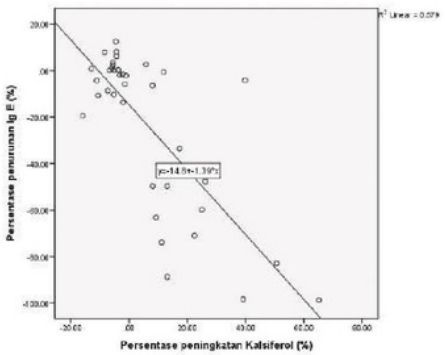
Wilcoxon test;Mann-Whitey U test, if superscript median % changes column is the same, it means that the result of Mann Whitney U test not significantly different (p>0,05); if different it means significantly different (p<0,05).*

Relationship Between 25(OH)D With Specific IgE Der p: The summary results of bivariate correlation analysis (Pearson correlation) and partial correlation in table 4 show that there was significant correlation (p <0.05) between% serum calciferol level change with% change of specific IgE Der p level with partial correlation coefficient of r = - 0,503.

Table 4: Correlation between Percentage Changes in Calciferol and IgE Specific Der p

Correlation between variables	Bivariat Correlation	Partial Correlation
	Correlation Coefficient r dan p	Correlation Coefficient r dan p
% change of klasiferol level with IgE Specific	r = - 0,746 dan p<0,001	r = - 0,503 dan p = 0,001

From graph 1 can be seen the relationship between percentages increased of calciferol with decreased of specific IgE Der p. The more increasing of levels of 25(OH)D, the more decreasing the levels of specific IgE Der p.



Graph 1: Scatter Plot Graph Between Percentage of 25(OH)D Increasing and Percentage of Spesific IgE Der p Decreasing

DISCUSSION

In this study we found insufficiency of 25(OH)D before therap Research conducted by Arshi[9] (2012) showed that serum 25(OH)D levels in patients with allergic rhinitis were significantly lower than normal people. This suggests that vitamin D has a role in inflammatory regulation based on type 1 hypersensitivity reactions and mediated by specific IgE. In vitro studies conducted by Pichler[10] (2002) and Staeva-Vieira[11] (2002) demonstrated that IL-4 production would be inhibited by 25(OH)D so that Th2 differentiation would decrease. A study conducted by Penna[12] (2008) found that IL-10 may rise up to 7-fold in dendritic cells given vitamin D, high levels of IL-10 prevent mast cell degranulation.

Most of the research sample work is office workers, students and housewives who are more in the room, causing a lack of exposure to ultraviolet light. This

may lead to low 25(OH)D levels in both groups. After therapy, there was an increase in serum 25(OH)D levels in the first group by 18.7%. While in the group not given vitamin D found a decrease in serum 25(OH)D level of 5.1%. This shows a significant difference of change between the two groups.

From the observation of specific IgE Der p, there was a significant decrease in specific IgE Der p levels in serum by 48.7% in the first group given vitamin D supplementation. While in the group not given vitamin D there was also a decrease of 0.81 % but not meaningful. Research conducted by Milovanovic[8] (2011) suggests that vitamin D has a major role in inhibiting IgE regulation through transcriptional ε germline barrier mechanisms.

In this study, bivariate correlation (Pearson correlation) and partial correlation found significant correlation between percentage change of serum vitamin D levels with percentage change of specific IgE levels which found that the higher the increasing of serum vitamin D level, the lower the specific IgE level. This is in contrast to the results of a study conducted by Tamasauskiene[13] (2014) which states that there is no significant correlation between total IgE levels and vitamin D serum levels.

The limitations of this study are that specific IgE constraints may also be caused by IFNγ, BCR, CTLA4, and IL-21. In this study these factors are not examined. Research d by examining the above cytokines can clarify the relationship between 25(OH)D serum and specific IgE. In this study additional vitamin D therapy was given for 21 days. Same with research conducted by Modh[3] (2014) which also provides vitamin D supplement for 21 days. Until now, it has not been known how long period of effective intake of vitamin D that can significantly decreasing specific IgE levels. More research is needed on this subject.

CONCLUSIONS

Through this study it can be concluded that there is a significant relationship between specific IgE of Der p levels with 25(OH)D serum levels, whereas the higher levels of 25(OH)D, the lower the specific IgE Der p levels. In this study it can also be concluded that the addition of vitamin D supplementation may decrease the specific IgE Der p level of patients with allergic rhinitis.

RECOMMENDATION

Due to the limitations in this study, further research is needed to clarify the relationship between vitamin D and specific IgE.

Conflict of Interest: There is no conflict of interest

Source of Funding: Researcher (Self)

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