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HEALTHY AGING RESEARCH

Allergic rhinitis in the elderly: A pilot study of the role of vitamin D

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Abstract

Background: Allergic rhinitis in the elderly is poorly understood as very few studies have investigated this patient group. Vitamin D insufficiency and deficiency are very common, and vitamin D appears to play a role in respiratory disease. We studied the role of vitamin D in elderly subjects with perennial allergic rhinitis.

Methods*:* Fifteen subjects with symptomatic perennial allergic rhinitis (Total Nasal Symptom Score, TNSS ≥5 out of 12) received vitamin D (4,000 I.U./day) and placebo each for 6 weeks in a crossover design. TNSS (instantaneous and in the previous three weeks) and Rhinitis Related Quality of Life Questionnaire (RQLQ) were evaluated at five study visits (baseline, and 3, 6, 9, and 12 weeks later). Associations between serum vitamin D and demographics, TNSS, and RQLQ were also assessed.

Results: Baseline serum vitamin D was 29.7±10.6 ng/ml. After the six-week vitamin D supplementation, its serum levels increased significantly (to 39.7±8.9 ng/ml, $p<0.01$), whereas serum calcium remained unchanged. Instantaneous TNSS, three-week TNSS, and RQLQ were unchanged compared to placebo. There was no association between serum vitamin D and age, body mass index, duration of rhinitis, or medication score. However, in subjects with poorly controlled nasal symptoms, there was a significant inverse association with serum vitamin D and the three-week TNSS ($r=-0.81$, $p=0.008$).

Conclusions: Vitamin D supplementation for six weeks did not improve nasal symptoms or RQLQ in elderly subjects with perennial allergic rhinitis. These results and the inverse association between vitamin D and nasal symptoms will require confirmation in larger studies.

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Introduction

It has been projected that the U.S. population older than 65 years will double by the year 2050 [1]. Allergic rhinitis is a very common disorder with direct and indirect costs calculated in tens of billions of dollars [2]. While the prevalence of allergic rhinitis seems to be decreasing with age, this condition affects 8.8% of individuals aged 65 to 74 years old [3].

There is a near complete lack of information about the treatment of allergic rhinitis in the elderly population. In fact, the vast majority of studies of this condition have focused on children and relatively young adults. The lack of trials targeting treatment of older patients with allergic rhinitis was discussed in a review article [4]. While some studies have included patients with rhinitis over 65 years old, only two studies, to our knowledge, have specifically looked at this group. Those include a 12-week study of an intranasal

steroid, mometasone, in perennial allergic rhinitis, and a 6-week, open label study of another intranasal steroid, fluticasone and azelastine (an intranasal anti-histamine) [5, 6].

It has been shown that vitamin D deficiency and insufficiency are very common, even in subjects with abundant sun exposure [7, 8]. Vitamin D can exert an immunomodulatory effect via its activity on T lymphocytes, dendritic cells, mast cells, monocytes and macrophages [9-14]. Among these cells, mast cells and lymphocytes are particularly key players in the pathogenesis of allergic rhinitis (15). Previous studies have shown that serum vitamin D levels are inversely related to allergic rhinitis [16, 17].

The main objective of this study was to investigate the effect of vitamin D supplementation on Total Nasal Symptom Score (TNSS) and Rhinitis Quality of Life Questionnaire (RQLQ) scores in elderly subjects with perennial allergic rhinitis. This was a double-blind, placebo controlled, cross-over study.

Secondary objectives of our study included investigating whether any association exists between serum vitamin D levels and age, sex, body mass index (BMI), disease duration, medication score, presence of asthma, TNSS and RQLQ scores.

Methods

This study included five study visits (baseline and 3, 6, 9, and 12 weeks later). It was performed during the period from November 1, 2013 to March 20, 2014 to try to avoid seasonal fluctuations of serum vitamin D due to sun exposure. 25-Hydroxy vitamin D2 and D3 were measured in the serum of the study subjects by chemiluminescence at the Main Line Health Laboratories. Subjects with serum vitamin D levels of less than 20 ng/ml were classified as deficient, whereas levels ranging between 20 and 29 ng/ml were considered to be reflective of vitamin D insufficiency. Serum vitamin D levels were measured at study entry, 6 and 12 weeks later. Serum calcium levels were also measured at such study visits.

The study subjects received placebo and vitamin D in a cross-over design. Each study subject took one 4,000 I.U. softgel of vitamin D3 (Carlson Laboratories, Arlington Heights, IL) or one softgel of placebo daily every morning for six weeks. The study subjects brought the study bottle to the third (6 week) and fifth (12 week, final) study visits. The bottles were collected and the remaining softgels were counted, recorded, and disposed. Compliance with the study based on softgel count was very good (>90%).

Fifteen subjects 65 years-old and older with perennial allergic rhinitis were included in the study. Allergic sensitization was verified by allergy skin tests for perennial allergens. Most common sensitivities were dust mites (12), house pets (8), and molds (4). Smokers were excluded. Additional vitamin D-containing supplements were allowed only if they were components of standard multivitamin preparations (≤500 I.U./day). Otherwise, such supplements were discontinued for at least one week prior to the initial study visit and for the duration of the study. The study subjects were recruited among interested and eligible patients with allergic rhinitis followed in our practice.

In order to qualify for the study, each subject had to have a minimal TNSS at baseline of ≥5 out of a maximum of 12. TNSS included the sum of the scores for nasal congestion, rhinorrhea, itchy nose/sneezing and post-nasal drip reported on a scale from 0 to 3 (none, mild, moderate, and severe, respectively). The TNSS collected during the study were related to the time of the study visit (instantaneous, TNSSi) and to the previous three weeks (TNSS3w). TNSS and RQLQ are the most common parameters assessed in studies of treatment of allergic rhinitis. Total medication scores (TMS) included nasal steroids (4), nasal antihistamines (6), oral antihistamines (8), montelukast (5), and ipratropium bromide (3). Drug treatment remained unchanged throughout the study period. Four subjects were on a stable dose of allergen immunotherapy during the study.

Data were expressed as the mean ± standard deviation and analyzed by the two-tailed, unpaired t-test and the Pearson correlation coefficient as indicated with significance accepted at alpha <0.05.

This study was approved by the Main Line Hospitals Institutional Review Board and registered on clinicaltrials.gov (NCT02272101).

Results

The baseline characteristics of the study subjects are summarized in Table 1 Only one subject had vitamin D deficiency and six subjects had vitamin D insufficiency.

Table 1. Subjects' characteristics at baseline

Age (years, range)	77.5±7.3, 68-92
Sex (F/M)	12/3
BMI	26.5±4.9
Duration of Rhinitis (years)	57.9±17.8
Asthma	9/15
TMS	1.7±1
TNSSi	7.3±2.2
TNSS3w	8±2.6
RQLQ Score	58.3±30.9
Serum Vitamin D (ng/ml)	29.7±10.6
Serum Calcium (mg/dl)	9.6±0.5

BMI: body mass index; RQLQ: Rhinitis Related Quality of Life Questionnaire; TMS: Total medication score; TNSSi: instantaneous Total Nasal Symptom Score; TNSS3w: three-week Total Nasal Symptom Score

After a six-week supplementation, serum vitamin D increased by 10 ng/ml (to 39.7± 8.9 ng/ml, $p<0.01$), whereas serum calcium was unchanged (9.68±0.38 mg/dl). As shown in Table 2, TNSSi, TNSS3w, and RQLQ scores did not change when compared to placebo after three or six weeks of vitamin D supplementation. The individual components of the RQLQ, including the nasal symptoms, were similarly unchanged compared to placebo (data not shown).

We found no significant association between serum vitamin D and age, BMI, duration of rhinitis, TMS, asthma, TNSS or RQLQ (Table 3). Serum vitamin D was similar in subjects with or without asthma (28.4±10.1 ng/ml vs. 31.7±11.9 ng/ml, respectively, p=0.60). However, in subjects with poorly controlled nasal symptoms (TNSS ≥8 of 12, RQLQ for nasal symptoms ≥16 of 24), there was an inverse association with serum vitamin D that was significant for the TNSS3w (Table 4).

Table 2. Effect of vitamin D supplementation on TNSS and RQLQ Scores vs. Placebo

	Baseline	Week 3	Week 6
TNSSi (Vitamin D)	7.3±2.2	4.3±3.4	5.3±2.9
TNSSi (Placebo)		4.6±2.7	3.5±2.1
TNSS3w (Vitamin D)	8±2.6	6.8±2.6	6.6±2.7
TNSS3w (Placebo)		6.9±2.9	5.3±2.8
RQLQ (Vitamin D)	58.3±30.9	44.2±30.3	41.9±24.6
RQLQ (Placebo)		46.8±25.7	40.9±29.5

RQLQ: Rhinitis Related Quality of Life Questionnaire; TNSSi: instantaneous Total Nasal Symptom Score; TNSS3w: three-week Total Nasal Symptom Score

Table 3. Associations between serum vitamin D and other parameters

	Correlation (r)	
Age	-0.02	p=0.94
BMI	-0.16	p=0.57
Duration of rhinitis	-0.14	p=0.62
TMS	-0.07	p=0.8
Asthma	0.15	p=0.59
TNSSi	-0.32	p=0.24
TNSS3w	-0.47	p=0.08
RQLQ	-0.29	p=0.29

BMI: body mass index; RQLQ: Rhinitis Related Quality of Life Questionnaire; TMS: Total medication score; TNSSi: instantaneous Total Nasal Symptom Score; TNSS3w: three-week Total Nasal Symptom Score

Table 4. Associations between serum vitamin D and TNSS and RQLQ for nasal symptoms (RQLQns) in subjects with uncontrolled symptoms

	Correlation (r)	
TNSSi	-0.56	p=0.25
TNSS3w	-0.81	p=0.008
RQLQns	-0.63	p=0.18

N=9 for TNSS3w and n= 6 for TNSSi and RQLQ.

RQLQns: Rhinitis Related Quality of Life Questionnaire for nasal symptoms; TNSSi: instantaneous Total Nasal Symptom Score; TNSS3w: three-week Total Nasal Symptom Score

Discussion

In this study, we investigated the role of vitamin D in elderly patients with perennial allergic rhinitis. This group of patients has been mostly ignored in previous studies of this condition.

We found that a six-week supplementation of daily vitamin D (4,000 I.U) significantly increased serum levels to about 40 ng/ml, but it did not lead to an improvement of the TNSS or RQLQ scores compared to placebo. Two very recent studies of vitamin D supplementation in adult asthmatics yielded conflicting results regarding the clinical benefit of this treatment [18, 19]. The results of these studies suggest that achieving high serum levels of vitamin D (close to 100 ng/ml) may be required to exert a clinical effect on respiratory disease.

It has been reported that vitamin D deficiency is common with obesity [20]. We did not find any association between serum vitamin D and BMI, age, or duration of disease. This difference could be explained by the fact that in our study only one subject was vitamin D-deficient and four were in the obese range (BMI≥30).

We did not find a significant association between TNSS or RQLQ scores and serum vitamin D. However, it is possible that a larger number of observations could have resulted in a weak, yet significant, inverse association.

In subjects with uncontrolled nasal symptoms, we did find a strong and significant inverse correlation between serum vitamin D and TNSS3w. Such finding suggests that vitamin D may play a role in patients with uncontrolled nasal symptoms. In our recent study of elderly asthmatics, we found that serum vitamin D was lower in subjects with uncontrolled asthma when compared to their counterparts with controlled symptoms [21].

Limitations of our study include the small number of subjects, exclusively Caucasian and mostly women, and the absence of daily symptom diaries. In addition, only one study subject was vitamin D-deficient.

Conclusions

This pilot study shows that vitamin D supplementation for six weeks does not lead to improved TNSS and RQLQ scores. These findings and the inverse association between serum vitamin D and TNSS will require confirmation in larger studies.

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