
Effect of vitamin E supplementation on the regular treatment of seasonal allergic rhinitis

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Background: Vitamin E supplementation is widely used in clinical practice for the prevention and treatment of different medical conditions. Evidence from basic science studies suggests that vitamin E may reduce immune allergic responses. However, only a few clinical studies of the effect of vitamin E on allergic conditions have been performed in patients with atopic dermatitis and asthma, and none have been performed in patients with allergic rhinitis.

Objective: To determine the effect of high-dose vitamin E supplementation in combination with the usual (“real-life”) treatment on the symptoms of seasonal allergic rhinitis during the pollen season.

Methods: In a double-blind, placebo-controlled, randomized study, 112 patients with documented hay fever received either vitamin E (800 mg/d) or placebo in addition to their regular antiallergic treatment during the pollen season. Patients recorded their daily nasal and eye symptoms and their daily need for other medications to control allergic symptoms.

Results: Although no effect was observed on ocular symptoms, nasal symptom scores were lower in patients who received vitamin E supplementation during the hay fever season. However, there was no reduction in the percentage of days with serious symptoms or in the percentage of days that medications were used to control allergic symptoms during the pollen season.

Conclusions: Vitamin E supplementation may be a valuable addition to the treatment of patients with seasonal allergic rhinitis. However, further clinical and basic science studies are needed to determine its real value.

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INTRODUCTION

Vitamin E supplementation is widely used in clinical practice for the prevention and treatment of various medical conditions.¹ However, its value in preventing disease is controversial. The use of vitamin E in preventing cardiovascular disease has been widely studied in different clinical investigations,^{2–7} but the results are contradictory. It has also been hypothesized that vitamin E reduces the risk of cancer; however, only 1 study⁸ found a significant reduction in the incidence of prostatic cancer but not other types of cancer. Evidence from animal studies suggests that vitamin E reduces IgE production,^{9,10} modifies the leukotriene pathway,¹¹ and reduces the level of immune response mediators.¹² A study¹³ done in a murine model of nasal allergy demonstrated that high-dose vitamin E supplementation suppressed nasal allergic responses and reduced the levels of the cytokines interleukin (IL) 4 and IL-5 and of total serum IgE. A nutritional study¹⁴ of 2,633 adults indicated that higher intake of vitamin E was associated with lower IgE concentrations and a lower frequency of allergen sensitization. Weber et al¹⁵ demonstrated that vitamin E down-regulates IL-4 expression in messenger RNA and protein levels in activated human peripheral blood T cells by interfering with transcriptional activity.

Although these studies may support supplementation of vitamin E for primary or secondary prevention of allergic conditions, only a few clinical studies have been done, mostly

in atopic dermatitis and asthmatic patients,^{16–18} and none have been performed in allergic rhinitis patients. Therefore, we designed a double-blind randomized study to compare the effect of high-dose vitamin E supplementation in combination with the regular (“real-life”) treatment on the symptoms of allergic rhinitis during a natural pollen season.

METHODS

Patient Population

Men and women aged 18 to 70 years with a documented history of seasonal allergic rhinitis during the pollen season for at least the 2 previous years were included in the study. Patients were eligible for inclusion in the study after confirmation of seasonal allergic rhinitis by skin prick testing for a panel of inhalant allergens (Center Laboratories, Port Washington, NY). The skin test results were considered positive if the diameter of the skin response was at least 5 mm greater than that of the saline control. Patients with skin test results positive for olive pollen or a mix of 8 southern grasses, which correlated to the patient’s seasonal history, were included in the study. Exclusion criteria included anticoagulant drug treatment, a history of bleeding disorders, congestive heart failure, a history of arrhythmia, malignancy, and a history of other allergic conditions, such as perennial allergic rhinitis, bronchial asthma, and atopic dermatitis.

Study Design

A randomized, double-blind, placebo-controlled study was conducted during peak pollen season between March and May 2002 in 4 allergy clinics in northern Israel. The study was approved by the Ethics Committee for Clinical Research

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Table 1. Patient Demographics (N = 112)

	Vitamin E group (n = 58)	Placebo group (n = 54)
Sex, M/F, No.	28/30	29/25
Age, median (range), y	32 (18–65)	36 (18–65)
Mean days of follow-up	70	65
Real-life treatment, No (%) [*]		
Specific immunotherapy	24 (41.3)	25 (46.3)
H ₁ antihistamines	26 (44.8)	16 (29.6)
Topical steroids	22 (37.9)	24 (44.4)
Vasoconstrictor nose drops	16 (27.6)	8 (14.8)
Vasoconstrictor eye drops	5 (8.6)	3 (5.6)
Positive skin prick test result [†]		
Grass pollen	51 (87.9)	41 (75.9)
Olive pollen	26 (44.8)	31 (57.4)
Grass and olive pollen	10 (17.2)	12 (22.2)
Other allergens	20 (34.5)	15 (27.8)

^{*} Some patients were treated with more than 1 medication.

[†] Some patients were sensitive to multiple allergens.

Studies of the Rambam Medical Center, and all patients provided written informed consent.

The study design consisted of 4 patient visits. At visit 1, patients were evaluated for signs and symptoms of allergic rhinitis and for current medical treatment for controlling allergic symptoms (real-life treatment, ie, drugs and immunotherapy). Physical examination and skin prick tests were performed. Eligible patients were randomized to receive either 800 mg/d of vitamin E (Evitol; Teva Pharmaceutical Industries Ltd, Petach Tikva, Israel) or placebo. They were also supplied with a questionnaire and instructed to record their daily nasal symptoms (sneezing, nasal blockage, rhinorrhea, and nasal itching) and daily ocular symptoms (watering, itching, redness, and eyelid edema). For each symptom, a 4-point scale was used: 0, absent; 1, mild symptoms that do not bother the patient; 2, moderate symptoms that do not prevent the patient from carrying out usual activities and that do not interfere with sleep; and 3, severe symptoms that prevent the patient from performing usual activities and that interfere with sleep. Patients were

instructed to continue their usual antiallergic treatment (immunotherapy, antihistamines, nasal glucocorticoids, and nasal and ocular vasoconstrictor drops). They were also instructed to record their daily use according to the number of tablets, inhalations, and drops used.

At visit 2, 15 days after enrollment in the study, the investigators recorded a list of symptoms similar to that given to the patients, collected the diary card, and instructed the patient to take medications to control symptoms in case it was necessary. Visits 3 and 4 each took place 1 month after the previous visit, and the same evaluation conducted at visit 2 was performed at each visit. The primary end point of the study was a reduction in the daily nasal and eye symptom score. The secondary end points were reductions in the total number of days with serious symptoms (symptom score 2 or 3) and in the use of medications to control allergic symptoms.

Statistical Analysis

The intent-to-treat population consisted of all individuals who were randomized for treatment and who received at least 1 of the study medications (vitamin E or placebo). Demographic characteristics of the 2 groups were compared using analysis of variance for continuous variables and the χ^2 test for categorical variables. A Mann-Whitney-Wilcoxon test was used to compare efficacy between the 2 study groups. $P < .05$ was considered to indicate a statistically significant difference.

RESULTS

One hundred twelve patients were randomized to the 2 treatment groups, which were comparable for all parameters (Table 1). Vitamin E supplementation produced an improvement in the total daily symptom scores (both nasal and ocular) evaluated by the patients ($P = .04$) but not those evaluated by the investigators (Table 2 and Figs 1 and 2). An improvement in the total nasal symptom score evaluated only by the patients was also noted ($P = .03$), but there was no statistically significant difference in eye symptoms between the 2 groups (Table 2 and Figs 3 and 4).

Table 2. Mean Daily Symptom Scores as Recorded by Patients

	Vitamin E group		Placebo group		P value
	Mean	95% CI	Mean	95% CI	
Total symptom score	5.03	4.01–6.06	6.56	5.39–7.73	.04
Total nasal symptom score	3.46	2.84–4.09	4.51	3.79–5.22	.03
Sneezing	0.82	0.63–1.01	1.05	0.84–12.5	.15
Nasal blockage	0.94	0.72–1.15	1.22	1.01–1.42	.04
Rhinorrhea	1.06	0.87–1.25	1.30	1.10–1.51	.08
Itching	0.65	0.48–0.82	0.94	0.73–1.15	.06
Total ocular symptom score	1.57	1.07–2.07	2.05	1.45–2.66	.25
Watery eyes	0.46	0.30–0.61	0.52	0.33–0.71	.70
Itching	0.59	0.42–0.76	0.70	0.51–0.90	.40
Red eyes	0.30	0.17–0.44	0.44	0.28–0.61	.60
Swollen eyes	0.22	0.09–0.34	0.39	0.22–0.55	.10

Abbreviation: CI, confidence interval.

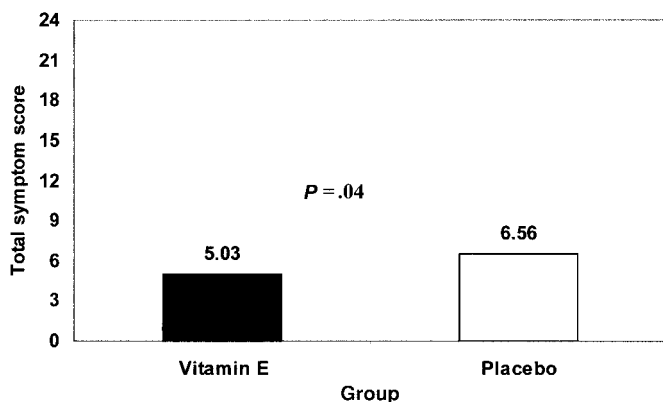


Figure 1. Mean total symptom score by patient report (maximum score = 24).

When each nasal and ocular symptom was considered individually, a statistically significant improvement was observed only in nasal blockage ($P = .04$); the other individual nasal symptoms improved, but without statistical significance (Table 2 and Fig 5). There was a nonsignificant reduction in the percentage of days with serious symptoms. Individual nasal symptoms, such as rhinorrhea ($P = .08$) and itching ($P = .06$), showed a trend toward significance (Table 2 and Fig 5). There were no differences between the 2 groups in the daily use of medications to control allergic symptoms (Fig 6).

DISCUSSION

This randomized, double-blind, placebo-controlled study evaluated the effect of vitamin E supplementation in 112 patients with seasonal allergic rhinitis who received conventional (real-life) treatment to control symptoms during the hay fever season. We demonstrated an improvement in the total (both ocular and nasal) symptoms of seasonal allergic rhinitis score reported by the patients but not in those recorded by the investigators who evaluated the patient at each visit. However, patient-reported improvement was statisti-

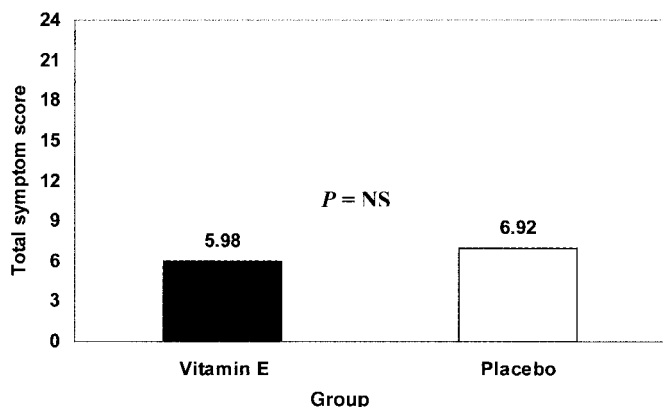


Figure 2. Mean total symptom score by physician examination (maximum score = 24). NS indicates not significant.

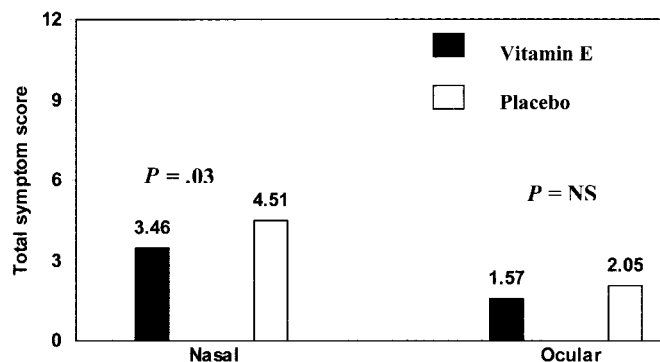


Figure 3. Mean daily nasal and ocular symptom scores by patient report (maximum score = 12). NS indicates not significant.

cally significant only for nasal symptoms. The fact that patients participating in the study could not be prevented from seeking further treatment to control their symptoms may explain the lack of medication reduction during the study despite the change in nasal and ocular symptom scores reported by the patients.

Vitamin E acts as an antioxidant in cellular membranes and scavenges free radicals by blocking the peroxidation of polyunsaturated fatty acids. It also modifies prostaglandin formation and thereby enhances the production of prostaglandin I_2 , known to inhibit the effects of histamine, the major chemical mediator in the cascade events of allergic rhinitis that causes itching, sneezing, and rhinorrhea.¹⁹ Numerous other types of cells and inflammatory mediators, such as prostaglandin D_2 , leukotrienes D_4 and C_4 , and platelet-activating factors, are involved in the pathogenesis of allergic inflammation.¹⁹ These mediators are derived from fatty acid metabolism, which may also be modulated by vitamin E.

Zheng et al,¹³ using a model of induced nasal allergy in mice, demonstrated that a diet supplemented with high-dose vitamin E led to a significant reduction in all the outwardly observable markers of nasal allergy compared with a diet supplemented with low-dose vitamin E. They also demon-

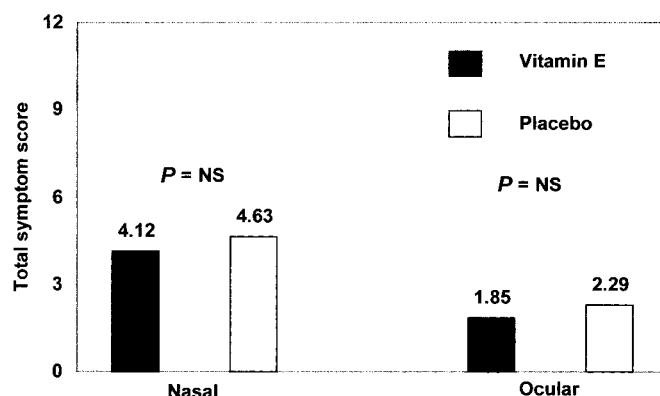


Figure 4. Mean daily nasal and ocular symptom scores by physician examination (maximum score = 12). NS indicates not significant.

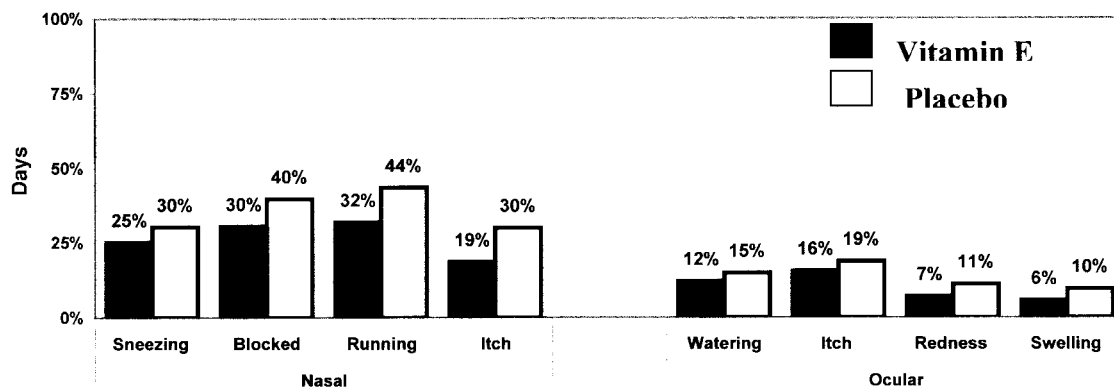


Figure 5. Percentage of days with serious nasal and ocular symptoms by patient report.

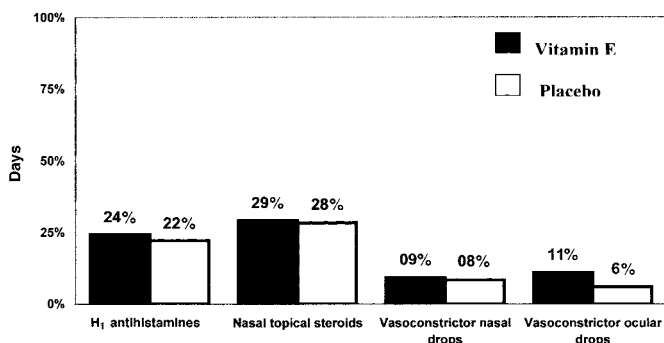


Figure 6. Percentage of days of medication use to control allergic symptoms.

strated decreases in lymphoproliferation, T_H2 cytokine production of IL-4 and IL-5, and serum IgE levels in mice treated with high-dose vitamin E. Fogarty et al¹⁴ demonstrated in an epidemiologic nutritional study of 2,633 adults that higher intake of vitamin E was associated with lower serum IgE concentrations and lower frequency of allergen sensitization and atopic diseases. Tsourelis-Nikita et al¹⁶ reported an improvement in subjective symptoms and a reduction in serum IgE levels in patients with atopic dermatitis treated only with vitamin E compared with patients who received placebo.

Recent studies point to the fact that 5-lipoxygenase shifts the T_H1 response to T_H2. Thus, by inhibiting 5-lipoxygenase and influencing the production of biologically active cysteinyl leukotriene, vitamin E may have the effect of directing the response toward a T_H1-type response instead of T_H2.¹¹

The daily treatment dose of vitamin E (800 mg) used in the study was much higher than the recommended daily allowance of 15 mg.¹⁷ However, previous studies¹⁻⁸ have used vitamin E dosages of 200 to 800 mg/d safely, and we adopted the higher dose.

In conclusion, to the best of our knowledge, this study is the first in which vitamin E supplementation was used as a component of the treatment of seasonal allergic rhinitis. Our

data demonstrate improvement in the symptom scores of patients with seasonal allergic rhinitis. We suggest that this improvement may have been caused by inhibition of IL-4, IL-5, and IgE production or by modulation of the leukotriene and prostaglandin pathway. We also suggest that the antioxidant role played by vitamin E reduced the oxidative stress of treated patients, thereby reducing the level of immune inflammation in these patients. In view of our data and considering the wide experience with vitamin E use in different medical conditions without serious adverse effects, further clinical and basic science trials are warranted to validate the effect of vitamin E supplementation in allergic conditions.

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