

Allergic Contact Dermatitis from Vitamin E: The Experience at Mayo Clinic Arizona, 1987 to 2007

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Background: Vitamin E, of which the most biologically active form is α -tocopherol, has become widely known for its antioxidant effects. It has been ingested or applied topically for purported anti-aging effects and for cosmetic enhancement.

Objective: To determine whether the incidence of allergic contact dermatitis from vitamin E has increased in recent years.

Methods: With the approval of the Mayo Clinic institutional review board, we retrospectively analyzed patch-test data from patients tested from June 1987 through December 2007.

Results: A total of 2,950 patients were patch-tested during this period, and 18 patients (0.61%) had positive reactions to α -tocopherol; 6 (0.53%) of 1,136 patients tested from June 1987 through December 1997 had positive results, and 12 (0.66%) of 1,814 patients tested from January 1998 through December 2007 had positive results ($p = .69$).

Conclusion: Vitamin E appears to be a relatively rare contact allergen in our experience.

VITAMIN E, of which the most biologically active form is α -tocopherol, is widely claimed to be a useful antioxidant. It has been ingested orally or applied topically for purported anti-aging effects and for cosmetic enhancement. Frequently, patients apply vitamin E to scars in an effort to improve cosmesis, although a double-blinded study showed no differences in cosmetic appearance for patients using an ointment containing α -tocopherol (320 international units per gram) as opposed to using an ointment alone.¹ In that study, 33% of the subjects developed contact dermatitis from vitamin E.

Recently, interest in complementary and alternative medicine has grown along with interest in “natural” products for improving cosmetic appearance. A recent study found that vitamin E was a component of 54.7% of moisturizers available at a local pharmacy.² Patients continue to use vitamin E either at the direction of their physicians or on their own despite its history of possible adverse reactions.

The purpose of this study was to examine our patient population data from 1987 through 2007. The patients

were divided into two groups: those tested from 1987 to 1997 and those tested from 1998 to 2007. This was done to explore a possible difference in the incidence of contact dermatitis over time.

Methods

This study was approved by the Mayo Clinic institutional review board. Patch-test data from June 1987 through December 2007 were reviewed. Patients with a positive patch-test reaction to α -tocopherol were noted, and charts were reviewed for additional information, including site of dermatitis and relevance of the reaction. Patients who were patch-tested more than once during this period were counted as only one patient; a positive reaction on any of a patient's numerous patch tests was counted as a positive reaction.

Because of changes in the patch test of allergen sources during the study period, patients tested from 1987 through 1999 were tested with α -tocopherol at various concentrations in petrolatum. Patients who were patch-tested from 2000 through 2005 were tested with α -tocopherol acetate 10% in petrolatum; patients who were tested after 2005 were tested with α -tocopherol 100%. Statistical values were calculated with a two-tailed chi-square test. All statistical analysis was performed with SAS software (SAS Institute Inc., Cary, NC).

Results

From June 1987 through December 2007, 2,950 patients were patch-tested with α -tocopherol. For our analysis, we

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divided the patients into two groups: (1) patients seen from 1987 through 1997 and (2) patients seen from 1998 through 2007. We hypothesized that these groups would represent patients with different levels of exposure to vitamin E and would therefore have differing incidences of positive patch-test reactions to vitamin E.

From June 1987 through December 1997, 1,136 patients were patch-tested with α -tocopherol. Of these, 723 (63.6%) were female. The mean age at the time of patch testing was 60.2 years. Six patients (0.53%) had positive patch-test reactions, and all reactions were considered relevant. Extremities were the most common site of rash ($n = 3$) although the following locations were affected in one patient each: generalized, oral, and face and neck. One patient with upper extremity involvement also had facial involvement. Of the patients who had positive reactions, four were female, and the mean age at application was 54.3 years. All but one patient had other positive reactions as well.

From January 1998 through December 2007, patch tests with α -tocopherol were performed on 1,814 patients. Of these, 1,155 patients (63.7%) were female. The mean age at application was 62 years. Twelve patients (0.66%) had positive reactions to either α -tocopherol in petrolatum ($n = 11$) or α -tocopherol 100% ($n = 1$), and all reactions were considered relevant. Of the patients who had positive reactions, 8 (66.7%) were female, and the mean age was 62.4 years. Extremities were the most common sites of rash involvement ($n = 4$). Dermatitis encompassing hands and feet ($n = 3$) or the face ($n = 3$) was noted, as was generalized dermatitis ($n = 2$). Of these patients, all but one had multiple positive patch-test results.

When both data sets were considered, the overall positivity rate was 0.61% (18 of 2,950 patients). As shown in Figure 1, the rate of positive patch-test reaction in the first part of the study (0.53% during a 10.5-year period) and the positive-reaction rate in the second part of the study (0.66% during a 10-year period) were not significantly different ($p = .69$).

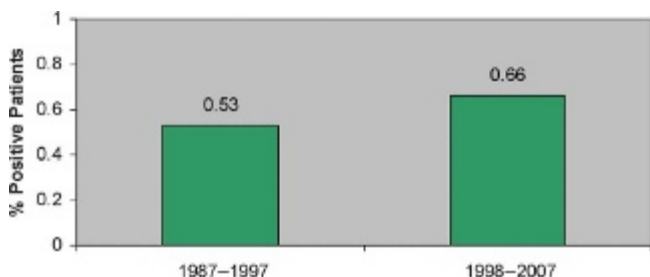


Figure 1. Percentages of patients with positive patch-test reactions.

The dermatology practice group at another campus of our institution began collecting data on α -tocopherol acetate and α -tocopherol in 2000. We compared our overall positivity rate (0.61%) with that of this other group (0.54% from 2000 to 2007) (Fig 2). The difference in rates was not significant ($p = .51$).

Discussion

According to the Environmental Working Group's Skin Deep cosmetic safety database, more than 14,000 currently marketed products contain tocopheryl acetate or tocopherol.³ These compounds are found in moisturizers, sunscreens, lip products, foundations, cleansers, conditioners, and other topical products. With the recent heightened interest in anti-aging and rejuvenation, this number likely has increased in the past decades. We initially hypothesized that we would identify a corresponding increase in cases of allergic contact dermatitis with time. However, we found no evidence of increased incidence of allergic contact dermatitis when we compared the initial patch-test data (1987 to 1999) with more recent data (2000 to 2007).

This study used a small population and included data from only two centers. Additionally, because exact concentrations of vitamin E were not recorded from 1997 to 1999, we were unable to analyze the effects of changes in the concentration of patch-test products over the years.

"Vitamin E" is a general term used to denote a family of eight antioxidants (four tocopherol compounds and four tocotrienol compounds); stereoisomers of individual compounds also exist.⁴ Additionally, because vitamin E chemicals are antioxidants, they are unstable compounds that are typically esterified to facilitate stability among other chemicals.⁵ Thus, α -tocopherol acetate is actually α -tocopherol that has been esterified by acetic acid. Esters

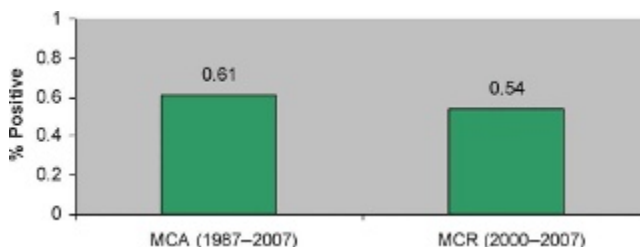


Figure 2. Comparison of overall positivity rates from the institution's home location and another campus. (MCA = Mayo Clinic, Arizona; MCR = Mayo Clinic, Rochester.)

must be hydrolyzed for activity, and this is easily accomplished in the human body.

Contact allergy to vitamin E was reported in 1965: an 18-year-old female developed dermatitis on her earlobes, where she had been applying a salve that contained vitamin E.⁶ Patch testing with the ingredients of the salve revealed a clinically significant reaction only to α -tocopherol. Subsequently, many other cases of allergic contact dermatitis from tocopherol acetate and linoleate were reported,^{7–12} including an epidemic outbreak in Europe that was ascribed to the inclusion of tocopherol in cosmetic preparations.¹³

In addition to allergic contact dermatitis, contact urticaria¹⁴ and erythema multiforme-type eruptions¹⁵ have been reported in connection with vitamin E. One report describes a xanthomatous reaction following a suspected contact dermatitis from vitamin E.¹⁶ According to *Fisher's Contact Dermatitis*, vitamin E almost never causes reactions when taken systemically, but it can cause contact urticaria when applied to the skin.¹⁷

The contact dermatitis in our study's patients consisted mainly of (1) dermatitis on the face or extremities or (2) a generalized eruption. This is consistent with the reports of allergic contact dermatitis from vitamin E in the literature.^{9,10,13,15}

The North American Contact Dermatitis Group (NACDG) reported a 1.1% rate of positive patch-test reaction to dl- α -tocopherol 100% in 2003 to 2004 and a relative rate of 1.00 in 2001 to 2002. Before 2001, dl- α -tocopherol 100% was not tested as part of a standard series.¹⁸ dl- α -Tocopherol was on the NACDG's list of the 20 most common allergens in cosmetics from 2001 to 2004; 3.1% of women and 0.6% of men had positive patch-test reactions to vitamin E that were attributed to a cosmetic not otherwise specified.¹⁹ This implies that users of cosmetics may have a greater risk of contact dermatitis than the general population.

In 2003, Oshima and colleagues described a young woman who had a positive patch-test reaction to dl-tocopheryl nicotinate but negative patch-test reactions to dl- α tocopherol and nicotinamide.²⁰ This implies that in some patients at least, there is antigen specificity within the vitamin E group. Thus, patients should be patch-tested with their own products. Patch testing with only α -tocopherol may be inadequate when evaluating allergic contact dermatitis from the other isomers or esters that make up the vitamin E family.²¹

An additional complicating factor in testing for allergic contact dermatitis from vitamin E is the fact that vitamin E is an antioxidant. This implies that it has the ability to

minimize inflammation; in fact, animal models have shown that vitamin E derivatives can effectively suppress contact dermatitis.²² A guinea pig study has also shown that sensitization to contact allergens can be reduced when an antioxidant preparation containing vitamin E is used.²³ Additionally, vitamin E is known to have photoprotective effects²⁴ and antiinflammatory effects²⁵ in mouse models.

Vitamin E derivatives in various products may actually suppress contact dermatitis; one such suspected case has been reported.²⁶ dl- α -Tocopherol acetate has been used to decrease paresthesias from synthetic pyrethroids in humans, and investigators speculated that this effect may stem from antiinflammatory properties of vitamin E.²⁷

Because of the role of vitamin E in the human body and because of its antioxidant properties, vitamin E and its derivatives likely will appear on ingredient lists for years to come. Although some patients will develop contact dermatitis after exposure to the ingredient, our findings suggest that this is rare. The results of future studies investigating the ability of vitamin E to act as both an allergen and a suppressor of contact allergy perhaps would allow physicians and scientists to exploit the positive effects of the antioxidant while avoiding the adverse contact dermatitis.

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