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The Effect of Vitamin D Supplementation on Atopic Dermatitis

Nell Rafalovich

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The Effect of Vitamin D Supplementation on Atopic Dermatitis

Abstract

**Background:** Atopic dermatitis is a very common dermatological condition affecting adults and up to 20% of children. Atopic dermatitis is thought to be regulated by the innate immune system which is controversially affected by vitamin supplements, specifically vitamin D. Does vitamin D supplementation improve symptoms of atopic dermatitis?

**Methods:** An exhaustive medical literature search was completed utilizing the following databases: Medline-OVID, Web of Science, and CINAHL. The terms “vitamin D” and “atopic dermatitis” were used and linked to further specify the search terms. The GRADE system for assessing research quality was used to determine strength of studies’ findings.

**Results:** Two studies were selected using the systematic review inclusion criteria for the review. One random control trial (RCT), of moderate GRADE quality, found a statistically significant improvement in atopic dermatitis symptomology with patients suffering from mild, moderate, and severe eczema on a vitamin D supplementation. The second RCT examined (also moderate in GRADE) did not show a significant improvement in symptoms with vitamin D supplementation, however, some improvements were noted and the authors suggest more research on the topic.

**Conclusion:** Vitamin D supplementation may cause a slight improvement in symptoms of atopic dermatitis but more research is needed to prove a direct link and to provide dosing guidelines in order for this recommendation to be adopted by medical providers.

**Keywords:** vitamin D, atopic dermatitis, supplementation, eczema, innate immunity

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Annjanette Sommers, MS, PA-C

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The Effect of Vitamin D Supplementation on Atopic Dermatitis

Nell Rafalovich

A Clinical Graduate Project Submitted to the Faculty of the School of Physician Assistant Studies Pacific University Hillsboro, OR For the Masters of Science Degree, August 08, 2015

Faculty Advisors: Dr. Vo & Prof. Olson

Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS
Biography

Nell Rafalovich is a first-generation college student who has a background in diet and exercise counseling, cardiac rehabilitation, and exercise science with a BS from Southern Oregon University and a MS from Texas Tech University. She was born in Helena, MT and travelled extensively with migrant working parents until settling in southern Oregon as a youth. Her nontraditional upbringing gave opportunities to volunteer in India for three months, work in Germany as an au pair for a summer, and later she lived in Vietnam for six months as a college student studying the Vietnamese language and their medical practices. After completion of her Masters of Science in Texas, she chose to stay home with her two young sons for six years. She currently enjoys studying medicine and spending time with her husband and two sons.
Abstract

Background: Atopic dermatitis is a very common dermatological condition affecting adults and up to 20% of children. Atopic dermatitis is thought to be regulated by the innate immune system which is controversially affected by vitamin supplements, specifically vitamin D. Does vitamin D supplementation improve symptoms of atopic dermatitis?

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Table I: Characteristics of Reviewed Studies
Table II: SCORAD and TIS Values

List of Abbreviations

AD.................................................................Atopic Dermatitis
SCORAD..........................................................SCORing Atopic Dermatitis
TIS..............................................................Three Item Severity Score
RCT.............................................................Random Control Trial
EASI..............................................................Eczema Area of Severity Index
IU..............................................................International Units
The Effects of Vitamin D Supplementation on Atopic Dermatitis

BACKGROUND

Atopic dermatitis (AD) also known as eczema is one of the most common skin disorders in children and adults, with a steep rise in diagnoses in children.\(^1\)\(^2\) Up to 20% of children are now affected in developing countries.\(^3\) Atopic dermatitis is a chronic and relapsing disease that is associated with inflammatory processes that often precedes asthma and allergic reactions. Patients with atopic dermatitis have a greater chance of acquiring infection by microbial organisms such as *Staphylococcus aureus* and herpes simplex virus due to defects in the innate immune system.\(^4\)

Treatment strategies have often focused on allergy avoidance or topical application of medications but now research has shifted to the connection to immune function and the skin’s natural role as a barrier.\(^3\) Atopic dermatitis is not only associated with defects in the immune system but often these defects worsen inflammation.\(^5\) Within the past five years, focus has moved from the known interactions of vitamin D and bone mineralization and osteoporosis to a broader role including cardiovascular, endocrine, cancers, and chronic diseases such as hypertension.\(^6\) Vitamin D appears to have important roles in the immunity, namely improving the innate and adaptive immune responses. In fact, vitamin D supplementation has been used to treat tuberculosis.\(^5\) Researchers are now interested in this relationship and some support the hypothesis that vitamin D insufficiency interferes with the innate immune system and may be an underlying cause of infectious disease and immune disorders.\(^6\) The innate immune system is responsible for the signaling of antimicrobial activity and antigen presentation.\(^4\)
It is known that vitamin D also induces cathelicidin production. Cathelicidins are antimicrobial peptides that are involved with the defense against skin infections which are one of the exacerbating factors and causes of resistance to steroid therapy in atopic dermatitis. Cathelicidin production is one piece of the immunity puzzle.

Because of vitamin D’s impact on innate immunity, it has received attention recently about the possibility of improvement of eczema with supplementation. Current recommended daily doses of vitamin D range from 800 IU per day to beyond 4000 IU per day, depending on the extent of insufficiency. Vitamin D levels are often varied among persons of differing skin shades, geographic locations, sunscreen use habits, diet, and hereditary factors. The multifactorial nature of vitamin D levels makes studying their effects on atopic dermatitis difficult.

Traditional treatment options for patients with atopic dermatitis include harmful ultraviolet B light treatment and/or topical vitamin D. These treatments may be effective due to the possible activation of the production of vitamin D3 in the skin. Ultraviolet light is a known cancer-causing agent and should not be used routinely to treat eczema in most patients. In addition, topical application of vitamin D has not been shown to significantly affect the symptomology of sufferers of atopic dermatitis. Recent research focus has been on oral supplementation of vitamin D, especially in higher latitude regions where vitamin D deficiency is widespread. Pilot studies are revealing a possible correlation to decreased serum vitamin D levels and increased severity of eczema, using SCORing Atopic Dermatitis (SCORAD) and Three-Item Severity (TIS) scales.

Patients often are interested in an adjunct or more natural method of treating a disorder and vitamin supplementation has been used for centuries in this manner.
Vitamin D is relatively affordable and well-tolerated with little to no risk in most patients and may be able to increase the quality of life of those who are affected by atopic dermatitis. Can vitamin D supplementation improve eczema severity?

METHODS

An exhaustive search of relevant medical articles was conducted utilizing the following search engines: MEDLINE-OVID, Web of Science, and CINAHL through the Pacific University Library Databases using keywords “vitamin D,” and “atopic dermatitis.” The search produced 108 articles that was narrowed by the following exclusion criteria: studies in the English language, random control trials with placebo groups and number of participants over 30, and studies conducted within the past three years. The abstracts and titles were used to narrow down the relevant studies for inclusion in the review to three articles. Relevant articles were assessed for relevance and quality using the Grading of Recommendations, Assessment and Development of Evaluation (GRADE). A search of the National Institutes of Health (NIH) revealed that there are no current studies or related trials examining the effects of vitamin D supplementation on atopic dermatitis symptomology.

RESULTS

The initial database search yielded 108 articles that were relevant using the keywords “atopic dermatitis,” and “vitamin D.” Once applying the inclusion criteria described above, two articles remained to include in the systematic review. Two RCTs were examined to review if vitamin D supplementation improves atopic dermatitis. See
Table I. One study\(^7\) was excluded because the authors did not fully separate the results of atopic dermatitis from other groups in regards to vitamin D supplementation.

**Amestejani et al**

This randomized, double blind study\(^1\) examined vitamin D supplementation in the treatment of atopic dermatitis in Iran in 2012 and was lead by Morteza Amestejani, MD. The purpose of the clinical trial was to evaluate the effects of vitamin D supplementation on symptomology in patients with atopic dermatitis. Sixty subjects began the study, with 30 in the vitamin D group and 30 in the placebo group which was randomized by a third party who was not involved with the trial. Group allocation was processed by a computer-generated program, which randomly assigned group numbers. These groups were randomized and group allocation was concealed. The trial was 60 days in length and the treatment group received 1600 IU of cholecalciferol (vitamin D3) daily. The severity of atopic dermatitis was measured using SCORAD and TIS values by the same trained physician before and after the trial.\(^1\)

The inclusion criteria included being over age 14 years with no systemic diseases, concomitant systemic pyretic or inflammatory processes, other than diabetes mellitus and chronic hepatitis.\(^1\) The exclusion criteria were pregnancy; systemic inflammatory disease; taking vitamins, minerals or supplements, oral contraceptive pills, steroid hormones, anti-epileptic agents, and anticoagulant drugs; and nursing mothers. The researchers did allow continuation of prescribed medications, both orally and topically that patients were already using specifically for atopic dermatitis treatment.\(^1\)

The SCORAD grading of severity of eczema is divided into three grades of severity: mild (<15 points), moderate (15-40 points), and severe atopic dermatitis (>40...
points). The TIS value of severity is assessed by the following for the three divisions: mild (0-2 points), moderate (3-5 points), and severe form (6-9 points). Statistics were completed using SPSS software and a p-value of <0.05 was considered statistically significant.1

At the end of the 60-day trial, 29 patients remained in the treatment group and 24 in the placebo group. The seven participants were excluded from statistical analyses at the end of the study. The age, height, weight, SCORAD index, and TIS value of the two groups did not differ significantly at the beginning of the study with a p<0.05.1

Amestejani, et al1 found that at the conclusion of the study, all three groups of patients with calculated mild, moderate, and severe SCORAD and TIS atopic dermatitis symptoms were improved after 60 days of supplementation at a p<0.05 level. See Table II. The placebo group did not show any significant changes in their SCORAD and TIS symptoms of atopic dermatitis at a p>0.05 level. These results confirmed their hypothesis that vitamin D supplementation did improve atopic dermatitis symptoms. The authors suggest that vitamin D has both enhancing and protective mechanisms of the skin and these qualities could possibly benefit patients who suffer from atopic dermatitis.1

The authors identified and reported a few limitations. A limitation of the study was that there was only one dose of vitamin D supplementation given during the trial. This did not help identify a therapeutic dose to recommend in order to meet a therapeutic threshold. It would also be helpful to have a study that was longer in duration to understand whether the protective mechanisms that vitamin D supplies to the skin are continual or need to be constantly supplemented in order to be achieved.1

Javanbakht et al
Javanbakht et al\textsuperscript{8} conducted a randomized controlled trial using vitamins E and D supplementation in atopic dermatitis that was published in the *Journal of Dermatological Treatment* in 2011. Forty-five subjects were divided into four groups which consisted of group P (placebo), 1600 IU of vitamin D supplementation for group D, 600 IU of vitamin E was for group E, and group DE was 1600 IU of vitamin D and 600 IU of vitamin E combined for 60 days. The pills were identical in size and shape and the patients were randomized into groups for which they remained in for the duration of the study.\textsuperscript{8}

The trial measured clinical improvement of atopic dermatitis using SCORAD and also measured serum levels of vitamin D and E before and after the study. The four groups were randomized to each group and allocation was concealed. The authors included patients with atopic dermatitis who had an initial score of 10-70 on the SCORAD scale between the ages of 13-45 years old. Exclusion criteria included patients taking vitamins, mineral and fatty acid supplements, oral contraceptive pills, steroid hormones, and anti-epileptic agents, pregnant or nursing mothers, and those who were on anticoagulant medications. The patients were encouraged to maintain their prescribed treatments for their atopic dermatitis, which may have included emollients, topical corticosteroids, and oral antihistamines.\textsuperscript{8}

The authors used one-way analysis of variance (ANOVA), ANCOVA, Kruskal-Wallis test and chi-squared tests to compute differences between groups and to look for significance. They used a p-value of <0.05 for significance and they utilized SPSS software. Forty-five out of the fifty-two participants completed the study and those that were lost were not included in the final calculations. The groups were not significantly
different at the beginning of the study including age, sex, SCORAD index, and topical corticosteroidal usage at baseline at p<0.05 level.8

In the intent-to-treat analysis, the results show an overall improvement in SCORAD in all four groups: 24%, 32%, 30%, and 54.4% for groups P, D, E, and DE, respectively, with a p-value of 0.032 at the completion of the trial. These reductions were significant, but include changes in the placebo group in addition to the treatment groups. In the per-protocol analysis, groups D, E and DE showed a significant reduction in SCORAD values of 34.8%, 35.7%, and 64.3% with a p-value of 0.004. Despite these improvements, the difference between groups P and D was not significant. The need for use of topical corticosteroids was decreased in all four groups, but least in the placebo group. Limitations discussed by the authors include a small sample size and only one dose of treatment (1600 IU vitamin D).8

DISCUSSION

Vitamin D seems to play an important role in the innate immunity process but little is actually known about its effects on skin and skin conditions.3 There are few background studies that examine the link between inflammation and vitamin D supplementation. The exact link is still controversial and sometimes even refuted altogether. The two studies1,8 that are reviewed show that a possible link exists, albeit small according to the compiled data.

Amestejani et al1 found that 1600 IU of cholecalciferol supplementation over 60 days did significantly improve the symptoms of AD in patients with mild, moderate, and severe atopic dermatitis. Similarly, Javanbakht et al8 found a reduction in symptoms in patients with AD after supplementation with vitamin D, however the differences between
the placebo and group with vitamin D were not significant. However, whether or not 1600 IU of cholecalciferol is the most effective dose in treating atopic dermatitis was not established with these studies. Moreover, the Javanbakht et al study demonstrated a lower need for topical corticosteroids with vitamin D supplementation and a possible synergistic benefit with the addition of vitamin E.

Vitamin D supplementation is a relatively safe, inexpensive option with potential to decrease symptomology in those patients who suffer from atopic dermatitis. The risk of vitamin toxicity is rarely seen. Occasionally a medical provider will find it in a patient who exhibits symptoms of hypercalcemia and is usually associated with medications that promote imbalances in calcium, not from overly aggressive vitamin D supplementation. Experts believe that the dose required to bring upon vitamin D toxicity is about 10,000 IU per day, which is far from even the upper end of aggressive vitamin D supplementation practices. Considering the known negative effects on immunity and specifically the possible relief in symptomology of eczema, medical providers should consider vitamin D supplementation in patients suffering from atopic dermatitis until further research is completed.

Both studies suffered from a somewhat small sample size with the Javanbakht et al study having 45 participants who were divided into four groups which made this study’s precision suspect. Another limitation was that only one dose of vitamin D was utilized which limits the ability to identify the most effective dose or whether or not more improvement is seen in higher but safe doses of vitamin D. Lastly, the results that were reported lacked a between group comparison to the extent where a magnitude of effect
could be ascertained (eg, relative risk and number-needed-to-treat). This results in an overall moderate quality of evidence (see Table I).

Implication for further research is supported by the studies’ results that show improved SCORAD and TIS scores, however not all were significant. Support for vitamin D supplementation would be bolstered with longer and more robust randomized controlled trials that include other vitamin D doses and reported the number of participants who improved on the therapy. More research is needed to confirm if vitamin D supplementation does in fact improve symptoms of atopic dermatitis and whether the addition of other vitamins (eg, vitamin E) would also benefit these patients.

CONCLUSION

Medical providers can now use the data regarding vitamin D’s role in immunity and systemic disease prevention to more aggressively treat vitamin D deficiency in their patients. The clinical practice implication of the review shows that vitamin D could play an additive role in the protection of the skin barrier that is affected by immunity and atopic dermatitis. Eczema is one of the most common skin disorders in children and adults alike and the traditional treatments often do not bring relief. Vitamin D supplementation is a relatively safe, inexpensive option with potential to decrease symptomology in those patients who suffer from atopic dermatitis. The studies that were reviewed for this paper show some promise that vitamin D can help decrease the symptoms of atopic dermatitis when used in dermatology clinics worldwide.¹,⁸ More research must be completed to examine the therapeutic dose that brings the greatest benefit for patients, and what other factors could be added to vitamin supplementation in order to maximize treatment of eczema.
References


### Table I. Characteristics of Reviewed Studies

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<tr>
<th>Quality Assessment</th>
<th>Downgrade Criteria</th>
<th>Quality</th>
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<tr>
<td>Study</td>
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<td>Limitations</td>
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<tr>
<td>Vitamin D Supplementation</td>
<td>RCT</td>
<td>Not serious</td>
</tr>
<tr>
<td>Amestejani et al1</td>
<td>RCT</td>
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</tr>
<tr>
<td>Javanbakht et al8</td>
<td>RCT</td>
<td>Not serious</td>
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* Small sample size

### Table II. SCORAD and TIS Values1

<table>
<thead>
<tr>
<th></th>
<th>Drug G Mean Score</th>
<th>Placebo G Mean Score</th>
<th>TIS Value Drug G Total Score</th>
<th>Placebo G Total Score</th>
<th>p-value</th>
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<td>After 15.3+/-3.1</td>
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<td>Before 3.5+/-0.5</td>
<td>After 1.9+/-0.4</td>
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<td><strong>TIS Value</strong></td>
<td>Before 3.8+/-0.4</td>
<td>After 4.02+/-0.5</td>
<td>p-value 0.22</td>
<td>Before 3.5+/-0.5</td>
<td>After 1.9+/-0.4</td>
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