

## Original Papers

# Evaluation of Topical Vitamin B<sub>12</sub> for the Treatment of Childhood Eczema

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### Abstract

**Objectives:** Topical vitamin B<sub>12</sub> is an approach that has been shown to successfully treat atopic dermatitis in adults; however, there have been no studies in children. Topical vitamin B<sub>12</sub> is thought to decrease the symptoms involved in eczema through reducing nitric oxide production. Atopic dermatitis affects 5%–20% of children in the United States. Various treatment options are available to treat atopic dermatitis in children, but there are drawbacks to some of these options. Children tend to need a larger dose of medication for body surface area involved and can be more adversely affected by agents such as topical steroids. This study was developed in order to find an alternative eczema treatment for children.

**Design:** This double-blinded, randomized, placebo-controlled study with intraindividual left/right comparison was set up to determine whether topical vitamin B<sub>12</sub> would be effective in children with eczema.

**Subjects:** Patients from the ages of 6 months to 18 years old were recruited from the Center for Family Medicine and enrolled for 4 weeks.

**Outcome measures:** Skin checks using a standardized scoring system were done at baseline, and 2 and 4 weeks by a single investigator. Twenty-one (21) patients completed the study.

**Results:** Skin treated with topical vitamin B<sub>12</sub> improved significantly more than placebo treated skin at 2 and 4 weeks ( $p=0.02$ ,  $0.01$  respectively).

**Conclusions:** Topical vitamin B<sub>12</sub> should be considered as a treatment option in children with eczema.

### Introduction

ATOPIC DERMATITIS IS A PREVALENT disease process in children, affecting 5%–20% of children.<sup>1</sup> Various treatment options are available to treat atopic dermatitis to include topical emollients, topical steroids, and topical calcineurin inhibitors. There are drawbacks to the use of some of these agents. For example, with the use of steroids, side-effects such as skin atrophy, striae, telangectasias, adrenocortical suppression, and pigmentation changes can limit the duration of their use.<sup>2</sup> The U.S. Food and Drug Administration placed a black box warning on the calcineurin inhibitors (pimecrolimus topical and tacrolimus topical) in January 2006,<sup>3</sup> which put physicians in a difficult position when trying to determine appropriate and optimal treatment of eczema in children,<sup>4</sup> especially in those less than 2 years of age. Given the fact that children have a larger body surface area versus size ratio, they are exposed to potentially higher doses of topical medications

when compared to adults. Therefore, it would be optimal to use as little steroids or calcineurin inhibitors as possible in this population in order to minimize any side-effects or adverse reactions. Topical vitamin B<sub>12</sub> may be one method to reduce the need for steroids in children with atopic dermatitis.

Topical vitamin B<sub>12</sub> is an approach that has proven to be useful to treat atopic dermatitis in adults. A study published in 2004 showed efficacy when compared to placebo with excellent tolerance and low safety risks to patients.<sup>5</sup> This study was done in adults with ages ranging from 18 to 70 years old. Statistically significant efficacy of the topical vitamin B<sub>12</sub> was seen against placebo after 4 weeks of treatment, and there was a trend at 2 weeks in the study.

The itching of atopic dermatitis has been shown to be related to increased cytokines and nitric oxide. The increased nitric oxide can be seen in the serum as well as the skin. As a nitric oxide scavenger, vitamin B<sub>12</sub> applied topically is presumed to reduce this formation and thereby reduce the

TABLE 1. BASELINE DEMOGRAPHICS

	Age	Baseline SCORAD
B <sub>12</sub>	1,326 days (range 157–5162)	13.19 (range 5–24)
Placebo	12.57 (range 5–24)	

SCORAD, scoring of atopic dermatitis.

symptoms associated with atopic dermatitis. As vitamin B<sub>12</sub> has poor systemic bioavailability, topical vitamin B<sub>12</sub> was used to increase efficacy.

Materials and Methods

The study was designed as a prospective, placebo-controlled, double-blinded study using intraindividual left/right comparison. The study was reviewed and approved by the Spartanburg Regional Health System’s Institutional Review Board. Using the Stata program (8th edition, College Station, TX), a total of 44 patients were anticipated to be enrolled in order to detect a difference in the modified SCORAD scale of three points given a power of 0.9 and an  $\alpha$ -value of 0.05.

Participants were recruited from the Center for Family Medicine over a period of 8 months. Children between the ages of 6 months and 18 years old were recruited through a poster advertisement in the Center for Family Medicine waiting room and direct physician referral to the primary investigator. Recruitment was open from March 2007 through December 2007. Once informed consent was obtained from the parent (assent was also obtained if the child was over age 8), the child was enrolled following verification of inclusion and exclusion criteria. Inclusion criteria included children age 6 months to 18 years with eczema and ability to understand the consent process. Exclusion criteria included: unwillingness of parent to consent to study protocol; pregnancy or lactation; eczema with superinfection present; known history of allergy to vitamin B<sub>12</sub> or components of the base cream; topical treatment with corticosteroids in the 4 weeks prior to enrollment; or inability to speak and read English.

The patient’s eczema was rated by using a modified SCORAD (Scoring of atopic dermatitis) scale. The SCORAD scale has been validated in previous pediatric eczema studies and is considered to be the “gold standard” for evaluation of disease severity in atopic dermatitis.<sup>6</sup> The modified SCORAD scale contains six objective items (erythema, edema, excoriation, oozing, lichenification, dryness) and three sub-

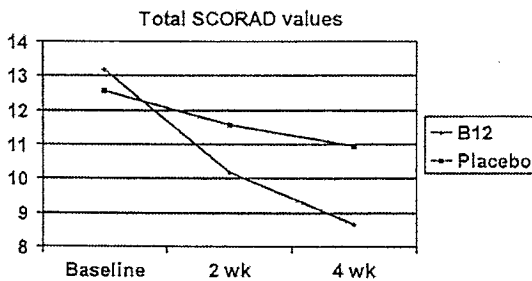


FIG. 1. Total SCORAD values.

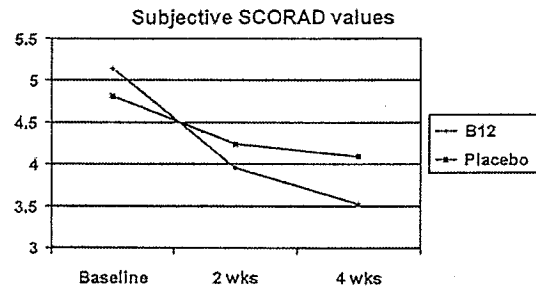


FIG. 2. Subjective SCORAD values.

jective items (pruritis, sleep loss, and overall parental rating), each on a scale from 0 to 3, thereby giving a range from 0 to 27 total. There was only one investigator who did the scoring to reduce any inter-rater variability. Baseline scores were recorded, and the scoring was repeated at 2- and 4-week follow-up visits.

The parent was given instructions to pick up two blinded containers of cream. The containers were labeled “L” and “R” and a random number generator created had the compounding pharmacy place either the active vitamin B<sub>12</sub> cream or a placebo vehicle in each separate container. Both the parents and the primary investigator were blinded as to the contents of each container. The parents were instructed to use the “L”-labeled medication on the child’s left side twice a day for the study duration and the “R”-labeled medication on the child’s right side. At the initial visit, the parents were instructed on the amount of material to be used, which followed normal dermatologic application processes (fingertip units). The parents would bring the containers to each visit so that compliance could be checked.

The vitamin B<sub>12</sub> and placebo creams were formulated according to the similar method as outlined in the adult study. Sher-Tech Pharmacy (Spartanburg, SC) created both creams. The vitamin B<sub>12</sub> cream contained 0.07% by weight concentration of cyanocobalamin in a moisturizer base. The placebo cream contained the same moisturizing base with a dermatologically neutral coloring agent mixed in so the creams would appear similar.

Results

A total of 26 patients were consented to join the study. Twenty-two (22) total patients were randomized and picked

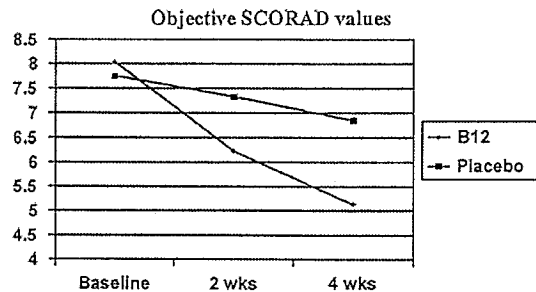


FIG. 3. Objective SCORAD values.

up the study medications and 21 patients completed the entire 4-week study period, with 1 patient withdrawing early for apparent side-effects to both the placebo and study creams. This was the only adverse event noted during the study. Initial demographics as seen in Table 1 showed a mean age of 1326 days old (3.6 years old  $\pm$  3.3 years) with a range from 178 days old (6 months old) to 5162 days (14.1 years old). Baseline SCORAD was similar in the two groups (13.19 in the active agent group versus 12.57 in the placebo group). Changes in SCORAD values were compared using Student's *t*-test assuming unequal variances. As shown in Figure 1, there was a drop in the total SCORAD values in both the active treatment and placebo groups. The decrease noted in the B<sub>12</sub> group was statistically significant at the 2- and 4-week measurements when compared to the placebo measurements. Total decrease in SCORAD at 2 weeks was three points in the intervention group and one point in the placebo ( $p=0.011$ ). At 4 weeks, the SCORAD value was decreased by 4.52 and 1.61 points, respectively, for the B<sub>12</sub> and placebo measurements ( $p=0.011$ ). The findings for the change in subjective SCORAD data were significant ( $p=0.032$ ) at the 4-week measurement periods as noted in Figure 2. The subjective change value approaches significance at 2 weeks ( $p=0.058$ ). Objective SCORAD data are presented in Figure 3 and show that the change is statistically significant ( $p=0.01$  at 2 weeks of use,  $p=0.014$  at 4 weeks of use).

#### Discussion

Given the results of the results of the study, it appears that topical vitamin B<sub>12</sub> provides an efficacious and safe treatment option for children with eczema. This treatment option appears to work quickly, within 2 weeks of starting treatment.

As noted in the study in adults, topical vitamin B<sub>12</sub> has minimal to no side-effects. The only dropout noted in this study had a localized skin reaction to the creams applied on both sides of the body, including the placebo side. There were no other specific systemic or topical reactions noted in the other patients. Oral vitamin B<sub>12</sub> has a potential side-effect of causing acneiform rashes,<sup>7</sup> but this was not noted in any of the study participants.

Some limitations of the study include a smaller number of participants than originally planned. Enrollment was limited by having only one primary investigator doing all of the examinations and SCORAD scales, rather than actual patient interest in the study. There were additional participants who were not enrolled because of this factor. Another limitation to be noted was the presumptive significant change in the SCORAD that was used. The study used a change in the SCORAD of three in order to calculate the original power statistics. The primary investigator felt that this was a significant value; however, one may have to clinically use the scale in order to judge whether this truly is the case.

The active medication used in the study was a compounded medication. This factor could limit the overall availability and use of the topical vitamin B<sub>12</sub>. It could also make this treatment option outside the reach of some patients because of the cost.

One additional limitation would be that the parents could have used what appeared to be the most efficacious cream on both sides of the body, which could have skewed the final results given the intraindividual comparisons being made.

#### Conclusions

Topical vitamin B<sub>12</sub> can be considered as a treatment option for children with eczema. At this time, there is no proprietary cream available in the United States; however, working with a knowledgeable compounding pharmacy will allow for an additional, safe treatment for pediatric atopic dermatitis.

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#### Disclosure Statement

The author reports that no competing financial interests exist.

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