

Corticosteroid application prior to nickel exposure prevents contact dermatitis in sensitized individuals

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Contact dermatitis in response to nickel is common in North America and Europe, with a prevalence of approximately 11%.¹ Allergen avoidance is the primary management strategy, with topical corticosteroids used as standard pharmacotherapy during disease flares.^{2,3} Anecdotally, clinicians may prescribe preemptive treatment with topical corticosteroids if the allergen cannot be avoided. However,

whether this strategy is effective in preventing contact hypersensitivity dermatitis has never been formally studied in previously sensitized individuals.

It has been suggested that nickel hypersensitivity may be abrogated by regulatory T cells (Tregs) systemically generated from oral nickel exposure.⁴ The function and number of Tregs in the mouse increases in

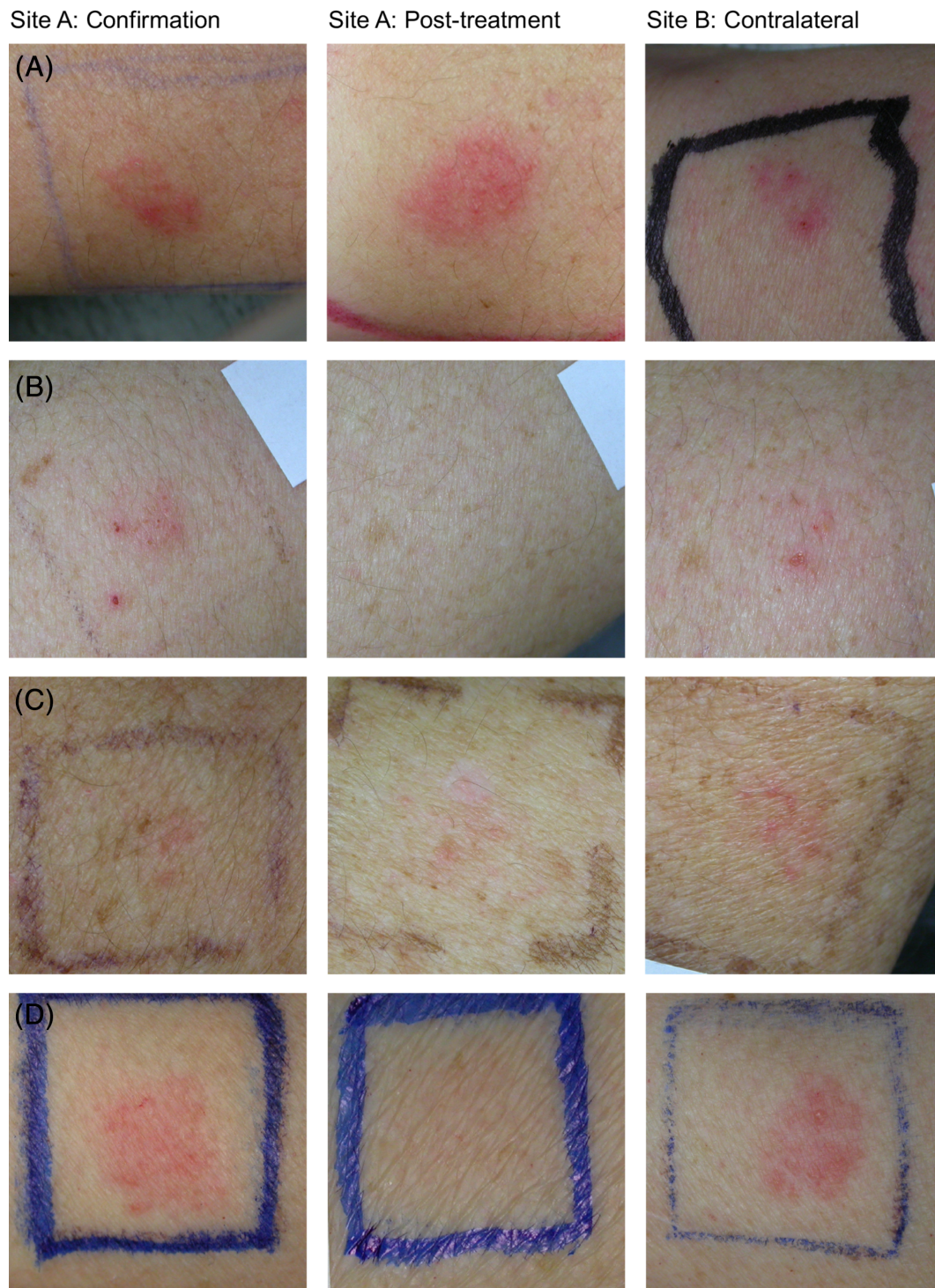


FIGURE 1 Representative images of patch tests on participant forearms treated with (A) vehicle, (B) betamethasone dipropionate, (C) calcipotriol, and (D) combined betamethasone dipropionate/calcipotriol ointment, taken 96 hours after nickel challenge

calcipotriol-treated skin,⁵ suggesting that calcipotriol may be efficacious in boosting local immunosuppression. The goal of our study was to determine whether preventative treatment with topical corticosteroids and/or calcipotriol can reduce nickel contact dermatitis at the site of treatment, and whether either can induce systemic protection upon challenging skin at a site distinct from the application area.

METHODS

We conducted a randomized, double-blinded, placebo-controlled study (ClinicalTrials.gov under NCT01413477) of 15 individuals with proven nickel contact dermatitis approved by the University of British Columbia (UBC)/Vancouver General Hospital (VGH) ethics committee.

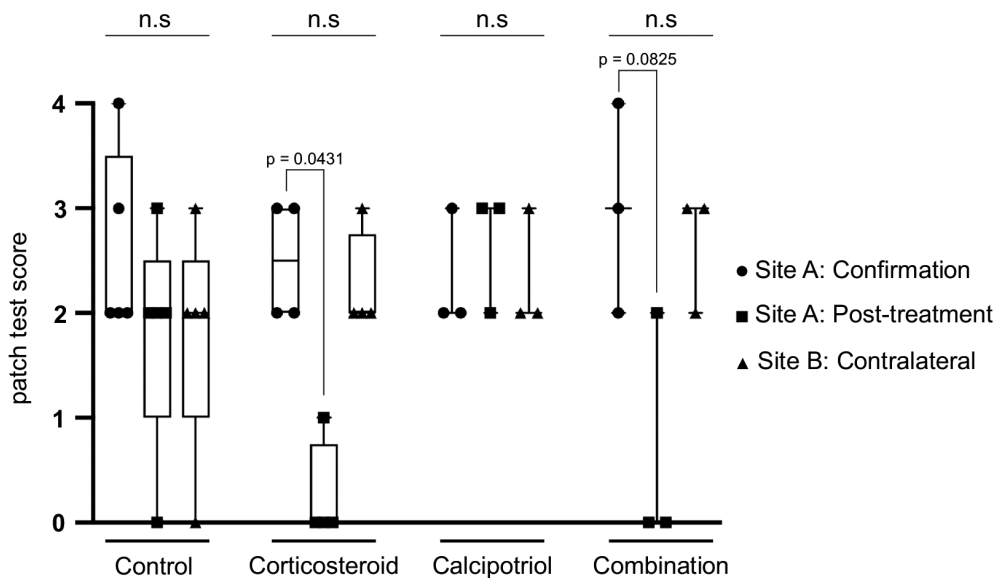


FIGURE 2 Pretreatment with calcipotriol alone is nonsuperior to corticosteroid or combination corticosteroid-calcipotriol ointments in preventing nickel contact sensitivity. Patch test scores were recorded at site A for confirmation, site A after drug treatment, and site B after drug treatment on the contralateral forearm. Data are represented as median $\pm$ range

Detailed methodology can be found in the online supplement in the Appendix S1.

RESULTS

All participants had clinically confirmed nickel hypersensitivity at site A. Topical treatment with vehicle at site A (Figure 1A) did not prevent dermatitis when administered prior to challenge, nor on untreated site B upon challenge. Conversely, treatment with the corticosteroid, betamethasone dipropionate (Figure 1B), but not calcipotriol alone (Figure 1C), resulted in a visible reduction in skin inflammation in some patients on the treatment site A. Combination betamethasone dipropionate/calcipotriol ointment similarly reduced skin inflammation at the site of treatment (Figure 1D). However, patch test reactivity was unchanged at untreated site B, suggesting a lack of systemic tolerance.

Corticosteroid pretreatment alone significantly reduced patch test grades on site A ($P = .043$) compared to vehicle or calcipotriol alone (Figure 2). Combination pretreatment reduced patch test grades on drug-applied sites, but the effect did not reach significance ($P = .083$), suggesting that calcipotriol does not improve corticosteroid-mediated protection. None of the treatment arms resulted in reduced patch test grades compared to baseline upon challenging site B, suggesting a lack of systemic protection.

DISCUSSION

We demonstrate that topical corticosteroids, alone or with calcipotriol, are superior to vehicle or calcipotriol alone in preventing recall of local contact hypersensitivity. Although topical corticosteroids are typically employed to treat ongoing cutaneous inflammation,⁶ our findings provide evidence that topical corticosteroids may be used preemptively to avoid an inflammatory reaction. When anticipating exposure to a contact allergen such as nickel or

hair dye, topical pretreatment with corticosteroids may aid with preventing contact hypersensitivity. In addition, our findings suggest the importance of avoiding corticosteroid treatment at sites where diagnostic patch testing will be conducted to avoid false-negative results. Future studies with an expanded sample size are warranted to validate the capacity of corticosteroids in preventing the elicitation of contact dermatitis in response to nickel and other contact allergens.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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1 ONLINE SUPPLEMENT:

2
3 **Methodology**

4 We conducted a randomized, double-blinded, placebo-controlled study
5 (ClinicalTrials.gov under NCT01413477) approved by the UBC/VGH ethic committee.
6 Participants (13 female, 2 male) were recruited from the UBC Contact Dermatitis Clinic
7 and provided informed consent. Inclusion criteria included: age >18 years and
8 confirmed nickel allergy diagnosis determined by patch testing. Exclusion criteria
9 included: treatment with immunomodulating medications concurrently or in the previous
10 one month, active skin disease (particularly at the study sites), hypersensitivity to
11 calcipotriol, corticosteroids, or vehicle; previous anaphylaxis to nickel, and pregnancy or
12 breast-feeding. Confirmation patch testing was conducted on the forearm (**site A**) using
13 IQ Ultra chambers with nickel sulfate 2.5% pet. (Chemotechnique Diagnostics, Malmö,
14 Sweden) worn for 48 hours. The degree of edema (1+/2+/3+) was documented at 96
15 hours and skin erythema photographed. The treatment arms included were: placebo
16 vehicle (N=5), calcipotriol (N=3), betamethasone dipropionate (N=4), or betamethasone
17 dipropionate/calcipotriol (N=3). Participants self-applied a ¼ fingertip of unlabeled
18 ointment within a 5x5 cm window on site A twice daily for 7 days. Site A was patch
19 tested and evaluated as at confirmation. Two weeks following site A testing, untreated
20 skin on the contralateral forearm (**site B**) was patch tested and subsequent
21 inflammation was assessed. Friedman exact test with Dunn's multiple comparisons post
22 hoc analysis was done using GraphPad Prism version 8.00 for MacOS, GraphPad
23 Software, California.