**Are Topical Non-Steroidals as Effective as Topical Corticosteroids in the Treatment of Atopic Dermatitis?**

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**Summary Statement:**

Topical corticosteroids are the standard of care in treating atopic dermatitis (AD) along with daily supportive care and application of moisturizers for generalized xerosis. There is limited data on the usage of corticosteroids such as concentration, duration, frequency, and application (5). However, the current established treatment of AD is using a topical corticosteroid for a short period until lesions are cleared, usually not exceeding two weeks of therapy (2). The cutaneous side effects of corticosteroids include atrophy of the skin, telangiectasias, skin pigment changes and striae. The non- cutaneous side effects of topical corticosteroids are reduction in linear growth in children, decreased bone density in adults and potential suppression of the hypothalamic pituitary axis. In children, topical corticosteroids are used with caution secondary to these side effects and potential long- term effects.

The alternative topical non- steroidal treatments of AD include topical calcineurin inhibitors and new skin barrier repair creams. The topical calcineuriin inhibitors, Tacrolimus and Pimecrolimus, are immunosuppressants that have anti-inflammatory properties. These calcineurin inhibitors are well studied in comparison to topical corticosteroids since their development. The newer skin barrier creams include Atopiclair (contains hyaluronic acid, telmesteine, Vitis vinifera, and glycyrrhetinic acid), EpiCeram (contains ceramides, free fatty acids and cholesterol), and MiMyx (contains N-palmytoylethanolamine). Currently, there is not much data of these new skin barrier creams as compared to the topical steroids.

Relevant studies for these alternative therapies were identified from PubMed using Mesh terms “atopic dermatitis” and “topical steroids” and “topical non- steroidal drugs.” Search was further refined using Mesh terms “steroids” and “atopic dermatitis” and “Atopiclair” or “epiceram” or “triple a lipid barrier” “zarzenda” or “anti-inflammatory agents, non-steroidal” or “calcineurin inhibitors” or “N- palmytoylethanolamide” or “lamellar matrix.” The validity of studies was assessed according to randomization, blinding, complete follow-up of subjects and intention to treat.

**Clinical Bottom Line:**

 Topical corticosteroids continue to remain the mainstay treatment for AD. There is some evidence that a provider may consider topical non-steroidal alternatives, such as the topical calcineurin inhibitors, for patients with increased frequency of flares or who are refractory to corticosteroid therapy. However, the cost of these topical non-steroidals may outweigh the benefits and the side effect profile as well as the long- term effects of these newer drugs remain unknown. There is potential consideration for using the new skin barrier creams as a maintenance therapy for AD, but the current cost may deter the patient population.

Further studies for the effectiveness of Atopiclair and MiMyx as compared to topical corticosteroids in treating AD has not yet been assessed. Expansion of research is needed to look at topical non-steroidals as a maintenance therapy in conjunction with topical corticosteroids for acute flares. Also, there currently is no research for the post- treatment rebound effects of theses topical non-steroidals. As mentioned above, the safety profile and long-term effects of topical non- steroidals is also a topic of further research.

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|  | Citation #1 | Citation #2 |
| Reference | Sugarman JL and Parish LC. Efficacy of lipid based barrier repair formulation in moderate to severe pediatric atopic dermatitis. *Journal of drugs and Dermatology*, 2009; 8(12): 1106-1111. | Udompataikul M and Srisatwaja W. Comparative trial of moisturizer containing licochalcone A vs. hydrocortisone lotion in the treatment of childhood atopic dermatitis: a pilot study. *Journal of the European Academy of Dermatology and Venereology*, 2011; 25: 660-665. |
| Study Question | Is a lipid based barrier repair formulation/EpiCeram effective in treating moderate to severe pediatric atopic dermatitis? | Is a moisturizer containing licochalcone A as effective as hydrocortisone lotion in the treatment of atopic dermatitis in children? |
| Study Design | Randomized, investigator blinded comparative study | Randomized, blinded, case- control study |
| Validity | Yes | +/- |
| Results | Δ= 0.069, slight risk reduction | Δ= -0.077Hydrocortisone (HC) was superior to licochalcone A (LA) lotion |
| Limitations | Some subjects used Fluticasone prior to the study, but not identified which group they were from | Small study  |
| Application | Yes | Difficult to apply secondary to small sample size and unavailability of LA in the US. |
| Clinical Bottom Line | With longer treatment of EpiCeram there may some alleviation of AD symptoms as compared to topical corticosteroids, but not very impressive. May think about use in a child who needs repeated courses of higher potency steroids, but safety profile needs to be reviewed. | HC lotion has faster resolution of erythema, excoriation and pruritis, but side effects include striae, atrophy of the skin and telangiectasias. LA lotion has no real harm in its use, unable to conclude if it is as effective as HC lotion. |

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|  | Citation #4 | Citation #5 | Citation #6 |
| Reference | El-Bataway MM, Bosseila MA, Mashaly HM and Hafex VS. Topical calcineurin inhibitors in atopic dermatitis: a systematic review and meta-analysis. *Journal of Dermatological Science*, 2009; 54: 76-87. | Doss N, Kamoun MR, Bubertret, Cambazard F, Remitz A, Lahfa M and de Prost Y. Efficacy to tacrolimus 0.03% ointment as second line treatment for children with moderate-severe atopic dermatitis; evidence from randomized, double-blind non inferiority trial vs. fluticasone 0.005% ointment. *Pediatric Allergy and Immunology,* 2009; 21: 321-329. | Beiber T, Vick K, Folster-Holst R, Belloni-Fortina A, Stadler G, Worm M and Arcangeli F. Efficacy and safety of methylprednisolone aceponate ointment 0.1% compared to tacrolimus 0.03% in children and adolescents with an acute flare of severe atopic dermatitis. *Allergy*, 2007; 62: 184-189. |
| Study Question | Are topical calcineurin inhibitors effective in treating atopic dermatitis?  | Is tacrolimus an effective second line treatment for mod-severe AD as compared to fluticasone? | Is a topical steroid as effective as a topical calcineurin inhibitor in treating an acute flare of severe atopic dermatitis? |
| Study Design | Systematic review | Randomized, double blinded comparative study | Randomized, double blinded comparative study |
| Validity | +/- | Yes | Yes |
| Results | Pimecrolimus less effective than topical corticosteroids | Δ = 1.62% | Δ = 9% (Success rate by Day 14)Δ = 0.3% (Patients clear by end of tx) |
| Limitations | Not all studies were comparative studies to the gold standard (topical steroids); Non-English studies excluded | Industry sponsored trial | Unclear what endpoints were measured exactly (success of tx vs. cleared by end of tx) |
| Application | Yes, but the review includes older studies that may make applicability more difficult | Yes | Yes |
| Clinical Bottom Line | Pimecrolimus in children with mild AD > 2 years may have value in long-term maintenance & steroid sparing effect in AD. Parents may prefer corticosteroids for faster relief of symptoms in the setting of an acute flare. | May use Tacrolimus in children with mod-severe AD >2yr depending on the patient’s clinical presentation and previous response to steroids; but still need to consider safety profile. | Topical corticosteroids remain gold standard as compared to Tacrolimus and leads to rapid relief of symptoms in patients with severe AD & very severe AD. |

**References:**

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3. Doss N, Kamoun MR, Bubertret, Cambazard F, Remitz A, Lahfa M and de Prost Y. Efficacy to tacrolimus 0.03% ointment as second line treatment for children with moderate-severe atopic dermatitis; evidence from randomized, double-blind non inferiority trial vs. fluticasone 0.005% ointment. *Pediatric Allergy and Immunology,* 2009; 21: 321-329
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