ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 16, Issue 7, 2023

Online - 2455-3891
Print - 0974-2441

Research Article

A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, AND CONTROLLED STUDY OF TREATMENT WITH HYDROCORTISONE-ETHANOL GEL OINTMENT IN CHILDREN'S WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS

ARTI BHABHOR[1], RUTU HARSH OZA[2], PRATIK MAKWANA[3], KRUNAL TRALSAWALA[1]*

[1]Department of Dermatology, Parul Institute of Medical Sciences and Research, Parul University, Vadodara, Gujarat, India. [2]Consultant Dermatologist, Ahmedabad, Gujarat, India. [3]Department of Dermatology, Dr. N. D. Desai Faculty of Medical Sciences and Research, Dharmsinh Desai University, Nadiad, Gujarat, India. Email: dermatology11111@gmail.com

Received: 06 February 2023, Revised and Accepted: 20 March 2023

ABSTRACT

Objectives: The objective is to see the effectiveness of hydrocortisone (*HC*)-ethanol gel (EG) ointment in treating children with Moderate-to-severe atopic dermatitis (*AD*).

Methods: Thirty children with moderate-to-severe AD participated in a 2-week double-blind, randomized, and controlled clinical trial. They were randomly assigned to apply either an ointment with 1% HC ointment or a novel ointment containing 1% HC and dispersed EG droplets HC. At the end of 2 *week*, SCORAD score was measured. SCORAD is a clinical tool used to assess the extent and severity of eczema (SCORing AD).

Results: A 2-week double-blind, randomized, and controlled clinical trial included 30 kids with moderate-to-severe AD. About 1% HC ointment or a new ointment comprising 1% HC and dispersed EG droplets were applied to them at random (HC-EG). The SCORAD score was calculated at the conclusion of 2 *week*s. A clinical tool called SCORAD is used to evaluate the severity and extent of eczema (SCORing AD).

Conclusion: We would want to draw the conclusion from our research that HC-EG ointment was superior to HC ointment in terms of reducing AD-related pruritus and visible rash.

Keywords: Atopic dermatitis, pruritus, hydrocortisone.

 DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i7.47497. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Atopic dermatitis (AD) is a severe, long-lasting Itchy inflammation condition of the skin that causes eczematous and devouring gashes on various parts of the body. Around 20% of both children and adults around the world are affected at some point in their lives [1]. In addition to skin barrier breakage, the pathophysiology of Atopic dermatitis combines ecological, genetic, and immunological considerations. Regular application of creams to aid in the recovery of the epidermal barrier is one way to prevent the disease [2].

One of the most common therapies for AD is topical corticosteroids. When treating children with this family of drugs, only low-potency corticosteroids should be utilised. The only exception to this rule is when low-potency corticosteroids are ineffective. Therefore, high-potency corticosteroids are utilised to prevent severe situations [3]. Users and providers of this class of medication need to be aware of how to manage them to reduce side effects (such as skin stretch marks or skin receding), which could lead to low patient compliance due to corticophobia [4,5]. To increase the effectiveness of corticotherapy, the doctor's advice and dose adjustments are essential.

The most significant adverse effect of the Drug on these patients' existence is tingling [6]. To lessen the general tingling, allergy medications are typically utilized. In any event, these drugs are used to increase the negative effects rather than effectively treat dermatitis [7]. Logical data are inconsistent in some way; for example, when compared to counterfeit treatments, certain data do not show the prevalence of allergy medications. Others, however, display an antipruritic effect [8]. Original allergy medications have a negative effect on the capacity to calm down, which might be useful for those patients who have a recurring restless sleep disorder [9]. In dangerous instances of AD, as when traditional medicines such as corticosteroids and phototherapy have lost their viability, methotrexate, mycophenolate mofetil, and azathioprine substances, having a place with the class of fundamental immunosuppressant drugs, are the elective methodology [10]. Emollients should be utilized in lined up with restore the water-lipid film of the skin.

While there is evidence that the delivery of hydrocortisone (HC) across the skin is improved when ethanol is dissolved in a solution with it, we were unable to locate any reports of this happening when ethanol is dissolved in an ointment as gel microbubbles. We anticipated developing a different skin plan that would prevent tingling, prevent potential absorption of ethanol and HC across eczematous skin, and attempt not to increase skin dryness to incorporate alcohol-based hand sanitizer gel (ABSHG) in the effective treatment of AD. The ethanol is present in the innovative ointment as distributed ABHSG microbubbles.

METHODS

From June 2018 to July 2019, the dermatology and pediatric departments of the Parul Sevashram Hospital in Vadodara, Gujarat, jointly undertook this double-blind, randomized, and controlled trial.

The pediatricians in the area who had examined and approved the research protocol recruited 30 patients. At both the beginning and completion of therapy, all 30 patients were present. Ages varied from 3 months to 12 years. A therapy group is chosen at random for the patients. Pre- and post-therapy visits are required of patients. The primary investigator calculates a modified SCORAD score at each visit.

Inclusion requirements

1. At the first visit, there may be lesions that are crusted and leaking on the face, limbs, or trunk.
2. A history of poor response to one or more prescription drugs, including topical corticosteroids, topical calcineurin inhibitors, and topical and oral antibiotics, as well as previously used over-the-counter ointments. Age of 6 months or older.

Intervention

The test creams were already prepared for application. (A) HC topical solution made from a combination of Aquaphor® and corticosteroid 2.5% ointment. A ratio of Aquaphor®, corticosteroid 2.5% ointment, and 70% ethanol gel (EG) produces 1% HC and 17% by volume EG in the HC-EG ointment.

Treatment

Patients applied at home a saturating dose of the assigned ointment to the affected areas twice a day for 2 week. A "saturating dose" meant apply ointment until no more will absorb and then wipe off the excess with a paper towel. During the clinical trial, the only allowed topical treatment was the assigned ointment.

Outcomes

The average SCORAD improvement in participants receiving HC-EG ointment as opposed to HC ointment was the primary objective. Additional endpoints included: (1) For pruritus, HC-EG ointment outperformed HC ointment in terms of the average pruritus score decrease. (2) Increased corticosteroid absorption: No distinction between the two treatment groups was detected in terms of cutaneous blanching. (3) Localized negative effects: Stinging at the time of application. (4) Systemic negative effects: There was no difference in the two groups' levels of mental disorientation, slurred speech, and trouble walking, which are signs of alcohol intoxication. (5) Parental worries regarding the medication's safety.

RESULTS

Primary endpoint

Average SCORAD improved 60.97% in the HCEG ointment treated patients versus 38.46% in the HC ointment treated patients. This is a statistically significant difference with p=0.01.

At entry into the study, the patients assigned to HC-EG ointment had a worse average SCORE than the HC ointment group (45.1 vs. 35.1). Despite starting with a worse average SCORAD at entry, the HC-EG ointment cohort ended treatment with a better average SCORAD score at the end of therapy (SCORAD of 17.60 with HC-ED ointment vs. 21.60 with HC ointment) (Table 1).

Secondary endpoints

Pruritus: Average score was 91.54% improved in the HC-EG ointment treated patients versus 26.74% in the HC ointment treated patients. This is a statistically significant difference with p=0.008 (Table 2).

Stinging: One of 15 of the HC-EG ointment treated patients experienced mild-to-moderate stinging when the ointment was applied. The remaining 14 patients and all the HC ointment patients reported no stinging. The stinging was relieved and the patient continued treatment by first applying a layer of Aquaphor® and then the ointment for the first 2 days of therapy. After day 2 of therapy, no further pre-application of Aquaphor was needed. Local corticosteroid effects through percutaneous absorption on eczematous skin: No patient in either cohort exhibited local blanching at the post-therapy examination or parent reported seeing blanching during treatment at home. Evidence of systemic ethanol effect through percutaneous absorption on eczematous skin: None of the treated patients in the study that used HC-EG ointment turned out to be a more severe group than the group who received HC ointment.

Table 1 : Change in SCORAD score either 1% HC ointment or 1% HC ointment EG

Average SCORAD score	15 Patients using HC-EG ointment	15 Patients using HC ointment
Pre-treatment	45.1	35.1
End-treatment	17.60	21.60
% change	−60.97%	−38.46%

HC: Hydrocortisone, EG: Ethanol gel

Table 2: Change in pruritus score either 1% HC ointment or 1% HC ointment-EG

Average pruritus score (0–10)	15 Patients used HC-EG ointment	15 Patients used HC ointment
Pre-treatment	7.1	7.1
End-treatment	1.60	5.20
% change	91.54%	26.74%

HC: Hydrocortisone, EG: Ethanol gel

DISCUSSION

AD is a chronic, itch-inducing skin disorder that primarily affects the face (cheeks), neck, arms, and legs while sparing the Groin and axillary regions (see illustration below). Although it typically begins in early childhood, AD also significantly impacts a large number of adults. Frequently, high levels of immunoglobulin E are linked to AD (IgE). The "atopic march" theory, which contends that AD is a component of a progression that may result in subsequent allergic disease at other epithelial barrier surfaces, was developed as a result of the fact that it is the first disease to present in a series of allergic diseases, including food allergy, asthma, and allergic rhinitis, in that order [11,12].

AD is commonly treated with the following substances: Petrolatum, Aquaphor, or more recent products such as Atopiclair and Mimyx are examples of moisturisers. Topical steroids (the current standard of care; frequently combined with moisturisers): In general, ointment bases such as HC, triamcinolone, or betamethasone are favored, especially in arid settings. Tacrolimus and pimecrolimus are examples of broad immunomodulators (calcineurin inhibitors; generally considered second-line therapy) specialized biologic treatments dupilumab (anti-IL-4Ra monoclonal antibody) (anti-IL-4Ra monoclonal antibody) [13]

The dispersed EG microbubbles in the HC ointment were supposed to boost efficacy in this trial by reducing the staphylococcal population on the eczematous skin. Although this investigation confirmed the expected rise in clinical efficacy, the antibacterial cause of the improvement was not looked into. The population of staphylococcal biofilm before and after therapy was not monitored. Therefore, additional research will be required to assess and evaluate this proposed mode of action. The 1% HC-EG ointment was superior to the 1% HC ointment in these individuals with moderate-to-severe AD in terms of both objective improvement and decrease in pruritus [14]. Local discomfort was barely noticeable and manageable. There were no ethanol intoxication-related systemic symptoms. Parents stated that they preferred HC-EG over other treatments due of its quick effectiveness and lack of prescription corticosteroids and antibiotics [15]. Due to the lack of parental cooperation, this is significant. The small sample size and possible bias by the principal investigator due to conflicts of interest are two limitations of this study.

CONCLUSION

We would want to draw the conclusion from our research that HC-EG ointment was superior to HC ointment in terms of reducing AD-related pruritus and visible rash.

ACKNOWLEDGMENTS

We acknowledge the whole department of our institute.

AUTHOR CONTRIBUTION

All authors have equally contributed in this study.

CONFLICTS OF INTEREST

None.

FUNDING

Nil.

REFRENCES

1. Spuls PI, Gerbens LA, Simpson E, Apfelbacher CJ, Chalmers JR, Thomas KS, *et al*. Patient-Oriented Eczema Measure (POEM), a core instrument to measure symptoms in clinical trials: A Harmonising Outcome Measures for Eczema (HOME) statement. Br J Dermatol 2017;176:979-84. doi: 10.1111/bjd.15179, PMID 27858989
2. Ersser SJ, Cowdell F, Latter S, Gardiner E, Flohr C, Thompson AR, *et al*. Psychological and educational interventions for atopic eczema in children. Cochrane Database Syst Rev 2014;2014:CD004054. doi: 10.1002/14651858.CD004054.pub3, PMID 24399641
3. National Institute for Health and Care Excellence. Atopic Eczema in Children: Management of Atopic Eczema in Children from Birth up to the Age of 12 Years. Available from: http://www.nice.org.uk/nicemedia/pdf/Cg057fullguideline.pdf [Last accessed on 2009 Mar 15].
4. Langan SM, Bourke JF, Silcocks P, Williams HC. An exploratory prospective observational study of environmental factors exacerbating atopic eczema in children. Br J Dermatol 2006;154:979-80. doi: 10.1111/j.1365-2133.2006.07153.x, PMID 16634905
5. Ellis C, Luger T, Abeck D, Allen R, Graham-Brown RA, De Prost Y, *et al*. International Consensus Conference on Atopic Dermatitis II (ICCAD II): Clinical update and current treatment strategies. Br J Dermatol 2003;148(Suppl 63):3-10. doi: 10.1046/j.1365-2133.148.s63.1.x, PMID 12694268
6. Darsow U, Laifaoui J, Kerschenlohr K, Wollenberg A, Przybilla B, Wüthrich B, *et al*. The prevalence of positive reactions in the atopy patch test with aeroallergens and food allergens in subjects with atopic eczema: A European multicenter study. Allergy 2004;59:1318-25. doi: 10.1111/j.1398-9995.2004.00556.x, PMID 15507101
7. Cho SH, Strickland I, Boguniewicz M, Leung DY. Fibronectin and fibrinogen contributes to the enhanced binding of *S. aureus* to atopic skin. J Allergy Clin Immunol 2001;108:269-74. doi: 10.1067/mai.2001.117455, PMID 11496245
8. Zollner TM, Wichelhaus TA, Hartung A, Von Mallinckrodt C, Wagner TO, Brade V, *et al*. Colonization with superantigen-producing *Staphylococcus aureus* is associated with increased severity of atopic dermatitis. Clin Exp Allergy 2000;30:994-1000. doi: 10.1046/j.1365-2222.2000.00848.x, PMID 10848922
9. Santer M, Ridd MJ, Francis NA, Stuart B, Rumsby K, Chorozoglou M, *et al*. Emollient bath additives for the treatment of childhood eczema (BATHE): Multicentre pragmatic parallel group randomised controlled trial of clinical and cost effectiveness. BMJ 2018;361:k1332. doi: 10.1136/bmj.k1332, PMID 29724749
10. Santer M, Rumsby K, Ridd MJ, Francis NA, Stuart B, Chorozoglou M, *et al*. Adding emollient bath additives to standard eczema management for children with eczema: The BATHE RCT. Health Technol Assess 2018;22:1-116. doi: 10.3310/hta22570, PMID 30362939
11. Schram ME, Spuls PI, Leeflang MM, Lindeboom R, Bos JD, Schmitt J. EASI, (objective) SCORAD and POEM for atopic eczema: Responsiveness and minimal clinically important difference. Allergy 2012;67:99-106. doi: 10.1111/j.1398-9995.2011.02719.x, PMID 21951293
12. Gaunt DM, Metcalfe C, Ridd M. The Patient-Oriented Eczema Measure in young children: Responsiveness and minimal clinically important difference. Allergy 2016;71:1620-5. doi: 10.1111/all.12942, PMID 27232584
13. Levin J, Friedlander SF, Del Rosso JQ. Atopic dermatitis and the stratum corneum: Part 1: The role of filaggrin in the stratum corneum barrier and atopic skin. J Clin Aesthet Dermatol 2013;6:16-22. PMID 24155988
14. Cerrato S, Ramió-Lluch L, Brazís P, Fondevila D, Segarra S, Puigdemont A. Effects of sphingolipid extracts on the morphological structure and lipid profile in an *in vitro* model of canine skin. Vet J 2016;212:58-64. doi: 10.1016/j.tvjl.2016.03.020, PMID 27256026
15. Koppes SA, Charles F, Lammers L, Frings-Dresen M, Kezic S, Rustemeyer T. Efficacy of a cream containing ceramides and magnesium in the treatment of mild to moderate atopic dermatitis: A randomized, double-blind, emollient-and hydrocortisone-controlled trial. Acta Derm Venereol 2016;96:948-53. doi: 10.2340/00015555-2395, PMID 26939522