EFFICACY AND SAFETY OF TOPICAL HALOMETASONE IN ECZEMATOUS DERMATOSES IN INDIAN POPULATION: AN OPEN LABEL, NONCOMPARATIVE STUDY

H R Jerajani, A S Kumar[1], Maria Kuruvila[2], H V Nataraja[3], Mariam Philip[4], D V S Pratap[5], T K Sumathy[6], Binny Krishnankutty[7], Shilpi Dhawan[7], Dennis Thomas[7]

Abstract

Background: Topical steroids remain the mainstay of treatment in eczema, an inflammatory skin reaction characterized by pruritus, redness, scaling, and clustered oozing papulovesicles. Halometasone is a new potent corticosteroid approved in the Indian market for topical application in the treatment of dermatitis. **Aims:** To evaluate the efficacy and safety of halometasone in the treatment of acute or chronic noninfected eczematous dermatosis in Indian population. **Materials and Methods:** A prospective, open, multicentric, phase 3, noncomparative clinical trial conducted at outpatient departments of seven centres. Two hundred endogenous eczema patients meeting study criteria were enrolled. Halometasone 0.05% cream was applied twice daily for 30 days in chronic and 20 days in acute eczema patients. Calculation of eczema area and severity index, and assessment of investigator's global assessment of severity of eczema and severity of pruritus score were done at each visit and compared with baseline. All adverse events (AE) were captured and documented. Laboratory investigations including haematological tests, urinalysis, renal and liver function tests were performed at baseline and at end of treatment. **Results:** Of the 200 patients enrolled, 180 were chronic and 20 were acute eczema patients. It was found that there was a significant (P<0.001) improvement in all efficacy parameters compared with baseline. The treatment was shown to be successful in 91% patients. AE were reported in 30 patients and there was no serious AE reported. There was no clinically significant difference in laboratory investigations with treatment. **Conclusions:** Halometasone was shown to be safe and very effective in Indian patients with acute and chronic eczema and the drug was well tolerated.

Key Words: *Dermatosis, eczema, halometasone, topical corticosteroid*

Introduction

Topical corticosteroids, like betamethasone have been extensively used for the treatment of eczema for over 30 years and are the mainstay of therapy for eczema. Halometasone 0.05% is a well-tolerated synthetic tri-halogenated corticosteroid for topical application possessing pronounced anti-inflammatory, antiexudative, antiepidermoplastic, antiallergic, and antipruritic properties which is approved in the European market for the treatment of various types of dermatitis. Halometasone cream 0.05% is a potent (Group III) corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. Halometasone monohydrate was launched[1] under the brand name "Sicorten." It has been approved in many European countries such as Spain, Germany, Switzerland, Austria, Netherlands, Belgium, and Portugal and other countries such as Hong Kong and Israel. Clinical studies of halometasone have targeted all types of dermatitis (atopic dermatitis, contact dermatitis, and seborrheic dermatitis), acute or chronic eczematous dermatitis and psoriasis, and halometasone has been found to be effective. However, it is a new topical corticosteroid launched in the Indian market.

In international multicentric comparative studies with halometasone 0.05% cream, halometasone has been shown to be superior to comparators such as betamethasone,[2] prednicarbate,[3] fluocortolone,[4] and fluocinolone.[5] It has

From the Department of Dermatology, LTM Medical College and LTM General Hospital, Mumbai; [1]Department of Dermatology, Owaisi Hospital and Research Centre, Hyderabad; [2]Departments of Dermatology and Venereology, KMC Hospital, Mangalore; [3]Department of Dermatology, STD and Leprosy, Victoria Hospital, Bangalore Medical College and Research Institute, Bangalore; [4]Departments of Dermatology, Venereology and Leprosy, Dr SMCSI Medical College, Karakonam; [5]Department of Dermatology, Osmania Medical College and Hospital, Hyderabad; [6]Department of Dermatology, MS Ramaiah Medical College, Bangalore; [7]Global Medical Affairs, Dr. Reddy's Laboratories Ltd., Hyderabad, India. ***Address for correspondence:*** *Dr. Binny Krishnankutty, TC 25/576, Housing Board Jn, Thampanoor, Trivandrum, Kerala, India. E-mail: drbinnyk@gmail.com*

Access this article online

Quick Response Code:

Website: www.e-ijd.org

DOI: 10.4103/0019-5154.91822

been shown to be safe and well tolerated in European population. Since halometasone was not marketed in India at the time of this study, no data were available on Indian population regarding the efficacy and safety of this medication.

The objective of this study was to evaluate the efficacy and safety of halometasone in the treatment of acute or chronic noninfected eczematous dermatosis in Indian population.

Materials and Methods

This was a prospective, open, multicentric, phase 3, noncomparative clinical trial conducted at seven centres. The study was conducted at dermatology outpatient departments of LTM Medical College and LTM General Hospital (Mumbai), Owaisi Hospital and Research Centre (Hyderabad), KMC Hospital (Mangalore), Dr. SMCSI Medical College and Hospital (Karakonam), Osmania Medical College and Hospital (Hyderabad), MS Ramaiah Medical College (Bangalore), and Bangalore Medical College (Bangalore). Male and female patients above the age of 12 years with acute or chronic noninfected endogenous eczema, who were willing to give informed consent and who agreed for regular follow-up were included in the study. The diagnosis of endogenous eczema was done based on taking detailed medical history and the presence of clinical signs and symptoms including itchy and dry skin.[6] Acute and chronic eczema cases were included as topical steroids are prescribed in both types. Infected cases were excluded by doing microbiological culture. Patients with history of hypersensitivity to topical steroids and patients with history of tubercular, syphilitic, or viral skin infections were excluded from the study. Patients (including severe/extensive eczema) in need of any form of treatment that influences the healing of the lesion such as topical treatment other than trial preparation, topical radiation therapy, systemic medication with antibiotics, antimicrobials, antihistaminics, cytostatics, corticosteroids, or ACTH were also excluded.

The type (acute/chronic), duration of eczema and body surface area (BSA) affected with eczema were assessed and documented. Treatment history as well as concomitant illness was also documented at the time of enrolment. Halometasone cream 0.05% was applied twice a day without any occlusive bandage to the eczematous skin using enough to cover the entire affected area lightly. The patients were told to avoid application on any atrophied or ulcerated skin. The treatment was given for 20 days in acute and for 30 days in chronic eczematous patients. A washout period of 2 weeks was given in chronic eczematous patients who were on anti-inflammatory treatments. There were four visits in total consisting of visit 1 (start of therapy), visit 2 (day 5 for acute/day 10 for chronic), visit 3 (day 10 for acute/day 20 for chronic) and visit 4 (day 20 for acute/day 30 for chronic). Emollients were permitted during the course of the study.

Efficacy was assessed on per protocol basis. Eczema area and severity index (EASI), a composite index, including an assessment of the disease extent and percentage of body surface area involved, converted to a proportional factor (scale of 0–6), in four body regions (head and neck, lower limbs, upper limbs, and trunk), was used to assess changes with treatment in eczema severity and area affected.[7] Investigator's global assessment (IGA) of severity of eczema was also performed at all visits on a 1–6 scale. Severity of eczema was graded as 1=normal clear skin, 2=Almost clear skin, 3=mild eczematous dermatitis, 4=moderate eczematous dermatitis, 5=severe eczematous dermatitis, and 6=very severe eczematous dermatitis. Severity of pruritus was assessed at all four visits using a three-point scale. Severity was graded as 0=none, 1=mild, 2=moderate and 3=severe. Based on the IGA scale for eczema severity, response to treatment was categorized into cure (attainment of grade 1 or grade 2 or reduction of two or more grades in IGA at end of treatment), improvement (reduction of one grade in the IGA scale with treatment) and failure (no change/increase in the IGA grade at the end of treatment).

Any patient who had applied halometasone cream on at least one day was evaluated for safety. All adverse events (AE), whether or not considered causally related to the study drug were documented immediately on appropriate AE forms in the patient's case report form (CRF). The incidence, severity and causal relationship of the AE to the study medication were reported in CRF. All AE were followed up either to resolution, or to a point where no further improvement was expected.

Study was initiated after procuring approval from Directorate General of Health Services and respective Institutional Ethics Committees. Two hundred patients were enrolled into the study. This sample size is accepted as it is expected to show a mean reduction of at least 30% in the EASI score in eczema patients with treatment. For efficacy assessment, paired *t*-test or Wilcoxon signed rank test was used with two-tailed analysis, with a significance level of $P<0.05$. Statistical analyses were performed using statistical software STATA version 10.0 (Stata Corp, College Station, TX).

Results

Demographic characteristics

Study period was from September 21st 2007 to 20th March 2008. Altogether 200 patients with endogenous eczema (178 atopic dermatitis, 19 seborrheic dermatitis, and 3 nummular eczema) were enrolled and 178 patients completed the entire therapy, while 22 patients dropped out at different stages during treatment. Nineteen patients were lost to follow-up during the treatment, one patient was withdrawn due to adverse experiences, and two patients refused treatment and opted out. One hundred eighty

patients with chronic eczema and 20 patients with acute eczema (57.73% males and 42.27% females) belonging to 12–83 year age group were enrolled. The demographic details are given in Table 1.

Efficacy evaluation

EASI score was evaluated at baseline, visit 2, visit 3, and visit 4. The paired *t*-test was used to analyze the change in EASI score at visits 2, 3, and 4 compared to the baseline. There was a significant reduction ($P < 0.001$) in EASI at visit 2, visit 3, and visit 4 compared to the baseline. Table 2 shows the measures of dispersion of EASI score in the study population at different visits.

There was a significant reduction of 31.06% in EASI score at visit 2 compared to that of the baseline value. At visit 3 and visit 4, there were reductions of 53.48% and 64.46% respectively, in EASI compared to baseline.

Severity of eczema was analysed using Wilcoxon signed rank test since data followed a non-normal distribution, with two-tailed analysis. There was a significant ($P<0.001$) reduction in the severity of eczema as shown in Figure 1.

There was significant ($P<0.001$) reduction of 16.43% and 26.48% in IGA scales at visit 2 and visit 3 respectively, compared to that of baseline visit. At visit 4, there was a reduction of 35.17% in IGA eczema scales compared to the baseline. Out of 164 patients who had eczema of moderate and severe intensity, in 63 (38.41%) patients skin became clear or "almost clear" with treatment. Severity of eczema reduced to "mild" in 82 (50%) patients at the end of treatment.

A similar picture was obtained in severity of pruritus also. A significant ($P<0.001$) reduction in the severity of pruritus was observed at visit 2, visit 3, and visit 4 compared to the baseline. Change in pruritus severity with treatment is shown in Figure 2.

There was a decrease of 42.29% and 60.76% of pruritus severity scores at visit 2 and visit 3, respectively, compared to that of the baseline. At visit 4, there was a reduction of 76.32% in pruritus severity scores with respect to that of the baseline. Of the 165 patients who had moderate or severe pruritus at baseline, 88 (53.33%) patients did not have pruritus at the end of therapy, while 67 (40.61%) patients had only mild pruritus at end of therapy. The treatment was shown to be "success" (cure and improvement together) in 91% patients. Figures 3a and b show the lesions on the ventral forearm of a 36-year old male patient, before and after treatment.

Safety evaluation

Thirty patients (15.00%) reported to have 39 AE during the study. Perilesional hypopigmentation was the most commonly observed adverse event (6.00%). 94.59%

Table 1: Demographic characteristics of study population

Parameter	Results
Average age (years)	39.51±15.87
Average weight (Kg)	57.49±12.08
Average height (cm)	159.92±12.18
Duration of eczema	
< 1 year	59 (29.50%)
≥ 1 year and < 2 years	52 (26.00%)
≥ 2 and < 3 years	34 (17.00%)
≥ 3 and < 4 years	15 (7.50%)
≥ 4 years	40 (20.00%)
Co-illnesses	
Hypertension	12 (6.00%)
Ischemic heart disease	1 (0.50%)
Diabetes mellitus	6 (3.00%)
Hypertension and diabetes mellitus together	2 (1.00%)

Table 2: Change in the EASI score with treatment

Visits	No. of patients (*n*)	Mean±SD	Change from baseline	*P* value
Visit 1	200	4.42±4.47		
Visit 2	192	3.06±3.49	-1.373	***
Visit 3	186	1.96±1.92	-2.364	***
Visit 4	178	1.31±1.49	-2.849	***

*** $P<0.001$

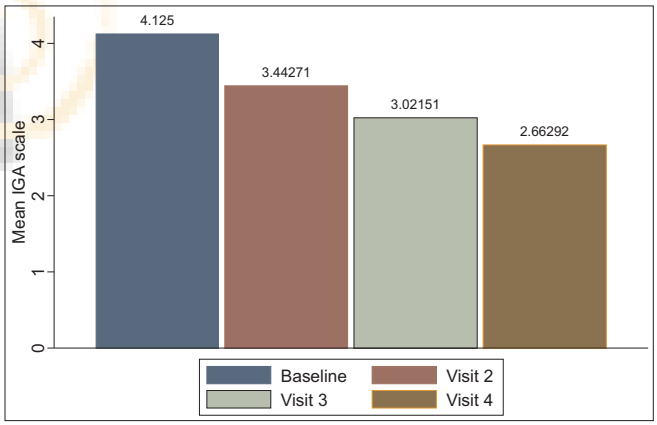

Figure 1: Change in the IGA eczema severity scale with treatment

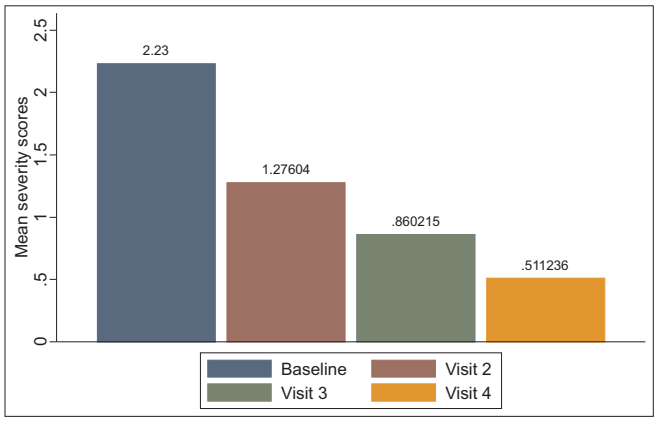

Figure 2: Change in pruritus severity with treatment

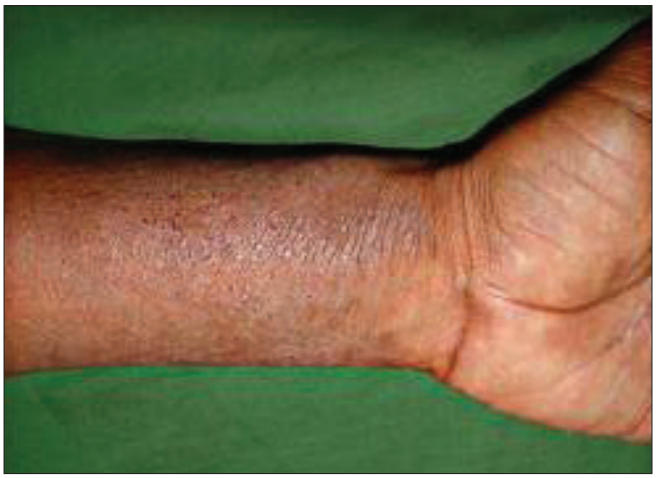

Figure 3a: Thirty-six-year old male with acute eczema at enrolment

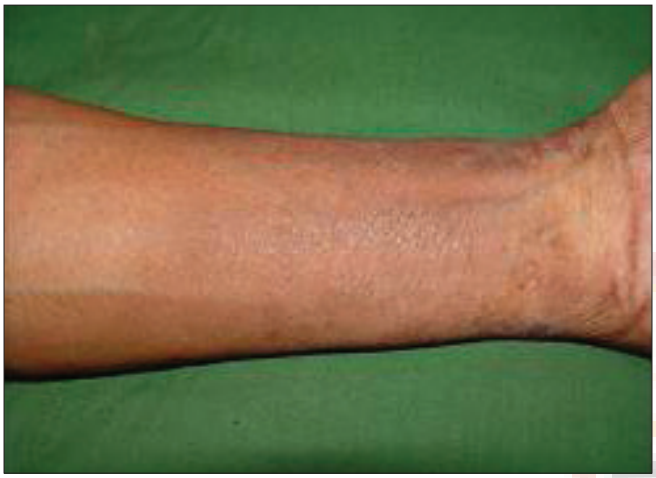

Figure 3b: Same patient at end of therapy

of all AE were either of mild or moderate severity. Two AE which were recorded as of severe nature were fever and increased serum glutamate pyruvic transaminase, which were unrelated to study drug. 69.24% of these AE got resolved or improved in due course without any intervention. There were no serious AE during the study. Pre- and post-treatment laboratory evaluation did not show any clinically significant change in haematological tests (CBC), urine, renal function tests, and liver function tests.

Discussion

Topical steroids remain the mainstay of treatment in eczematous dermatoses.[8] Emollients and steroids control the symptoms associated with eczema. Halometasone monohydrate 0.05% has been found to be effective in treating endogenous eczema. Halometasone was found to be superior to clobetasol 17-propionate in a double blind comparative clinical trial.[9] In pediatric patients with acute eczema (acute atopic dermatitis, seborrheic dermatitis, nummular dermatitis and contact dermatitis), halometasone produced "good" or "very good" results in 90% of patients and gave an overall cure rate of 74.3%.[10] Sixty-two percent patients got an early cure (in less than 20 days).

In international multicentre comparative clinical trials carried out by dermatologists in 717 patients with noninfected acute eczematous dermatoses at 28 trial centres in Austria, Germany, Holland, Switzerland, and Yugoslavia, halometasone cream exhibited a very satisfactory therapeutic effect in acute contact dermatitis, atopic dermatitis, nummular dermatitis and sebrrhoeic dermatitis. It yielded "good" to "very good" results in 89.7% of the 333 patients treated with halometasone cream. The onset of therapeutic effect was more rapid in patients treated with halometasone cream than in those on treatment with comparative preparations.[4] In another multicentric comparative trial on halometasone cream, the success rate was 93.1%[2] whereas the success rate was 90% in an open noncomparative trial with 247 eczema patients.[11] This is similar to the results obtained in the present study, where we got a success rate of 91%.

In this study, halometasone cream showed an average reduction of 60% in the EASI score and an average reduction of two grades in IGA eczema severity. It can be presumed from these results that halometasone would be more useful for curing the condition in endogenous eczema patients with mild and moderate severity than in patients with severe eczema, even though the drug was successful in reducing the intensity of the condition in severe eczema patients. It was observed that halometasone was very effective in reducing the severity of pruritus even in patients with severe pruritus. There was an average reduction of two grades of pruritus severity. Pruritus being a very inconvenient symptom associated with eczema, halometasone being effective in reducing itching, might provide faster relief to the patient. Within 1-month treatment, pruritus severity scores were reduced by more than three-fourth. Moreover, the overall compliance to treatment was more than 90%.

Halometasone monohydrate 0.05% cream has been found to be effective in reducing the area and severity of endogenous eczema, severity of itching associated with eczema and an early onset of therapeutic response, good tolerability and enhanced compliance. It was shown to be safe and very effective in Indian population and the drug was well tolerated.

References

1. Halometasone - Online Database of Chemicals. Available from: http://wordpress.org/. and http://www.chemicalall.com/chemicals-name-h/halometasone.html. [Last accessed on 2008 Oct 21].
2. Schuppli R, Dressler H, Yawalkar SJ, Weirich EG. Comparative clinical trial of a new trihalogenated dermatocorticoid (halometasone) versus betamethasone dipropionate. Z Hautkr 1983;58:230-7.
3. Ulrich R, Andresen I. Treatment of acute episodes of atopic dermatitis: Double-blind comparative study with 0.05% halometasone cream versus 0.25% prednicarbate cream. Fortschr Med 1991;109:741-4.

4. Yawalkar SJ, Macarol V, Montanari C. An overview of international clinical trials with halometasone cream. J Int Med Res 1983;11(Suppl 1):1-7.
5. Yawalkar SJ, Macarol V, Montanari C. An overview of international clinical trials with halometasone ointment in chronic eczematous dermatoses. J Int Med Res 1983;11(Suppl 1):13-20.
6. Williams HC, Burney PG, Pembroke AC, Hay RJ. The UK Working Party's Diagnostic Criteria for Atopic Dermatitis, III: Independent hospital validation. Br J Dermatol 1994;131:406-16.
7. Hanifin JM, Thurston M, Omoto M, Cherill R, Tofte SJ, Graeber M. The eczema area and severity index (EASI): Assessment of reliability in atopic dermatitis: EASI Evaluator Group. Exp Dermatol 2001;10:11-8.
8. Weinberg JM. Formulary review of therapeutic alternatives for atopic dermatitis: Focus on pimecrolimus. J Manag Care Pharm 2005;11:56-64.
9. Schwarz KJ, Konzelmann M, Yawalkar SJ, Schoenenberger PM. A double-blind comparison between a new trihalogenated dermatocorticosteroid (halometasone) cream and clobetasol 17-propionate (Dermovate) cream. Br J Clin Pract 1982;36:192-6.
10. Blum G, Yawalkar SJ. Evaluation of halometasone cream in the treatment of paediatric patients with acute eczematous dermatoses. J Int Med Res 1983;11(Suppl 1):8-12.
11. Majerus JP, Reiffers-Mettelock J. Sicorten: A synthetic corticosteroid for topical treatment of common dermatoses. J Int Med Res 1986;14:46-9.

How to cite this article: Jerajani HR, Kumar AS, Kuruvila M, Nataraja HV, Philip M, Pratap D, *et al*. Efficacy and safety of topical halometasone in eczematous dermatoses in Indian population: An open label, noncomparative study. Indian J Dermatol 2011;56:652-6.

Received: September, 2010. **Accepted:** November, 2010.
Source of support: This study was sponsored by Dr. Reddy's Laboratories Ltd, Hyderabad, **Conflict of Interest:** Authors HRJ, ASK, MK, HVN, MP, DVSP and TSK have received research funding for the conduct of this trial from Dr. Reddy's Laboratories Ltd. Authors BK and SD are employees and are stakeholders by means of salaries and/or shares at Dr. Reddy's Laboratories Ltd, which sponsored the study. DT is an ex-employee of Dr. Reddy's Laboratories.