Halometasone monohydrate (0.05%) in occupational contact dermatitis

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ABSTRACT

Objective: The impact of occupational contact dermatitis (OCD) is often underestimated because of underreporting, and its management is also inadequate, especially in developing countries. Topical corticosteroids have remained the first line treatment but till date, there is no study on efficacy and safety of halometasone in OCD, and there is a paucity of data on its comparative efficacy in allergic and irritant variety. This study aims to evaluate the efficacy and safety of halometasone in OCD and to compare its effect in allergic and irritant types of OCD.

Methods: The present study is a prospective, interventional, single arm clinical study conducted on 150 patients of OCD. Detailed history and clinical examination was done at baseline, and all enrolled patients underwent patch test with the Indian Standard Battery of allergens. Eczema severity was assessed by the Investigator’s Global Assessment (IGA) scale, SCORing Atopic Dermatitis (SCORAD) index, and patient-oriented eczema measure (POEM). Change in quality of life was assessed by using the Dermatology Life Quality Index (DLQI). After baseline assessments, they were prescribed halometasone 0.05% ointment and were followed up after 4 weeks, and efficacy variables were evaluated.

Results: At follow-up, 19 patients were lost, and data of 131 patients were analyzed. After 4 weeks of halometasone therapy, there was statistically significant ($P < 0.001$) improvement in SCORAD index, IGA, POEM, and DLQI. Considering improvement in IGA as treatment success criteria, treatment was found to be successful in 87.8%. Subgroup analysis revealed no significant difference in effect of halometasone in allergic and irritant OCD.

Conclusions: Halometasone is efficacious with a good safety profile in patients with OCD, and there is no significant difference in efficacy of the drug in allergic and irritant OCD.

KEY WORDS: Dermatology Life Quality Index, halometasone, Investigator’s Global Assessment scale, occupational contact dermatitis, patient-oriented eczema measure, SCORing atopic dermatitis

Introduction

Occupational contact dermatitis (OCD) is a pathological entity for which occupational exposure can be presented to be a primary cause or contributory element. The two most common types of OCD are allergic and irritant contact dermatitis.1-3 In most cases, both types present as eczematous lesions on
Halometasone monohydrate is a well-tolerated, antiallergic, and antipruritic property. It has been approved for use in allergic and irritant OCD. Depending on change in IGA score, the impact of OCD on its efficacy and safety in eczematous dermatoses till date. Our literature search revealed that there is a paucity of data on OCD in Indian population, and there was no study on efficacy and safety of topical halometasone in OCD. Hence, we planned this study to assess the efficacy and safety of halometasone in OCD and to compare the efficacy of the drug in allergic and irritant OCD.

Methods

The present study was a prospective, interventional, single arm, Phase IV study on the effect of 0.05% halometasone monohydrate in OCD conducted in a single centre.

Study Setting

The study was conducted on patients attending the outpatient clinic of Department of Dermatology, All India Institute of Medical Sciences, Bhubaneswar, India (a tertiary care center). The study was registered with the Clinical Trials Registry-India (CTRI registration number: CTRI/2014/08/004876).

Participants

Patients aged 18–65 years of either sex attending the Dermatology Outpatient Department of our institution with OCD (both allergic and irritant) were enrolled for the study. All patients with pruritic eczematous conditions that started or aggravated for the 1st time after joining the present occupation were included. The diagnosis of OCD was done based on taking detailed medical and occupational history and the presence of clinical signs and symptoms including pruritus and eczema. Lesions over all areas, including exposed as well as covered areas, were included unless they are solely restricted to covered areas/groins or genitalia. The diseases excluded were infective diseases such as scabies, fungal infections, and bacterial infections; and all noneczematous dermatoses such as psoriasis and lichen planus, even if associated with itching. Other exclusion criteria were lesions solely affecting the groins, genitals, or covered areas; patients who are already under treatment for the presently presenting conditions; patients with history of hypersensitivity to topical steroids; 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 study preparation, topical radiation therapy, systemic medication with antibiotics, antimicrobials, antihistaminics, cytostatics, corticosteroids, or adrenocorticotropic hormone were also excluded. Pregnant and nursing women, patients with a history of cardiovascular, hematological, metabolic, neurological, or clinically significant laboratory abnormalities, which would interfere with patient participation in the study or evaluation of patient’s response to therapy, were also excluded from screening.

Study Design

This was a prospective, interventional, single arm clinical study conducted in a single center. Patients aged 18–65 years of either sex with pruritic eczematous conditions were screened and enrolled following inclusion and exclusion criteria. Detailed history, clinical examination, laboratory investigations were done at baseline and at the end of therapy. All enrolled patients underwent patch test with the Indian Standard Battery of patch test allergens, and eczema severity was assessed by the Investigator’s Global Assessment (IGA) scale, SCORing Atopic Dermatitis (SCORAD) index, and patient-oriented eczema measure (POEM). Change in QoL was assessed by using the Dermatology Life Quality Index (DLQI). After baseline assessments, they were advised to apply commercially available halometasone 0.05% ointment twice daily locally as a thin layer over the affected area of skin with gentle rubbing. All patients were followed up after 4 weeks and during follow-up visit, efficacy parameters were evaluated.

Outcome Measures

- IGA scale: IGA of severity of eczema was done at both visits on a 0–5 scale. Depending on change in IGA score, the response to treatment was categorized into “success” and “failure.” Success included two classes: “Cure” and “improvement.” Cure was defined as either attainment of either Grade 0 or Grade 1 at the end of the study or reductions by two or more grades in IGA scale at the end of the study compared to the grades in IGA scale at baseline. Improvement was defined as a reduction of one grade in IGA scale at the end of the study compared to baseline. Failure was defined as either an increase in IGA grade or no change in the IGA grade at the end of the study compared to baseline.

- SCORAD index: SCORAD index is a clinical tool used to assess the extent and severity of eczema by considering the affected area as a percentage of the whole body, the intensity of the signs (redness, swelling, oozing/crusting, scratch marks, skin thickening/lichenification, dryness) and subjective symptoms (pruritus, sleeplessness).

- POEM: POEM is a simple, valid, easily interpreted, and reproducible tool for monitoring aspect of eczema that is important to patients in routine clinical practice or in the clinical trial setting. The measure captures the fluctuating and chronic nature of atopic eczema and provides a more comprehensive assessment of patient symptoms than that obtained by measuring itch and/or sleep disturbance alone, the two most commonly measured symptoms of the disease.

- DLQI: DLQI is a dermatology-specific QoL instrument. It is a simple 10-question validated questionnaire that can be used in different skin conditions.
**Safety Evaluation**

The occurrence of adverse effects was sought by nondirective questioning of the patient at follow-up visit. Patients had free access to the investigators for reporting any adverse effects experienced by them. There was a plan to record all adverse effects, whether previously known or not, with their description, intensity, action taken, duration, outcome, and opinion about the causal relationship to halometasone.

**Ethics Statement**

The study was conducted following the Indian Council of Medical Research’s ethical guidelines for biomedical research on human subjects (2006) after getting written approval of the Institutional Ethics Committee. A voluntary written informed consent was obtained from each patient after explaining the benefit and harm of joining the study and the freedom of withdrawing from the study at any moment they would like to. Prior permission was taken from Finlay for using DLQI questionnaire which is copyright protected.

**Statistical Method**

Continuous data has been presented as a mean ± standard deviation, whereas categorical data has been presented as a median and interquartile range. Comparison of means of continuous variables was done using two-sided paired t-test. Wilcoxon rank‑sum test and Fisher’s exact test were used for categorical variables. Statistical analyses were performed using statistical software Instat+ Version 3.036 statistical software (Statistical Services Centre, University of Reading, Reading, England) considering a significance level of \( P < 0.05 \).

**Sample size calculation**

Literature survey could not find any data on the prevalence of occupational contact dermatitis in India. The studies done in other countries reported the prevalence of OCD around 4–9%. Taking prevalence as 9%, we calculated the sample size as 136 and assuming around 10% attrition, we have finalized the total sample size as 150.

**Results**

**Patient Disposition and Baseline Demographics**

A total of 150 patients were recruited, and 131 patients were followed-up after 4 weeks. Recruitment of subjects started in April 2014 and completed in January 2015. Postbaseline values were missing in 19 patients who did not turn up at follow-up. The baseline demographic data and clinical characteristics of study subjects have been presented in Table 1. The patients age ranged from 18 to 65 years (mean age, 40.7 years), and 40% were female and 60% were male. The mean duration of suffering from contact dermatitis was 2.5 years. Out of 150 patients, 37 patients (24.7%) showed positive result in Patch test and thus diagnosed as allergic contact dermatitis. In remaining 113 patients, the etiology was irritant substances. During the study period, a total of 12.690 patients attended Dermatology outdoor clinic and out of which 620 patients were diagnosed to suffer from contact dermatitis and finally 273 patients with OCD were screened for recruitment. The percentages of contact dermatitis and OCD among the patients attending our dermatology outpatient clinic are 4.9 and 2.2, respectively. Recruited patients were found to be from different job profiles. A maximum number of patients (29) were engaged in construction works followed by agriculture workers (28) and homemakers (27). The characteristics of job and the corresponding suspected allergen/irritants have been listed in Table 2.

**Efficacy Analysis**

**Change in Investigator’s Global Assessment score**

IGA of the severity of eczema was done at both visits on a 0–5 scale. At first visit (baseline), the median value was 3.0, and it was found to decrease to 2.0 at follow-up (after 4 weeks). The change in IGA score was found to be significant (\( P < 0.001 \)). Subgroup analysis also revealed a significant change in IGA in both irritant and allergic OCD groups [Table 3].

Following the definition of success and failure of treatment, it was found that out of 131 patients, treatment was successful in 115 patients (87.8%) whereas failed in 16 patients. Subgroup analysis revealed that in allergic OCD, there was failure in three patients and treatment failed in 13 patients in irritant OCD. These findings were put in a 2 x 2 contingency table and tested by the Fisher’s test and were found to be statistically nonsignificant (\( P = 0.5 \)).

**Change in SCORing Atopic Dermatitis index**

At first visit (baseline), the mean value was 44.5, and it was found to decrease to 25.9 at follow-up (after 4 weeks). The change in SCORAD index was found to be significant (\( P < 0.001 \)). Subgroup analysis also revealed significant change in SCORAD index in both irritant and allergic OCD groups [Table 3 and Figure 2].

**Change in patient-oriented eczema measure scoring**

POEM is a questionnaire (seven questions) for monitoring aspect of eczema and scoring is done on a 0–4 scale for each question. At first visit (baseline), the median value was 13.0, and it was found to decrease to 7.0 at follow-up. The change in POEM score was found to be significant (\( P < 0.001 \)). Subgroup analysis also revealed significant change in POEM in both irritant and allergic OCD groups [Table 3].

**Change in Dermatology Life Quality Index**

DLQI is simple 10-question validated questionnaire, and each question is scored on 0–3 scale. At first visit, the median

| Characteristics | Values |
|-----------------|--------|
| Number of patients recruited | 150 |
| Number of patients at follow-up | 131 |
| Female sex (%) | 40 (60/150) |
| Mean age in years† | 40.7±14.4 |
| Mean duration of eczema (in years)* | 2.5±1.5 |
| Patch test positivity (%) | 24.7 (37/150) |
| IGA scale† | 3.0 (3-4) |
| SCORAD index* | 44.5±11.1 |
| POEM† | 13 (11-15) |
| DLQI† | 13 (11-15) |

*Data are in mean±SD, †Data in median and interquartile range. SCORAD=SCORing atopic dermatitis, IGA=Investigator Global Assessment, POEM=Patient oriented eczema measure, DLQI=Dermatology Life Quality Index, SD=Standard deviation
value was 13.0, and it was found to decrease to 7.0 at follow-up visit. The change in DLQI was found to be significant (P < 0.001). Subgroup analysis also revealed significant change in DLQI in both irritant and allergic OCD groups [Table 3 and Figure 3].

**Safety Evaluation**

The drug was well-tolerated and among 150 recruited patients, there was no complaint of any adverse drug reaction or any event which could have warranted discontinuation of the therapy.

**Discussion**

Occupation is a crucial risk factor for contact dermatitis in adults. OCD is prevalent in population and the long-term prognosis is poor unless harmful exposures at workplace are addressed. Not only they continue to have disease and their overall QoL may be impacted, but also they may have significant work disruption. Topical corticosteroids have remained the mainstay in the treatment of eczema for more than three decades and are still the preferred agents in the symptomatic management of this clinical entity. In the present study, we have assessed the efficacy and safety of Halometasone monohydrate 0.05% in OCD.

This outdoor-based study has been conducted in our institute, which is a tertiary care center. Percentage of contact dermatitis patients in our outdoor is 4.9% whereas the percentage of OCD was found to be about 2.2%. The true prevalence of OCD is difficult to determine as many workers never report minor ailments. Those with more severe conditions are initially managed and sometimes mismanaged by primary care physicians, and some end up referred to dermatologists and allergists. Recruited patients were found to have different job profiles. A maximum number of patients were found to be engaged in construction works and different industries. As our city is experiencing rapid urbanization and growth of industries since last few years, there is an increase in incidence of contact dermatitis among the industrial workers. Exposure in the workplace was responsible for cutaneous problems in all these study subjects, and proper care was taken by the dermatologist for cure and prevention.

IGA was recorded at baseline and after 4 weeks to reflect the dermatologists’ perception of efficacy, which revealed that there was statistically significant decrease in severity of eczema after 4 weeks treatment with halometasone. The effect of the drug was also clinically significant as the treatment success rate was 87.8%. In a prospective, multicentric, Phase III clinical trial, Jerajani et al. reported treatment success rate of halometasone treatment as 91% which is close to our study results. Yawalkar et al. obtained satisfactory results with halometasone in 717 patients with noninfected acute eczematous dermatoses. Therapeutic effect was good to very good in 89.7% of these patients; these trials also showed that halometasone exhibited early-onset therapeutic response than other comparators under study. Subgroup analysis showed that there was no significant difference in effect of the drug in allergic and irritant OCD. The SCORAD index combines...
objective symptoms (extent and intensity) and subjective criteria (daytime pruritus and sleep loss). Change in SCORAD index over 4 weeks was found to be statistically significant denoting improvement both in subjective and objective symptoms. The treatment was found to be equally efficacious in both allergic and irritant OCD in subgroup analysis. In a previous study by Jerajani et al., reduction in severity of eczema by halometasone therapy was 64.46% whereas in our study, we observed a reduction of 41.79%. This difference in result may be contributed to the fact that in the study by Jerajani et al., all types of eczematous dermatoses were included whereas we evaluated the drug only on OCD. The POEM is a tool for assessing atopic eczema and monitoring aspects of the disease that are important to patients. The total score (maximum 28) accurately reflect eczema-related morbidity whereas analysis of individual variables can provide useful information on whether acute (weeping, bleeding) or chronic (itching, dryness) changes are predominant and can help target therapy accordingly. The change in POEM score in our study population over 4 weeks was found to be statistically significant indicating the ability to perform household works and the necessity to pursue time-consuming treatment. These all affect the QoL. DLQI is a dermatology-specific QoL instrument that can be used in different skin conditions including contact dermatitis. The change in DLQI in our study group was found to be statistically significant over 4 weeks. The drug was well-tolerated by the study subjects, and there was no complaint of any adverse drug reaction.

Analyzing the change of all four efficacy parameters and safety issues, in our study, we have found halometasone therapy in OCD was successful. Previous studies have also revealed its efficacy, safety, and tolerability in Indian population with eczema.

Halometasone was well-tolerated without any systemic effect, and there were no reports of skin atrophy, which is usually associated with the topical use of corticosteroids. In the earlier studies, the inclusion criteria were broad including different types of eczematous dermatoses or contact dermatitis. However, the present study was conducted exclusively on OCD and 1-month halometasone therapy was found to be effective and safe. The efficacy and safety of halometasone may be attributed to its structure (i.e., chlorine and fluorine atoms, the C1, 2 double bond, and the free OH moiety in C11 increases the affinity and potency of the steroid) and its varied effects like anti-inflammatory, antipruritic and antiallergic properties.

The main limitation of the study is its single arm design without any standard comparator and conducted in single center.

Conclusion

Analysis of results of all the parameters of safety and efficacy indicate that halometasone is efficacious with a good safety profile in patients with OCD, and there is no significant difference in efficacy of the drug in allergic and irritant OCD. Because the present study is a single arm study, the drug can be compared with other standard topical corticosteroids through multicentric, randomized, double-blind, large population-based study.

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Conflicts of Interest

There are no conflicts of interest.

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