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SAFETY AND EFFICACY OF DEWDERM AD CREAM IN PATIENTS WITH ATOPIC DERMATITIS: A 60-DAYS, PROSPECTIVE, OPEN-LABEL CLINICAL STUDY.

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ABSTRACT

Objective: To evaluate the safety and efficacy of a formulation, Dewderm AD cream, in patients with mild-to-moderate atopic dermatitis (AD). **Methods:** Thirty six subjects with mild-to-moderate AD aged between 5–55 years were enrolled in the study. All 36 patients were instructed to apply Dewderm AD cream twice daily on the affected area for 60 days irrespective of their visits to the clinic. Subjects underwent evaluation of efficacy parameters, such as effect of skin surface hydration and assessment of disease severity, quality of life at the end of the treatment, and photographs were taken before and after the treatment (i.e. on day 60) to assess clinical improvement of the severity of AD. **Results:** Treatment with Dewderm AD cream showed statistically significant improvement in all the efficacy parameters at different time points from baseline to end of the study. A statistically significant ($p < 0.05$) increase in mean skin surface hydration with 54.86% improvement at visit 5 was observed when compared to baseline. SCORAD score showed 80.22% reduction in the severity of skin lesions by the end of the treatment period suggesting progressive improvement in the disease severity. Similarly, the investigator's global assessment (IGA) scale also showed a statistically significant reduction of 67.01% from baseline 2.69 ± 0.47 to 0.88 ± 0.40 at the end of the study ($p < 0.05$). The DLQI score also demonstrated a statistically significant decrease ($p < 0.05$) from baseline to end of the study. Additionally, photograph comparing before and after treatment showed gradual clinical improvement in severity of AD of the affected area at the end of the study in subjects who had skin lesions at baseline. No adverse events were reported during the study. **Conclusion:** Dewderm AD cream was very effective in treating mild-to-moderate AD by significantly reducing the disease severity without any side effects. Hence, the formulation is an effective and safe treatment option in patients with mild-to-moderate AD.

KEYWORDS: Atopic dermatitis, Investigator's Global Assessment, Quality of Life.

INTRODUCTION

Atopic dermatitis (AD) also called as eczema and is considered as the most common, chronic, itchy and relapsing inflammatory skin disease. The term '*Atopy*' means an inherited tendency to produce immunoglobulin E antibodies in response to minute amounts of common environmental proteins, such as pollen, house dust and food allergens. Dermatitis is derived from the Greek word "*derma*," which means skin, and "*itis*," which means inflammation.[1] The lifetime of AD has been well documented and represents a major public health problem, mostly in industrialized countries. Atopic dermatitis not only affects children but also adults with prevalence varying from 1% to 20% in different regions of the world.[2]

The clinical features of AD include multiple lesions with erythema, excoriation, erosions accompanied by a serous exudate, accentuated skin markings, fibrotic papules, extremely dry skin, and susceptibility to cutaneous infections.[3]

The pathogenesis of this inflammatory skin disease is not completely understood; nevertheless it appears to result from the complex interaction between defects in skin barrier function, environmental and infectious agents, and immune abnormalities.[2] Skin barrier abnormalities appear to be associated with mutations within the filaggrin gene, which encodes a structural protein essential for skin barrier formation. An individual with AD has also been shown to be deficient in ceramides as well as antimicrobial peptides, which correspond to first-

line of defense against many infectious agents. These skin barrier abnormalities lead to transepidermal water loss and increased penetration of allergens and microbes into the skin. *Staphylococcus aureus* is the most common infection involved in AD, which colonizes in approximately 90% of AD patients.[4-6]

In AD the clinical features varies with age and may differ with the course of the disease. Atopic dermatitis cannot be cured; however, prompt and effective management can improve the disease condition and quality of life of affected individuals. The main treatment goals include elimination of inflammation and infection, preserving and restoring the barrier function and controlling exacerbating factors.[7] The current therapies involve use of topical corticosteroids (first-line treatment) and/or topical calcineurin inhibitors (TCIs), first-generation antihistamines and phototherapy to manage sleep disturbances and skin infections.[2]

Because effective medical treatments for this condition are limited in number, due to few side effects like skin thinning, skin aging, skin cancer etc.[8] Many patients have turned to therapies which include natural and herbal products.[9] Thus, this prospective, open-label, multi-centre clinical study was conducted to assess the safety and efficacy of Dewderm AD cream for 60 days in patients with mild-to-moderate AD. The Dewderm AD cream is formulated with *Niacinamide, Aloe vera juice, Allantoin, Amaranthus caudatus extract, Panthenol, Hydrogenated Avocado oil, Avena Sativa (Oat) kernel oil, Hordeum vulgare extract and Tocopheryl acetate*.

PATIENTS AND METHODS

STUDY DESIGN

A prospective, open-label study for a period of 60 days was carried out at three centers: Meenakshi Multispecialty Hospital, Chennai, Vijaya Super Specialty Hospital, Nellore and Anbu Clinic, Chennai to evaluate the efficacy and safety of Dewderm AD cream in patients with mild-to-moderate AD.

All 36 subjects enrolled in the study were instructed to apply topical Dewderm AD cream twice daily on the affected area for a period of 60 days. Subjects were followed up on Day 15, Day 30, and Day 60. All subjects enrolled in the study were evaluated for the effect of the formulation on AD at the end of the study or at the time of discontinuation of the treatment compared to baseline with the Investigator's global assessment rating scale, SCORAD (Scoring Atopic Dermatitis) Score, Dermatology Life Quality Index (DLQI), and standardized clinical photographs. Principal investigator of the study monitored safety data throughout the course of the trial. The safety measurements include monitoring of adverse effects, physical examination results and vital signs. All statistical testing were planned to be two-sided and performed using in-house software. All analyses were performed on available data from the intent-to-treat (ITT) population, defined as all subjects who received at least one dose of the test product. Student t test and repeated measure ANOVA were used for assessing the efficacy of Dewderm AD cream. The drop out patients' data was analyzed by last observation carried forward (LOCF) method.

PATIENT SELECTION

Thirty six male and female subjects (age: 5–55 years) who were diagnosis with mild-to-moderate AD participated in the study. Before taking part in the study, all volunteers read and signed an informed consent form approved by Institutional Ethics Committee. Subjects were included in the study if indicated "Yes" to all of the inclusion criteria and "No" to all of the exclusion criteria.

Inclusion criteria: (1) Male and female subjects (age: 5–55 years) with a diagnosis of AD based on the criteria of Hannifin and Rajka were eligible; (2) Diagnosis of mild-to-moderate AD as defined by a SCORAD score of up to 50; (3) Healthy as determined through physical examination; (4) Willing to follow the protocol requirements and come for all follow-up visits; (5) Not participated in a similar investigation in the past four weeks; (6) Willing to refrain from current active therapy for at least 10 days prior to the application of the study cream.

Exclusion criteria: (1) History of skin disorders other than AD; (2) Current complication of AD, such as erythroderma or overt bacterial or viral infection for which treatment with anti-infectives are indicated; (3) History of superficial skin infections of viral etiology; (4) Topical or transdermal treatments, such as but not limited to retinoids, nicotine or hormone replacement therapies, on or near the intended site of application within 14 days prior to first application of study medication; (5) Systemic treatment for AD within 28 days of the first application of the study medication; (6) History of skin allergy to any of the actives used in the formulation; (7) Report of pregnancy, breastfeeding and women of child bearing potential not following adequate contraceptive measures.

STATISTICAL VARIABLES

Efficacy Variables: Efficacy assessments were Investigator's Global Assessment (overall severity of AD), SCORAD Score (the extent and severity of eczema - Scoring Atopic Dermatitis), Skin surface hydration, and Dermatology Life Quality Index (Questionnaire used to know about the impact of AD).

Safety Variables: Safety of the study was assessed mainly on the intensity and the occurrence of adverse events.

RESULTS

There were no subject withdrawals or dropouts during the study. The subject disposition and patient demographic data are presented in Fig.1 and Table 1,

respectively. The mean skin surface hydration was measured by corneometer and found to be increased from 19.75 ± 9.79 (baseline) to 43.75 ± 8.16 at visit 5. The difference demonstrated a statistically significant ($p < 0.05$) improvement of 54.86% from baseline to end of the study, confirming subjects' dry skin status to normal level (Fig. 2).

SCORAD is a tool used to assess the severity of skin lesions and it demonstrated 80.22% reduction from screening by the end of the treatment period confirming improvement in severity of the disease. It also showed a statistically significant ($p < 0.05$) reduction from screening (41.46 ± 5.60) to 35.14 ± 5.98 at visit 3 (15.26%), 22.53 ± 7.10 at visit 4 (45.66%) and 8.2 ± 4.88 at the end of the study (80.22%). The score showed a progressive improvement from moderate severity condition to mild at the end of the study (Fig. 3). The investigator's global assessment also showed a statistically significant reduction of 67.01% from baseline 2.69 ± 0.47 to 0.88 ± 0.40 at the end of the study ($p < 0.05$) (Fig. 4). Representative photographs comparing before and after treatment showed clinical improvement (i.e. gradual reduction) of severity of AD of the affected area after 60 days in subjects who had skin lesions at baseline (Fig. 5). The mean DLQI score at baseline was 10.78 ± 3.50, which gradually reduced to 9.42 ± 2.67, 6.14 ± 2.03 and 2.25 ±1.71 at visit 3, 4 and 5, respectively. The DLQI score demonstrated a statistically significant decrease ($p < 0.05$) from baseline to end of the study (Fig. 6).

During screening, a physical examination was performed, yielding normal findings for all subjects and no changes were observed at the end of the study. Thus, results of this study demonstrate that 60 days treatment with Dewderm AD cream is safe and well tolerated with no adverse effects in patients with mild-to-moderate AD.

Tables

Table 1: Baseline and demographic characteristic.

Parameter	Statistics	Dewderm AD cream N = 36
Age (years)	Mean± SD	33.42 ± 15.88
	Median	36
	Min; Max	7;57
Gender, n (%)	Male	19 (52.78%)
	Female	17 (47.22%)
Age group	Children (5–17)	10 (27.78%)
	Adult	26 (72.22%)
Body weight (kg)	Mean ±SD	59.35 ± 16.36
	Median	60.1
	Min; Max	26.1; 98.5
Height (cm)	Mean ±SD	156.28 ± 12.28
	Median	156
	Min; Max	121; 172
BMI (kg/m^2)	Mean ±SD	23.86 ± 4.52
	Median	23.65
	Min; Max	14.5; 34.1

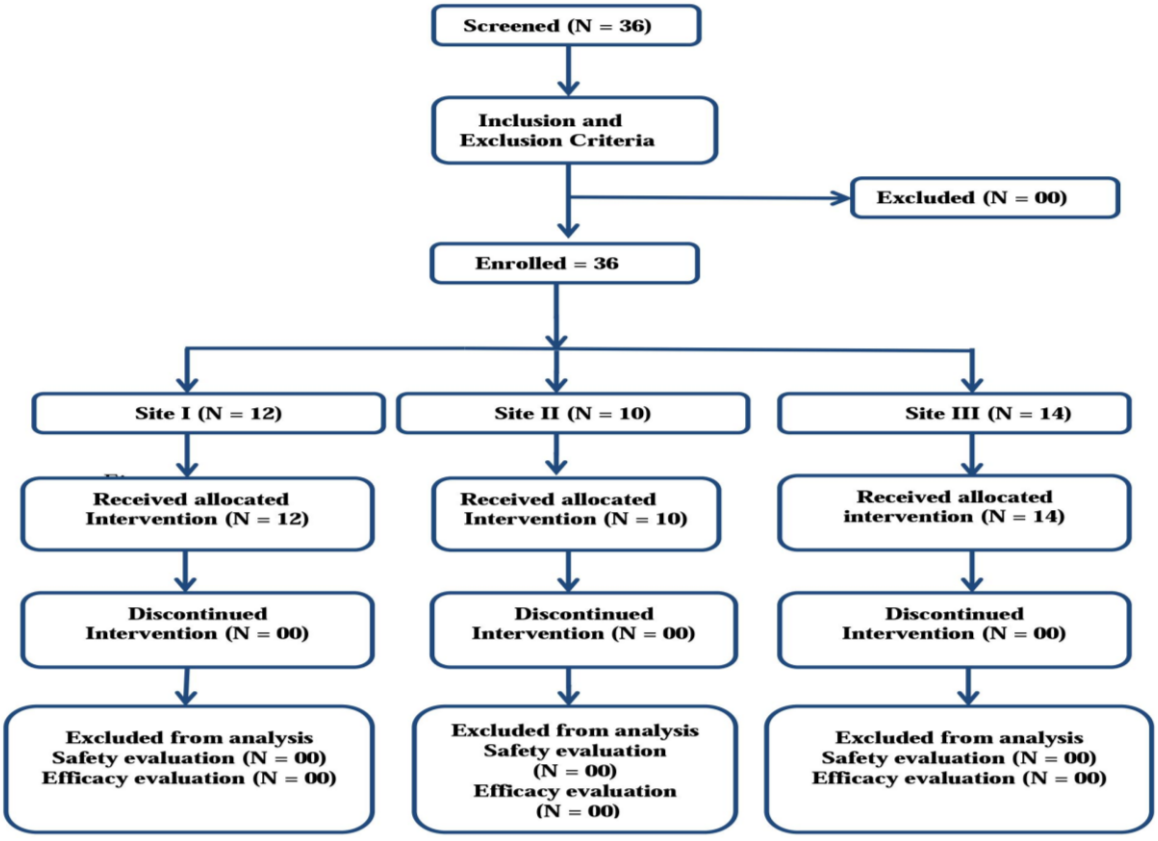

Figure 1: Flow chart of study procedures.

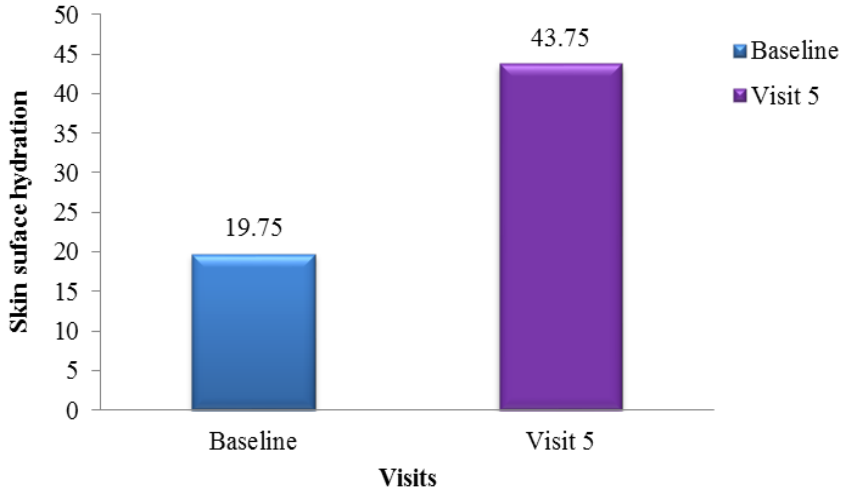

Figure 2: Changes in skin surface hydration content.

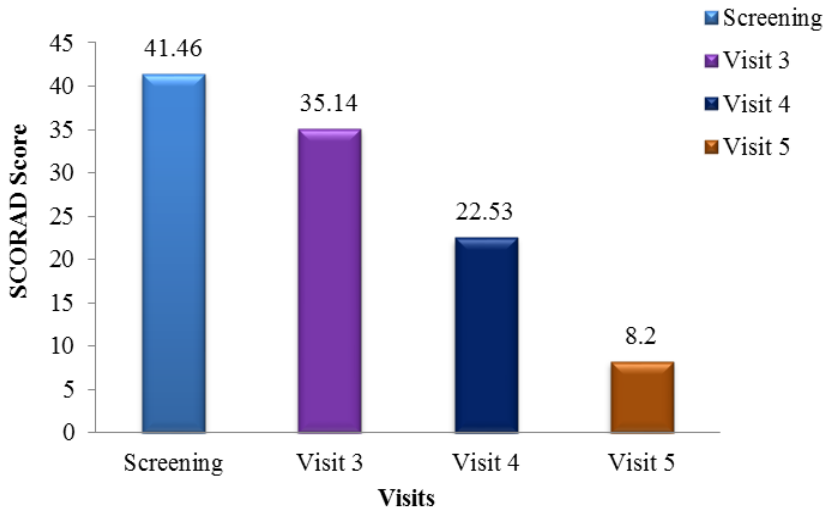

Figure 3: Treatment effect on the extent and severity of Atopic Dermatitis.

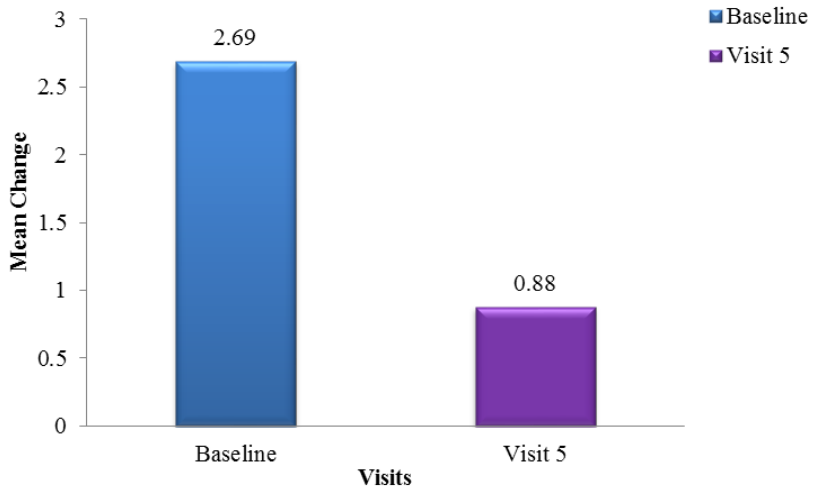

Figure 4: Treatment effect on the overall severity of Atopic Dermatitis (using Investigator's Global Assessment Rating Scale).

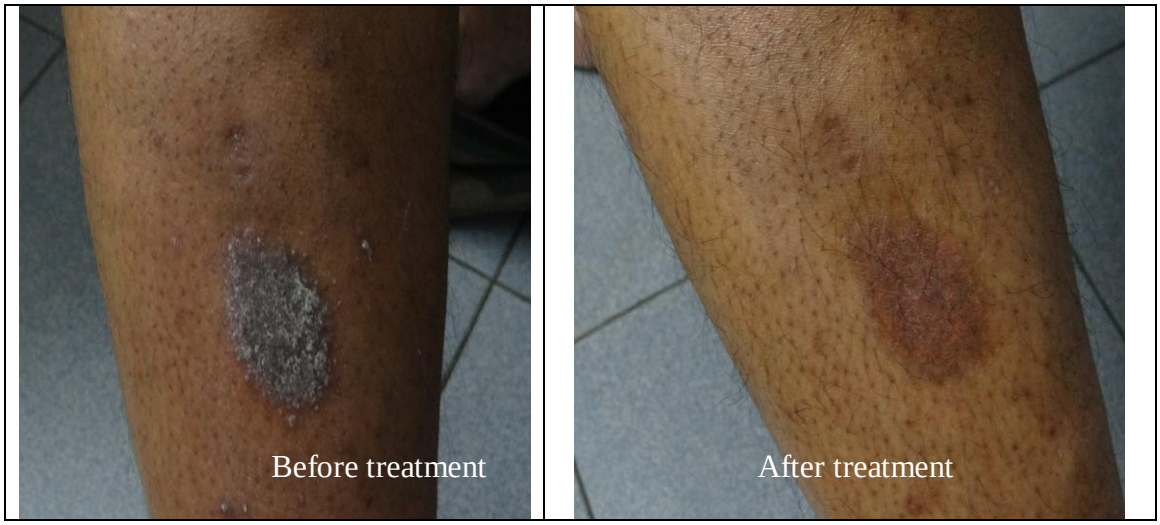

Figure 5: Comparison of before and after treatment on day 60 (Representative Image).

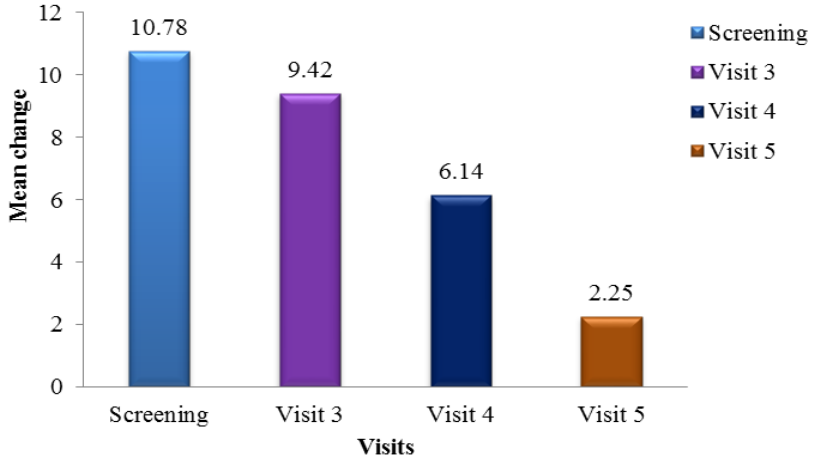

Figure 6: Treatment effect on health-related quality of life (measured by using Dermatologic Life Quality Index).

DISCUSSION

Atopic dermatitis is the major global public health problem affecting several people worldwide, which usually develops in early childhood. Reasons for increase in the prevalence and the cause of AD remain unclear, but environmental factors or genetic-environmental factors seem to play a major role. The symptoms vary from person to person, and the most common symptoms are dry itchy skin with rashes and cracks present over the skin. People with dermatitis seem to be sensitive to itching and feel the need to scratch. Atopic dermatitis affects patient's quality of life and the treatment depends mainly on the severity, distribution and extent of the condition as well as patient's age. The major causes could be due to immunological disorders and mutation in the filaggrin gene as per the reported, but concurrent incidence of infection with these inflammatory lesions reinforces the significance of treatment. Emollients, corticosteroids, and calcineurin inhibitors are a few methods used for the treatment but traditional and complementary approaches may also help to control the disease.[8]

Thus, considering various distinguishing attributes in respect of its efficacy and tolerability, the Dewderm AD cream would be a valuable addition in the treatment of mild-to-moderate AD. Most of the subjects were relieved of the symptoms and it could be mainly due to the combined action of actives present in the formulation which hydrates and prevents transepidermal water loss of the skin[10-13], soothes and conditions the skin, thus promoting rapid healing of skin lesions in dermatitis. Overall, current study data suggest that Dewderm AD cream is clinically effective and safe in patients with mild-to-moderate AD when applied twice a day.

Competing Interests:

The authors declare that they have no competing interests.

Ethics and Consent

This study was approved by the local ethics committee and all patients were notified about this study and participated with the written consent. This clinical study was registered at Clinical Trials Registry- India (www.ctri.nic.in) under the identifier CTRI/2017/03/008055 [Registered on: 09/03/2017].

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