A DOUBLE - BLIND RANDOMISED MULTICENTRE CONTROLLED STUDY OF TOPICAL 0.05% CLOBETASOL PROPIONATE WITH 2.5% ZINC SULPHATE PREPARATION

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The aim of this study was to compre the efficacy and safety of topical clobetasol propionate and clobetasol propionate with zinc sulphate cream preparation. Steroid responsive dermatoses were primarily considered in both the treatment groups. From the analysis of 291 patients, from five different centres,it was noted that though the out come was Positive in both the trial groups significant differences existed in the treatment group which received clobetasol propionate with zinc sulphate preparation. During evaluation the outcome was even between both treatment groups on the day 7. However towards the end of the study significant differences existed. Interestingly both the treatment groups did not have any adverse effects.

Key Words : Double - Blind, Multicentre, Clobetasol Propionate, Zinc Sulphate

Introduction

A variety of skin disorders like eczema, Psoriasis,and lichen planus show immediate and dramatic recovery following the use of topical steroids. Such steroid responsive dermatoses were taken up to evaluate the comparative efficacy of adding 2.5% zinc sulphate along with 0.05% clobetasol propionate cream based preparation. Conditions like subacute and chronic eczemas, chronic lichen planus and limited psoriasis (affecting not more than 15% ofbody suface area) were primarily considered for the study. This study was conducted in 5 centres in India, with a lead investigator to randomize and blind the trial progress and evaluation. A total of 291 patients who were suffering from mild to severe degree of the above condition were recruited for the study. It was prospectively determined that results of the individuals will be made after decoding CREAM-A and CREAM-B at the end of clinical evaluation from all the centres.

Materials and Methods

Outpatients aged above 12 years with a primary diagnosis of chronic and sub-acute eczema, lichen planus and limited psoriasis were screened by the investigators to fulfill the inclusion criteria. Clinical evaluation was done to exclude hypersensitivity to either clobetasol propionate or zinc sulphate,and to exclude co-existing medical illnesses like diabetes and hypertension. Patient who had lesion over the face, hands, flexural areas,scrotum and genitalia were excluded from the study. A minimum washout period of 2 weeks, in which no therapeutic intervention were carried out, was considered a prerequisite to enter into this trial.

Inclusion criteria:

1. above the age of 12 years
2. steroid responsive condition preferably patients with sub acute and chronic eczemas, chronic lichen planus and limited psoriasis.
3. intervention-free period of 2 weeks(washout period)

Exclusion criteria:

1. hypersensitivity to clobetasol or zinc sulphate
2. patients below the age of 12 years
3 hypertensives
4. diabetics
5. patients on other drug.
6. patients with lesion over face,hands,flexural

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areas,scrotum and genitalia

Each centre selected 60 patients and evaluated them for the inclusion and exclusion criteria. After obtaining informed consent from willing patients they were randomly assigned to Trial - A or Trial - B. From each center 30 patients each were taken up into Trial - A and Trial - B. The cream containing tubes were simply coded as A and B with manufacturing dates alone indicated on the crimps.

Table I. General characters of Trial A and Trial B

Parameters	Trial - A	Trial - B
Age	37.25 (14.49)	38.24 (14)
	Mean & S.D	Mean & S.D
	Frequency & Percentage	Frequency
Eczema	46 (31.7%)	57 (39.3%)
Psoriasis	44 (30.3%)	35 (24.1%)
Lichen planus	46 (31.7)	43 (29.7%)
Contact dermatitis	2 (0.7%)	2 (0.7%)
Prurigo nodularis	6 (4.1%)	7 (2.4%)
	Frequency	Frequency
Sex	& Percentage	& Percentage
Male	79 (54.5%)	86 (59.3%)
Female	66 (45.5%)	59 (40.7%)
Duration in months	Mean	Mean
	& S.D.	& S.D
	14 (4)	15 (3.75)

A separate investigator was given the task of blinding the trial till final outcome measures were assessed.

In the preliminary assessment, the investigator rated the severity of the disease condition under -4 parameters of erythema, lichenification, scaling and itching. In the Ist module of preliminary assessment the parameters were rated to assess the severity on the days 0,7, 14 and 28. To reduce the inter - observer bias and variation, the Ist module was reverse scaled unlike that of 2nd and 3rd modules. The second module was that of patient's assessment, where based upon the subjective description and visual analog cues patient's responses were rated from 1 to 5. The second and third modules measured the therapeutic responses on the days 0,7,14 and 28. Patients were advised to report adverse effects, if any, immediately and were prospectively determined to be dropped out of the study.

The investigator rated the severity in the Ist module and the progress in 3rd module under the same parameters of erythema, lichenification, scaling and itching. Module 1 measured the parameters in the range of 0 -3, 0-not significant, 1-mild, 2-moderate, and 3-severe. Module 2 and 3 were useful to assess the progress as they measured therapeutic responses in the range of 1 to 5,

1- Same, 2 - slight improvement (<25% clearance of symptoms), 3 - moderate improvement of symptoms (<50% clearance of symptoms), 4-good response (>75% clearance of symptoms) and 5 - complete recovery (100% clearance of symptoms).

Module 3 was the overall assessment module which was entered by the investigator taking into account the initial assessment and patient's assessment.

Results

Outcome over the 4 weeks of treatment were analyzed for the scores in each variables on the day 0,7,14, and 28. The scores on each parameter in three different modules, initial assessment, patient's assessment and overall physician's assessment were analyzed using suitable statistical methods. Frequency and descriptive approaches were used to summarize the findings in the same. Categorical variables like items in the socio-demographic profile and sex were compared between two groups using

Table II. Trial -A: Cream -A: 0.05% clobetasol propionate Trial -B Cream - B: 0.05% clobetasol propionate with 2.5% zinc sulphate

	Mild improvement	Moderate improvement	Good response	Complete recovery
Day	Trial - A 21.38% Trial - B 32.53%	Trial - A 13% Trial - B 18.13%	Trial - A 8.18% Trial - B 19.4%	Trial - A 10.65% Trial - B 6.65%
Day - 14	Trial - A 22.85% Trial - B 7.83%	Trial - A 17.55% Trial - B 11.05%	Trial - A 16.1% Trial - B 24.85%	Trial - A 21.47% Trial - B 37.3%
Day - 28	Trial - A 8.9% Trial - B 3.45%	Trial - A 19.92% Trial - B 5.1%	Trial - A 19.68% Trial - B 20.45%	Trial - A 37.6% Trial - B 57.25%

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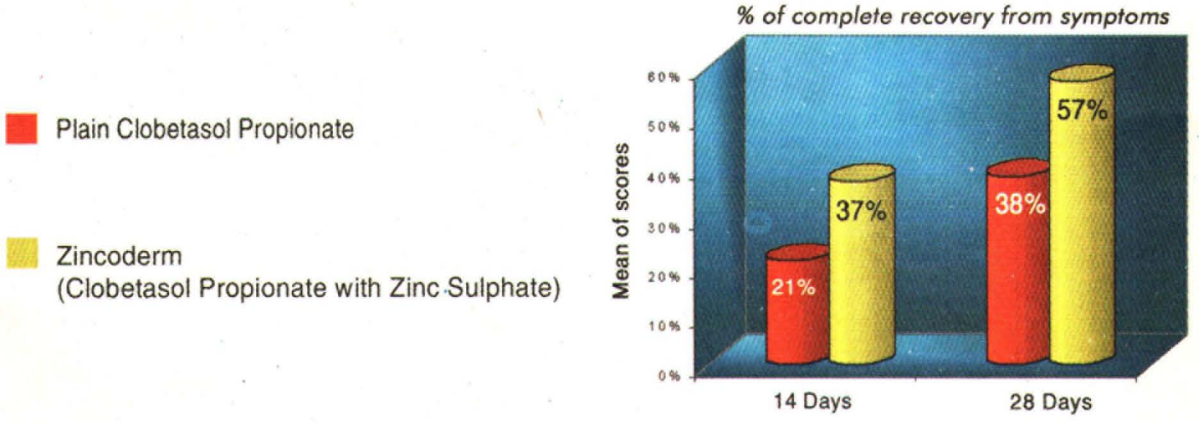
"Therapeutic responses were significantly high in the study among the patients who underwent treatment with 0.05 % clobetasol propionate with 2.5 % zinc combination as compared to plain 0.05 % clobetasol propionate cream". Addition of topical zinc augments the efficacy of clobetasol propionate in the treatment of psoriasis, eczema and lichen planus*

Ref: Jayakar Thomas, Sanjiv Kandhari, Chetan Oberoi, Elizabeth Jayaseelan, and Yogi Raj K
*A Double - Blind Randomised Multicentre Controlled Study of Topical 0.05% Clobetasol Propionate with 2.5% Zinc Sulphate preparation (*Data on file)*



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Chi-squared statistic. For ordinal outcome measures, which do not assume any particular family of distribution (non - parametric tests) Mann - Whitney U test was employed to compare between the groups and between baseline and final outcome scores. The data was not consistent with both the groups A and B, reflecting statistically significant outcomes in both the groups and within the groups. (p Value: <0.001 for all variables).

Of the 300 patients who entered the trial, 9 persons dropped out during the second week, and data was missing, yielding total treatment group to 291. The treatment groups did not differ in demographic patterns, diagnosis sub-types, sex distribution and duration of illness. (Table I).

The scores on individual parameters like itching, scaling, lichenification and erythema were tabulated based upon the responses, like mild improvement (less than 25%), moderate improvement (above 25% and less than 50%), good (above 50% and less than 75%) and complete recovery (100% recovery) on the day 7, 14, and 28.

Final scores represented the average of frequencies of all the 4 parameters summed up in the respective weeks. Trial-B showed significant differences, when compared to the Trial-A throughout the period of study. Marked differences were noticed in the day 14 and 28.

57.25% of persons in Trial - B(clobetasol propionate with zinc sulphate combination) showed complete recovery on the day 28, as compared to 37.6% of persons in Trial - A (plain clobetasol propionate preparation), and the differenecs remained significant statistically as evident by non-preparation), and the differences remained significant statistically as evident by non-parametric tests of significance. (Mann-Whitney U test). The scores for responses like good and complete recovery were high throughout the period of study for clobetasol propionate with zinc preparation as compared to plain clobetasol preparation. (Table II).

Discussion

There are controlled and comparative studies to evaluate the use of topical clobetasol propionate in inflammatory skin disorders.[1,2] Reports have also shown the antinflammatory properties of topical zinc sulphate. Zinc sulphate directly reduces keratinocyte activation markers associated with inflammation.This action is involved in the anti-inflammatory effect of zinc -associated therapies in cutaneous inflammatory diseases.[3]

The addition of zinc sulphate to clobetasol propionate in a topical preparation improves efficacy as compared to either of the chemicals when used alone. The side effects encountered with clobetasol are also reduced when combined with zinc. With these properties, besides being economical, the combination is user-friendly, contributes to patient compliance, and naturally proves to be of far better therapeutic outcome. Apart from the study of Eakin et al using topical clobetasol propionate with zinc pyrithione in psoriasis,[4] this is the only similar one. Also, to the best of the author's knowledge this is the first ever report comparing the efficacy of plain clobetasol propionate with that of a combination preparation of clobetasol propionate with zinc sulphate in dermatoses like eczemas and lichen planus.

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