

Comparision Efficacy of Hydrocortisone Acetate Cream in Patients

*Manickam Tamilselvi, Ankanagari Srinivas

Quest Life Sciences Pvt Ltd, Tambaram, Chennai 600045

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ABSTRACT

In a double-blinded, randomized, clinical trial lasting two weeks in 20 patients with skin infections (Eczema, Dermatitis, and pruritus), inflammatory and Pruritic manifestations of corticosteroid responsive dermatoses Pruritus, Eczema and Atopic Dermatitis were treated and compared between 1% w/w hydrocortisone cream and reference 1% w/w cutisoft hydrocortisone acetate cream and reductions of the basic criteria, i.e. itching, erythema and scaling, were evaluated. Effects were compared using Visual Analogue Scale, Patients compliance and Physician Global Evaluation of efficacy. All treatment regimens significantly reduced itching, erythema and scaling after 4 visits. The patients were assessed on day 01 (Visit 1), day 05 + 01 (Visit 2), day 10 + 01 (Visit 3) and on day 14 + 01 (Visit 4) for the analyses of infection. The basic criteria scores were decreased from visit 1 to visit 4. All patients were well tolerated. The results of therapeutic outcome proved the better results for test cream over reference cuti soft cream, the statistical analysis based on Generalized Linear model shown that both the products are clinically equivalent in terms of anti-inflammatory effect of hydrocortisone cream in this study.

Keywords: Hydrocortisone Acetate, Visual Analogue Scale (VAS), Global Score Index (GSI), Clinical response

INTRODUCTION

Topical corticosteroids have been used for therapy in dermatology nearly 50 years ago¹, ranging from low to high potency due to structural modifications, corticosteroids have resulted in compounds that are more effective. Use of steroids to² alleviate inflammation, irritation and itching caused by skin ailments are well known. They are commonly used as the first-line therapy in a range of inflammatory skin diseases^{1,3}. It is also known that use of steroids compromises patient's immune system and exposes them to bacterial infections. Numerous single-dose treatments, both topical and systemic, are currently employed for the treatment of skin inflammations.

In high doses hydrocortisone may increase the excitability of brain tissue and contributes to lowering the threshold of convulsive readiness. It stimulates the excessive production of hydrochloric acid and pepsin in the stomach that promotes the development of peptic ulcers. Therapeutic activity of hydrocortisone is due to anti-inflammatory, anti-allergic and antiexudative (due to vasoconstrictor effect) action. Hydrocortisone, as a weak steroid, is rarely associated with undesirable effects and is the steroid of choice for infants, the face, mucous membranes and for individuals with sensitive skin, or possibly when the steroid-responsive condition is not severe^{4,5}.

Topical glucocorticosteroids are still an important choice for the treatment of acute exacerbations in Atopic Dermatitis ⁶Aside from an anti-inflammatory effect, treatment with topical steroids contributes to a reduction of skin colonization with *S. aureus* and, therefore, might

affect a further trigger factor of Atopic Dermatitis^{7,8}. The skin of patients with Atopic Dermatitis is heavily colonized with *S. aureus*, even at uninvolved sites and toxins secreted by the majority of *S. aureus* on the skin behave as superantigens and can directly influence the disease activity, although clinical signs of bacterial super infection might be absent^{9,10}.

Most patients with Atopic Dermatitis are colonized with *S. aureus* and experienced exacerbation of their skin disease after infection with this organism¹¹. In patients with Atopic Dermatitis with bacterial infection, treatment with antistaphylococcal antibiotics can result in reduction of skin disease¹². The aim of this study was to compare the both test and reference products by inference, the clinical anti-inflammatory effectiveness efficacy, tolerability and healing of hydrocortisone in test and reference formulations: 1% hydrocortisone.

PATIENTS AND METHODS

This study is a randomized, parallel, double blinded; active controlled trial was done in the year of 2013 for 2 weeks. Twenty Male and females were having Eczema, Dermatitis, Allergies and Rash enrolled in the study. All twenty patients were explained about the study procedures and patients consent was taken before the study participation. The study was approved by the Ethics committee. Dosage and Administration of the cream was explained to all the patients: Topically the cream was applied 1-3 times a day.

A detailed instruction on topical hydrocortisone cream (1%) was given to each patient as follows: the patients in

Table 1. Visual Analogue Scale (VAS):

	Least Square Mean		P-Value
	Test (N= 10)	Reference (N= 10)	
LS Mean (SD)	-3.96 (0.3442)	-5.14 (0.3442)	0.0268
Difference and 95% CI of LS Mean	1.19 (0.15, 2.22)		

Table 2: Patient’s compliance

Parameter	Level 1	DF	Estimate	Stderr	95% Lower Wald CL	95% Upper Wald CL	Wald Chi-Square	P Value
Intercept1		1	1.4047	0.611	0.2071	2.6022	5.29	0.0215
Intercept2		1	4.6679	0.8806	2.9418	6.3939	28.1	<.0001
Intercept3		1	8.4131	1.4637	5.5442	11.282	33.04	<.0001
Product_code	C173	1	-2.3079	0.6031	-3.4899	-1.1259	14.64	0.0001
Product_code	X173	0	0	0	0	0	.	.
Visit	2	1	-3.739	0.853	-5.4108	-2.0672	19.21	<.0001
Visit	3	1	-0.051	0.7129	-1.4483	1.3463	0.01	0.9429
Visit	4	0	0	0	0	0	.	.
Scale		0	1	0	1	1	-	-

Note: LOCF method is used if visit value is missing.

Table 3: Physician’s Global Evaluation of efficacy

Parameter	Level 1	DF	Estimate	Stderr	95% Lower Wald CL	95% Upper Wald CL	Wald Chi-Square	P Value
Intercept1		1	-3.6742	0.7703	-5.1839	-2.1644	22.75	<.0001
Intercept2		1	-0.7312	0.5817	-1.8713	0.4088	1.58	0.2087
Product_code	C173	1	1.8979	0.5706	0.7795	3.0162	11.06	0.0009
Product_code	X173	0	0.0000	0.0000	0.0000	0.0000	.	.
Visit	2	1	0.6284	0.6566	-0.6586	1.9154	0.92	0.3385
Visit	3	1	-0.4746	0.6961	-1.8391	0.8898	0.46	0.4953
Visit	4	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000	-	-

both arms were instructed to apply a thin layer of the topical agents thrice a day over the skin patches, on the day of beginning the treatment and continued up to 2 weeks. All of the patients were followed up for 2 weeks and each patient was examined in all the five visits.

Affected area of the skin and patients’ age were recorded in the data sheet before the commencement of intervention. Subsequently, the dermatitis area (cm²) was measured independently up to 5 visits. Irregular dermatitis area was estimated in each patient using a grid paper. The patients’ complaints was scored from 0 to 3 in the data sheet in each examination (subjective scores were defined as: 0: no complaint; 1: mild; 2: moderate; and 3: severe complaint). In this study, the rate of dermatitis healing was the objective criterion. The primary end point of the study was the speed of dermatitis healing. Dermatitis healing was defined as complete epithelialization of moist desquamation (dermatitis grades 2 and 3) areas.

The healing rate of dermatitis was measured by comparing the rate of the decrease in the dermatitis area (cm/week) between the test and reference products. The mean dermatitis area (cm/week) was compared between the test and reference products during 2 consecutive weeks of intervention. A minimum sample size required is 20 patients in both arms to ensure 80% power at the 5% significance level for detecting a 40% improvement in the healing rate from 30% to 70%. The statistical analysis

was done using Generalized Linear Model for count data based on multinomial distribution assumption. The data was analyzed to compare the treatment, visits and its interactions. between the test and reference products and P value less than 0.05 was considered statistically insignificant.

RESULTS

There was no meaningful difference in terms of baseline variables, including age, sex, dermatitis grade and dermatitis area (cm²) between the test and reference products. The mean age of the control and study arms was 29 (range=19-55) years. Based on the Visual Analogue Scale (VAS). The mean dermatitis area after four visits was -3.96 in test product and -5.14 in reference product (Table No. 1). It is done for the assessment of wound, based on the severity.

All the patients were tolerated the topical treatments well, and no systemic or local reaction or dermatitis aggravation was observed. The analysis of data showed that after” 5 visits” use of topical application of test product thrice a day was more effective on the healing of dermatitis than that of topical hydrocortisone cream of reference product (1%).

The statistical analysis was done using Generalized Linear Model for count data based on multinomial distribution assumption. The treatments, visits and its interactions were used in this model. The statistical

analysis was done using change at visit 4, from baseline data. The ANOVA was used treatment with a fixed effect and tested at 5% level of significance. From the obtained results have shown that the least square mean (LSM) of two treatments C173 and X173 were not significantly different at 5% level significance and corresponding point estimate and confidence interval of difference between two treatments was 1.19 (0.15, 2.22) Table No.1. From the table No.2, Patients compliance, it is noted that the two treatments C173 and X173 were not significantly different at 5% level significance (t_1^2 with one d.f. 14.64, P-value = 0.0001). From the table no. 3, Physician's Global Evaluation of efficacy (PGES) it is noted that the two treatments C173 and X173 were not significantly different at 5% level significance, (t_1^2 with one d.f. 11.06, P-value = 0.0009). Hence the absence of significant difference suggests that Test and Reference products are clinically equivalent in terms of anti-inflammatory activity of the API.

DISCUSSION

Patients with the age group of 19-55 were included in this trial and the patients were having. Skin infections (Eczema, Dermatitis, Allergies and Rash), and inflammatory, Eczema and Atopic Dermatitis and have received little attention for the treatment of the above mentioned diseases were included in the study. The study was a double blinded clinical trial, in which 20 patients were received either test or reference product as per the randomization. These patients were assessed by following scores/ scales. A preliminary outcome analysis was done based on Visual Analogue Score, All the patients were followed up on Visit 01 (Day 01), Visit 02 (05th \pm 01 day), visit 03 (10th \pm 01 day) and visit 04 (14th \pm 01 day). There was no significant difference between the two groups with respect to their baseline demographic data. The statistical analysis was done using change at visit 4 from baseline data (Table 1). The ANOVA was used with treatment as a fixed effect and tested at 5% level of significance. From the obtained values, it is noted that least square mean (LSM) of both treatments were not significantly different at 5% level significance and corresponding point estimate and confidence interval of difference between two treatments were 1.19 (0.15, 2.22) Table 1.

The absence of significant difference suggests that Test and Reference products are clinically equivalent in terms of anti-inflammatory activity of the API. The statistical analysis was done by using Generalized Linear Model also shown that the absence of significant difference between that Test and Reference products suggests that both products are clinically equivalent in terms of anti-inflammatory activity of the API.

In this study, scoring criteria are based on visual inspection. This objective measurement assesses the efficacy and tolerability of the patient influencing the anti-inflammatory effect of dermatitis. Anti-inflammatory effects of corticosteroids may play an important role in relieving patients' symptoms [13], [14]. In this study, the

primary end point was the rate of wound healing between the test and reference product.

Many of today's modern drugs have their origin in traditional plant medicine. It also plays an antioxidant and immunomodulatory role and lacks the potential acute and late adverse effects of corticosteroids [15]. There is some evidence supporting the safety and efficacy of natural henna in wound healing [15], [16]. In our study, test product cream is more effective on the healing of dermatitis than reference product in the second week of intervention. In addition, test product significantly decreased the patients' complaints such as pain, and discharge compared to topical hydrocortisone cream (1%). Treatments suitable for use on psoriasis on the face and other sensitive skin areas are very few. Low-strength topical corticosteroids and vitamin D3 analogues may be regarded as first-line treatments for these areas [17]. When considering the treatment of sensitive skin areas such as the face and skin folds, use of a low potency corticosteroid may be considered optimal because these areas respond more rapidly to corticosteroid therapy and show greater overall improvement than psoriasis lesions on other locations. But they are more susceptible to corticosteroid-related adverse drug reactions [18], which is why potent steroids are not recommended for use on these areas. As per Jean-Paul Ortonne et al., [19], results indicate that a topical combination product containing calcipotriol with hydrocortisone exhibits an improved risk/benefit profile compared to calcipotriol as monotherapy.

Since less number of patients were returned for the visit No.5, score obtained during this visit has been considered as insignificant. While doing a retrospective analysis with the investigators, out of urge to understand the study results better, we found that the test product have shown a better efficiency in terms of Visual Analogue Scale Score, patient's compliance, Physician's Global Evaluation Score and Pruritus Severity Scale than the reference product. On an average, based on the clinical end points and the clinical response to the treatment administered, test product has scored better, adding value to the treatments given so far to the patients with Skin infections (Eczema, dermatitis, allergies, rash), inflammatory and Pruritic manifestations of corticosteroid responsive dermatoses. This is also supported with the investigator's quantitative evaluation. Based on all the above assessments and evaluations conducted on 20 patients, it is concluded that test product scored better results than reference product.

CONCLUSION

Based on the results obtained in this study, two weeks' use of topical hydrocortisone Test cream was more effective on the healing of dermatitis than the reference topical hydrocortisone cream (1%) in this patient's trial. This result was obtained from the preliminary evaluation of clinical trial.

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