COMPARISON OF EFFICACY AND SAFETY OF TOPICAL 0.1% ADAPALENE GEL WITH 0.05% ISOTRETINOIN GEL IN THE TREATMENT OF ACNE VULGARIS

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ABSTRACT

Introduction: Acne is a disease of the pilosebaceous unit with involving abnormalities in sebum production, microbial flora changes, abnormal keratinization, and inflammation. Topical retinoids play a very important role in the treatment of acne vulgaris. Adapalene a new third generation topical retinoid is a good choice for the treatment of acne vulgaris with less side effects and high efficacy .

Objectives: To compare the efficacy and tolerability of topical Adapalene gel with Isotretinoin in treatment of mild to moderate acne vulgaris.

Methods: The patients were divided into two groups. Group A was given topical Adapalene 0.1% and group B was given topical Isotretinoin 0.05%. Patients were followed up at 2, 4, 8 and 12 weeks.

Results: Sixty six percent of patients in group B (Isotretinoin group) showed response versus 65.66% of patients in group A (Adapalene group)(P>.001). Adapalene was, however, better tolerated with 12 of patients having side effects as compared to 22 of patients in group B isotretinoin although statistically insignificant ($p>0.005$).

Conclusion It can be concluded from our study, that Isotretinoin (non-selective retinoid) and Adapalene both are efficacious .Adapalene, has better tolerability profile than Isotretinoin..

Key words: Acne vulgaris, Isotretinoin, Adapalene, Retinoids.

INTRODUCTION

Acne is a common problem in adolescents and young adults. The disorder is caused by abnormal desquamation of follicular epithelium that results in the obstruction of the pilosebaceous canal. This obstruction leads to the formation of comedones, which can become inflamed because of overgrowth of Propionibacterium acnes[1],

Consensus guidelines advocate the use of topical retinoids as the primary treatment for most forms of acne vulgaris. However, all topical retinoid preparations may be irritating, and this may contribute to underutilization in clinical practices. Topical adapalene fosters topical retinoid treatment of acne with less irritation. Worldwide prevalence of acne varies from 35-90%, primarily in adolescent years[2], Morbidity arising due to acne vulgaris is considerable, with negative impact on self image and confidence especially at the time of adolescence[3,4]. It produces profound physical, social and psychological problems leading to restriction of social interactions[5,6,7].

For years, first-generation retinoids, prominently isotretinoin, 'has been used in the treatment of acne, with variable tolerability profile[8]. The efficacy of isotretinoin is largely the result of the effects on sebaceous gland differentiation and proliferation as well as modulation of skin androgen receptors[9]. In some studies, significant anti-inflammatory and desquamative effects of isotretinoin have also been observed[10].

Adapalene, a third generation retinoid, is known to have similar efficacy in curing acne vulgaris of mild to moderate severity, when applied topically[11]. It has the same biological properties as isotretinoin with distinct physico-chemical profile with high lipophility and increased chemical and photostability leading to higher acceptability and tolerability[12]. This agent is associated with decreased erythema, scaling, burning and pruritis as compared to isotretinoin[13].

The mechanism of action of isotretinoin and adapalene differs only in selectivity of action. Isotretinoin exerts majority of its actions through all types of retinoid acid receptors, whereas adapalene binds with high affinity to and subtypes only. Adapalene is considered superior to isotretinoin, due to its stability and significant anti-inflammatory activities, along with greater tolerability[13].

Limited data is available regarding clinical fea-

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tures, consequences and response to therapy of acne vulgaris in Asian skin types. The present study is aimed at evaluating differences in efficacy and tolerability of topical isotretinoin topical gel with adapalene gel in the treatment of mild to moderate acne vulgaris in our population.

MATERIAL AND METHODS

This randomized control trials were done on 200 patients presenting to the outpatient Department HMC Dermatology, Unit. Patients were included in the study from Jan 2011 to Dec 2011. Written informed consent was taken prior to enrollment of patients. Grouping was done randomly by using the random number table, group A weretreted with Adapalene and group B were treated with Isotretinoin. A detailed history, regarding the type of lesions, previous treatment undertaken, hypersensitivity reactions if any, was taken and the grade of acne vulgaris was recorded in the proforma following clinical examination. In female patients, where applicable, a Pregnancy test at the start of treatment was done to rule out pregnancy and were advised to use non-hormonal methods of contraception after being counselled in details about potential threats to the developing fetus by the treatment.

Patients were excluded from the study if they had severe (grade IV) acne, known hypersensitivity to any of the ingredients of adapalene gel 0.1% or isotretenoin or if they were pregnant or lactating women. Patients of both groups were advised to clean and dry the face before application of the isotretinoin and adapalene on the affected areas at night.

Assessment of efficacy and safety was conducted at the end of weeks 2, 4, 8 and 12. Evaluation of the overall response to therapy was recorded according to the following scale:

Cleared = 100% improvement
Marked improvement = >75% improvement
Moderate improvement = 50 - 75% improvement
Slight improvement = 25% - 50% improvement

The disease severity was defined as mild acne when there were comedones (less than 20) or less than 15 inflammatory papules or a comedone/ papule count of less than 30 on the face and moderate acne when papules and pustules (15-50 lesions) with comedones and rarely cysts were present. Total lesions (comedone, papule, and pustule) count ranged from 30 to 125 on the face[14].

Safety was assessed by the presence of erythema, scaling, burning, and pruritus on any of the follow up visits. Side Effects were subsequently assessed over four follow up visits spaced at 2, 4, 8, and 12 weeks following presentation and start of treatment.

Pregnant or lactating females, known hypersensitivity to adapalene and / or isotretinoin,patients with history of topical and systemic treatment of acne within 6 months of starting treatment, History of use of hormonal preparations or antibiotics over the last 3 months were excluded because these are the confounders and leads to make the study results biased.

Data Analysis

The information collected through proforma was regularly transferred to SPSS data editor files and was analyzed according to it. Qualitative variables like sex, gender, tolerability and efficacy between the two groups were assessed by applying Chi-Square test. Quantitative variables like total number of lesions and their percentage reduction at visit 4 were assessed by applying the independent sample T-test. The p-value ≤ 0.05 will be considered as significant.

RESULTS

A total of 200 patients with mild to moderate acne vulgaris were included in this study. In group A there were 26(26%) male and 74(74%) female while in group B there were 48(48%) male and 52(52%) female. There were 42% patients in group A with mild acne while in group B there was 56 patient with mild acne. Moderate acne was present in 58 patients of Group A while in group B, 44 patients presented with moderate acne.

Table 1

	Group	N	Mean	Std. Deviation
Age	Adapalene	100	21.0600	4.68572
	Isotretinoin	100	19.7800	4.39600
Total lesion counts	Adapalene	100	4.6200	1.59405
	Isotretinoin	100	3.8000	1.53083
Percent centage Reduction of Leasion	Adapalene	100	65.1600	21.64578
	Isotretinoin	100	66.0000	13.14257

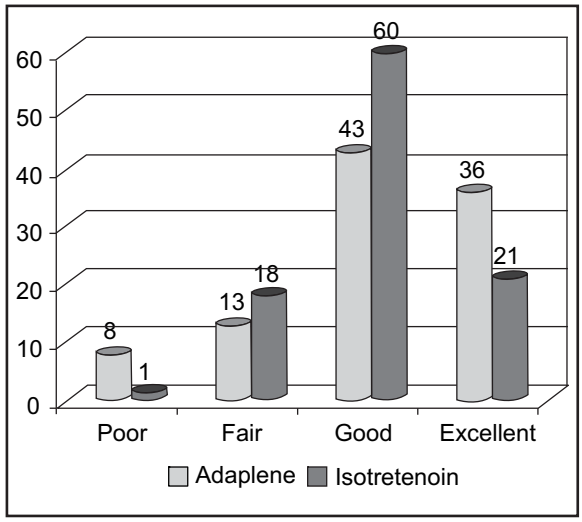

Fig. 1 Response in both the groups

Table 2: Grade of Acne Wise Distribution of Percentage Reduction of Leasion in both the groups

Grade of Acne			Percentage Reduction of Leasion				Total
			poor	fair	good	excellent	
Mild	Group	Adapalene	3	8	15	16	42
		Isotretinoin	0	8	36	12	56
	Total		3	16	51	28	98
Moderate	Group	Adapalene	5	5	28	20	58
		Isotretinoin	1	10	24	9	44
	Total		6	15	52	29	102

Table 3: SIDE EFFECT IN BOTH THE GORUPS

			Group		Total
			Adapalene	Isotretinoin	
Side Effect	Yes	Count	12	22	34
		% within Group	12.0%	22.0%	17.0%
	No	Count	88	78	166
		% within Group	88.0%	78.0%	83.0%
Total		Count	100	100	200
		% within Group	100.0%	100.0%	100.0%

Mean age of patient in adapalene group was 26.06 years ± 4.68SD while in Isotretenoin group mean age was 19.78years± 4.396 SD. (Table 1)

Mean number of lesion in group A were 4.62±1.594 SD. Mean of total lesion in Group B were 3.80±1.53 SD. Mean percentage reduction of lesion in Group A was 65.16 with SD 25.64 while in Group B mean percentage reduction was 66.00 ±13.14 SD. Which were insignificant with P-value 0.74 in both the groups.(Table 1)

In Adapalene group poor response was seen in 8(8%) patients, fair in 13(13%) patients, good in 43(43%) patients while 36(36%) showed an excellent response. In isotretenoin Group poor response was shown by 1(1%) patient, fair in 18(18%) patients, good in 60(60%) and 21(21%) patients showed an excellent response. p-value 0.005 (Fig 1)

Total number of patients with mild acne in both groups were 98.Total number of patients in adapalene group with mild acne were 42,out of which 3 showed poor response, fair in 8 patients, good in 15 while 16 patients showed excellent response. In isotretenoin group there were 56 patients with mild acne out which no patient showed poor response, fair in 8 patient, good in 36 patients and excellent in 12 patients. P value 0.015 in mild acne and p value of .071 in moderate group which were insignificant in both the groups.

Total number of patients with moderate acne in both groups were 102.In adapalene group 58 patients presented with moderate acne. Among them 5 showed poor response, 5 showed fair response, good in 28 and excellent in 20. In isotretenoin group total number of patients were 44,poor response was shown by one patient, fair by 10 patients, good by 24 while excellent response was shown by 9 patients.(Table 2)

Side effects were found in 12(12%) patients from Group A and 22(%) patients from Group B. which were not significant with P value of 0.058. (Table 3)

DISCUSSION

The development of topical retinoids has proved to be essential in the management of acne. As such, our review of adapalene is important from a therapeutic perspective because topical retinoids are underutilized in practice 15 The most compelling predictor of the use or nonuse of topical retinoids was physician specialty, with nondermatologists significantly less likely to use topical retinoids than dermatologists (39.4% vs. 23%)[16]

The differences in three generation of retenoids use depent on their tolerability as the newer generations are less irritant

The results of our study indicate that topical Adapalene and Isotretinoin are highly effective in the treatment of mild to moderate acne vulgaris.

Isotretinoin gel showed greater reductions in total lesion counts and comedone counts than topical Adapalene, but the results were not statistically significant. This difference may be due to that isotretenoin has action on all retinoid receptors including á â and ã, while Adapalene has action on all except á receptors. It is possible that RAR á receptors might have some additional role in sebaceous follicle keratinization or keratinocyte hyperproliferation.

Study conducted by D *Ioannides et al* showed adapalene to be more effective but the results were not statistically significant. while our study showed isotretenoin to be more effective in reducing inflammatory and non inflammatory lesions but here also results were not statistically different.

This difference in the results might reflect difference in the skin types of the two study populations. Secondly, the sample size in our study was much greater than the one used by *D. Ioannides et al* (200 vs. 80), which may account for differences in treatment outcomes observed.

Adapalene is an effective acne treatment. A multicenter, randomized, investigator-blinded study with 297 enrolled patients compared the efficacy of adapalene Royalty .1% solution to that of tretinoin. 025% gel in a once-daily dosage regimen for 12 weeks. Both agents provided significant mean im-provements in inflammatory lesions (47% and 50%, respec-tively), and noninflammatory lesions (57% and 54%). Our study showed comparable improvement with above study[17].

Regarding side effects isotretenoin produce more more burning and erythma than adapalene which is according to finding with *D. Ioannides et al*. Our study also showed more side effects in isotretenoin group(22vs 12). This effect may be due to isotretenoin effect on RAR receptors and these receptor may be possible for increase redness and burning. These results are analogous to most of the studies, which show greater tolerability profile of Adapalene versus tretinoin[18,19]. Side effects of topical retinoids are usually photo-associated, which may be the reason why more patients experienced the side effects during treatment. The skin type of our study population was type III,IV.

CONCLUSION:

It can be concluded from our study, that Isotretinoin (non-selective retinoid) and Adapalene both are efficacious. Adapalene, has better tolerability profile than Isotretinoin

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