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Original Article

Comparative efficacy and safety and efficacy of systemic 13-cis retinoic acid 20mg/day vs. 40mg/day in acne vulgaris

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Abstract

Background Early and effective treatment in acne vulgaris is essential to prevent facial scarring and psychological distress.

Objective To evaluate the safety and efficacy of two different doses of 13-cisretinoic acid in the treatment of acne vulgaris.

Patients and methods Sixty patients of moderate to severe acne vulgaris were selected from the dermatology out patient clinics of Abbassi Shaheed hospital, Aga Khan Hospital, Burhani Hospital and Taj Medical Complex, Karachi. They were randomly divided into two groups. Group I was given 20mg systemic 13-cis retinoic acid daily and group II, 40mg daily for 24 weeks. Assessment of the severity of acne was done using Global Acne Grading System (GAGS). Clinical improvement was measured on physician acceptance scale, every two months till 24 weeks. Safety was evaluated on the basis of side effects and lab abnormalities at the baseline and end of therapy.

Results Marked dose related decrease in acne lesions was noted within 8 weeks of the onset of therapy in all patients. In group I, out of 30 patients 24 showed 70% clearance in 8 weeks, 90% clearance in 16 weeks and 100% in 24 weeks, with residual pits in four patients. Six female patients were prescribed Diane 35® at 24 weeks, who still had premenstrual flare of acne. In group II, 26 patients out of 30 showed 90% clearance in 8 weeks and 100% clearance from 16-24 weeks. Mild scarring was noted in six patients at 24 weeks of treatment. Three female patients still had new eruption and were given Diane 35® after 24 weeks and in one male patient the dosage was increased to 60mg/day, which cleared the acne in 32 weeks. The results of two groups were insignificant ($p>0.5$). Side effects noted were chelitis, dryness pruritus and desqumation of skin, more in group II. A mild mood change with irritability was noted in 3 female patients.

Conclusion 13-cis retinoic acid is safe and efficacious in the treatment of acne vulgaris. A dose-dependent faster response is seen, although 20 mg/day works equally well than 40mg/day till 24 weeks.

Key word 13-cis retinoic acid, acne vulgaris.

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Introduction

Acne is a very common condition, particularly in adolescents and young adults. There is no mortality associated with this disease, but often there is significant psychological morbidity.[1] It is costly and because of relapses over a long period of time these costs are high.[2]

Effective treatment in acne is import prevent facial scarring and psychological distress. Since decades, people are using topical and systemic anti acne medicines like antimicrobials, tretinoin, benzoyl peroxide etc, which can control acne in some patients; but in relapsing, nodulocystic, and acne with complications like pigmentation and scarring, one should not waste time by prescribing conventials anti-acne treatment for months and years. Modalities like antiandrogens play a role but their use is gender limited.[3]13-cis retinoic is one compound which produces miracle response in acne vulgaris in short period of time and prevents complications.[4]

Studies show that 13-cis retinoic acid produces changes in surface skin lipids composition[5]. These changes result from marked inhibition of sebaceous gland activity[6]. 13-cis retinoid acid has unique activity on sebaceous glands, but it's a mystery because it doesn't bind to cellular retinoic acid binding proteins or to retinoic acid receptor.[7]

The molecular basis for it's anti sebotropic activity has not been fully elucidated. 13-cis retinoic acid is the most effective drug in reducing sebaceous gland size up to 90% by decreasing proliferation of basal sebocytes, suppressing sebum production and inhibiting sebocytes differentiation *in vivo*. Half-life ranges from 7-37 hrs. 13-cis retinoic acid crosses the placenta and is a strong teratogenic compound. It is excreted in feces and urine. The epidermal level of the drug is low and no progressive accumulation either in serum or skin is found. After discontinuation of therapy, it disappears from serum and skin within four weeks. 13-cis retinoic acids cause significant reduction in the microbial flora. This reduction persists for quite some time after discontinuation of therapy.[8]

The present study was undertaken to compare the efficacy and safety of systemic 13-cis retinoic acid in doses 20mg/kg and 40mg/kg in the treatment of moderate to severe acne.

Patients and methods

Sixty patients of moderate to severe acne vulgaris were selected from the outpatient clinics of Abbasi Shaheed Hospital, Aga Khan University Hospital, Burhani Hospital and Taj Medical Complex, Karachi. Their acne was graded on the Global Acne Grading System (GAGS).[9] All were placed in moderate to severe group. They were randomly divided into two groups II and I. Group I with 30 patients was given 20mg 13-cis retinoic acid (Ro-accutane®) daily and Group II with 30 patients had 40mg 13-cis retinoic acid daily for 24 weeks. They were followed up every 8 weeks, till 24 weeks.

Assessment of the patients was done using acceptable physician assessment scale every 8 weeks till 24 weeks. Clinical improvement were graded as: 1: excellent (>80%); 2: good (>50%); 3: moderate (30%-50%); 4:

Table 1 Comparison of improvement in two groups during 24 weeks of follow-up

	8 weeks	*16 weeks*	*24 weeks*
Group I (n=24)	60%	90%	100%
Group II (n=26)	90%	100%	100%

slight (<30%); and 5: no change. Any side effects appeared was noted. Lab investigations like hepatic profile and lipid profile were done at the baseline and at the end of the study. Chi-square test was applied for statistical analysis.

Results

At the end of study, results were evaluated in 60 patients (30 in group I and 30 in group II). None of the patients were lost to follow-up.

The Global Acne Grading Score (GAGS) placed the patients of both group in moderate to severe acne. In group I, 24 patient showed good (>50%) result in 8 weeks and excellent 90% at 16 weeks and 100% clearance at 24 weeks with slight residual pits. Six patients with moderate acne, with improvement had persistent new eruption at each pre-menstrual phase were given Diane35® after 24 weeks.

In group II, 26 Patients showed excellent 90% clearance at 8 weeks and 100 % clearance at 16 weeks till 24 weeks. Three female patients with moderate acne, with improvement had persistent new eruptions till 24 weeks and were given Diane 35®, in one male patient dosage of 13-cis retinoic acid was increased to 1mg/kg and he showed clearance at 32 weeks.

Statistically the difference in the results of two groups was not significant (p>0.5). Dose dependent, faster response was however noted in group II patients (**Table 1**).

Adverse effects noted on each follow-up visits were cheilitis 100%, pruritus and desquamation of skin in 30% and myalgia in one patient. The severity being more in group II. Emollients were given as treatment for chelitis and desquamation. Three female patients in group II noted frequent mood changes, these effects persisted throughout therapy. The laboratory investigations like hepatic and lipid profile at baseline and end of treatment were unremarkable in all patients.

Discussion

Our results confirm the notion that 13-cis retinoic has revolutionized the management of acne vulgaris. The clearance of acne lesions were dose dependent, but excellent improvement in both treatment groups at 16-24 weeks proves 20mg/day to be as effective as 40mg/day in our study clearance of facial lesions were faster than those on the back and chest and can be compared to that reported by Farreli.[3]

Adverse effects observed were similar to those previously reported with this drug.[4] The serum lipid profile at the baseline and end of therapy was unremarkable. This is in contrast to the data presented by Farreli[3] and Katz *et al.*[10] The hyperlipidemia appears to be dose-related and their patients received higher dosage of 13-cis retinoic acid than did our patients.

Depression, a major side effect also concerns the doctors and patients both.[11,12] Three of our female patient in group II noticed frequent mood changes, but none complained of depression during therapy. The lower dosage, close family ties, proper patient selection can be some criteria for such response.

13-cis retinoic acid is expensive and creates financial burden on many families. So, 240 dosage of 20mg/day, cuts down the cost to 1/3rd, and the amount spend in years on antibiotics and various topical modalities in relapsing acne makes it more cost-effective.

The sooner the therapy is started the better the results, one gets in terms of post acne pigmentation and scarring. Our patients even on 20mg / day did show concern about the cost, but all were so tired and miserable with efforts made to clear their acne in the past that all completed the therapy, even the ones who had new eruption, which proves its efficacy and tolerability.

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