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Original Article

Isotretinoin versus weekly pulse dose azithromycin in the treatment of acne-a comparative study

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Abstract

Background: Acne is a multifactorial disease and represents a spectrum of disease severity from a couple of blackheads and pustules to severe nodulocystic fulminant acne. The severity of the disease differs from patient to patient and treatment must therefore be tailored to the individual patient with the goal of preventing physical and/or psychological scarring.

Objective: To compare the efficacy of isotretinoin vs. weekly pulse dose azithromycin in the treatment of moderate to severe acne.

Patients and methods: An experimental study was done to compare the efficacy of isotretinoin and pulse dose azithromycin in the treatment of acne (Moderate to severe type). The study was conducted among 60 (sixty) patients of acne aged 15-30 years in the Department of Dermatology and Venereology in Bangabandhu Sheikh Medical University, Shahbag, Dhaka and Combined Military Hospital, Dhaka, during a period from January, 2004 to May, 2007. Cases having moderate to severe types of acne were included (categorized by the Global Acne Grading Score, GAGS). Patients were randomly allocated into two equal groups. Group A was given isotretinoin at a dose of 0.5-1mg/kg body weight according to severity of the disease for 5 (five) months and group B was given azithromycin 500mg three days a week for 3 months.

Results: Among the 60 cases included in the study, 33 (55%) were male and 27 (45%) were female. The mean age of group A was 21.03±4.21 years and in group B was 21.5±4.16 years. Maximum number of patients were having moderate type of acne i.e. 20 (66.7%) in group A and 25 (83.3%) in group B. The mean duration of the disease was 9.57±5.52 months in group A and 12.93±6.20 months in group B. In group A, all cases responded and the clinical response was rated as excellent in 24 (80%), good in 5 (16.67%) and fair in 1 (3.33%) case. In group B, 24 (80%) cases responded and the response was categorized as excellent in 6 (20%), good in 9 (30%), fair in 3 (10%) and poor in 6 (20%) cases. There was no response in 6 (20%) cases. Group A (isotretinoin) responded better than group B (azithromycin) [$p<0.05$].

Conclusion: Both isotretinoin and azithromycin can be useful for the treatment of moderate and severe acne but isotretinoin appears to be superior to weekly pulse dose of azithromycin.

Key words
Isotretinoin, azithromycin, acne.

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Introduction

Acne is the commonest cutaneous disorder affecting nearly 80% of persons at sometime between the ages of 11-30 years. It is a chronic inflammatory disorder of pilosebaceous follicles and this can occur anywhere on the body apart from palms and soles, but frequently affects face, back, chest, neck and upper arms.[1,2] The basic cause of acne is unknown. It is a multifactorial disease and its pathophysiology centers on the interplay of increased sebum production, follicular hyperkeratinization, colonization with *Propionibacterium acnes* and inflammation.[3] Acne represents a spectrum of disease severity from a couple of blackheads and pustules to severe nodulocystic fulminant acne. The severity of the disease differs from patient to patient and treatment must therefore be tailored to the individual patient with the goal of preventing physical and/or psychological scarring.[4,5]

Acne may be noninflammatory, marked by white or black comedones or inflammatory varying from papules and pustules to nodules and cysts. Regarding the treatment of acne, four major principles govern the therapy: a) decrease sebaceous gland activity, b) correct the altered pattern of follicular keratinization, c) decrease the follicular bacterial population, and d) anti-inflammatory effects.[6,7]

There are many topical and systemic modalities for acne. These include topical retinoids, benzoyl peroxide, antibiotics, salicylic acid, azelaic acid, intralesional steroid infiltration, black light, laser etc. and systemic antibiotics, hormones, retinoid, low dose steroid, fenasteride etc.[8,9]

The use of oral retinoid (isotretinoin) has revolutionized the management of severe and treatment-resistant acne. The remarkable aspects of isotretinoin therapy are the completeness of the remission in almost all cases and the longevity of the remission which lasts for months to years in the great majority of the cases at a dose of 0.5 to 1mg/kg body weight for a period of 16-20 weeks.[1,8]

Azithromycin belongs to the azalide group of antibiotics and is closely related structurally to macrolides like erythromycin. It is more tissue stable, penetrates deeply into tissues and has a higher terminal half life than erythromycin.[8] Azithromycin has recently been introduced to treat acne at a weekly pulse dose schedule for a period of 3 months. Pulse regimes significantly increase patients' compliance because of the reduced total number of administered drugs.[9] In Bangladesh no such study was done earlier. The present study was undertaken with a view to compare the efficacy of isotretinoin and weekly pulse azithromycin in the treatment of acne.

Patients and methods

An experimental study was done to compare the efficacy of isotretinoin and pulse dose azithromycin in the treatment of acne (moderate to severe type). The study was conducted among 60 patients of acne, aged 15-30 years in the Department of Dermatology and Venereology in Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Combined Military Hospital Dhaka Cantonment, Dhaka and Community based Medical College and Hospital, Mymensing during a period from January, 2004 to May, 2007. Cases having moderate to severe acne as categorized by the Global Acne Grading Score, GAGS, were included. All cases were diagnosed clinically. Patients were educated regarding compliance, regular follow up, side effects, avoidance of other oral medication and importance of contraception

(females only) whilst on treatment. Written consent for the treatment was obtained from all patients. Baseline complete and differential blood counts, liver function tests, renal function tests, complete lipid profile and urine pregnancy test (for females) were done for all the patients of group A before starting isotretinoin. These tests were repeated every month for the whole duration of isotretinoin therapy. Here, null hypothesis was that there was no difference of effectiveness between isotretinoin and pulse dose azithromycin in the treatment of moderate to severe acne.

Patients were randomly allocated into two equal groups, A and B. Group A was given isotretinoin at a dose of 0.5 to 1mg/kg body weight according to severity of the disease for 5 months and group B was given azithromycin 500mg three days a week for 3 months. Patients were followed up monthly for evaluation of the disease. After completion of the treatment both the groups were followed up at two monthly intervals for another year. Topical adjuvant therapy e.g. erythromycin lotion initially and then adapalene was given in both the groups. The improvement was noted on the basis of Global Acne Grading score as excellent: complete clearing of lesions; good: 75% clearing of lesions; fair: 50-75% clearing of lesions; poor: <50% clearing of lesions; and no response**.**

Results

In total, 60 cases (30 in group A and 30 in group B) were included in the study (**Table 1**). 33 (55%) were males and 27 (45%) were females. The age in both the groups ranged from 15 to 30 years. The mean age of group A was 21.03±4.21 years and in group B was 21.5±4.16 years. In both the groups, the maximum numbers of patients were in the age group of 15 to 20 years. Maximum number of patients had moderate type of acne, 20 (66.7%) in group A and 25 (83.3%) in group B. The duration of disease ranged from less than 6 months to more than 12 months whereas the mean duration of the disease was 9.57±5.52 months in group A and 12.93±6.20 months in group B.

Table 1 Demographic data and disease characteristics in the two groups.

	Group A (n=30)	*Group B (n=30)*
Male	17 (56.7%)	16 (53.3%)
Female	13 (43.3%)	14 (46.7%)
Age		
Mean (years)	21.03 ± 4.21	21.50±4.16
15-19 years	14 (46.7%)	13 (43.3%)
20-25 years	10 (33.3%)	12 (40%)
26-30 years	06 (20%)	05 (16.7%)
Severity of acne		
Mild	-	-
Moderate	20 (66.7%)	25 (83.3%)
Severe	10 (33.3%)	05 (16.7%)
Duration of disease		
3-6 months	9 (30%)	13 (43.3%)
6-12 months	15 (50%)	12 (40%)
12-24 months	6 (20%)	5 (16.7%)
Mean (months)	9.57 ± 5.52	12.93±6.20

Data represented in **Table 2** assessed the efficacy of both drugs. In group A, all patients responded. The clinical response was found excellent in 24 (80%), good in 5 (16.7%), and fair in 1 (3.3%) patient in group A. In group B, clinical response was seen in 24 (80%) cases and it was excellent in 6 (20%), good in 9 (30%), fair in 3 (10%) and poor in 6 (20%).

Clinical response in patients with different disease severity is also shown in **Table 2**. In group A, out of 20 patients with moderate type of acne the response was excellent in 16 (80%) and good in 4 (20%), whereas in 10 cases with severe type of acne, it was excellent in 8 (80%), good in 1 (10%), and fair in 1 (10%). In contrast, in group B, clinical improvement, in 25 patients with moderate acne, was rated as excellent in 6 (24%), good in 8 (32%), fair in 2 (8%), poor in 4 (16%) and nil in 5 (20%) cases. In 5

Table 2 Clinical response in moderate and severe disease, group A (n=30) and group B (n=30) by clinical response in moderate type and in severe type of lesions.

Clinical response	*Group A (n=30)*			*Group B (n=30)*		
	Total	*Moderate acne*	*Severe acne*	*Total*	*Moderate acne*	*Severe acne*
Excellent	24 (80%)	16 (80%)	8 (80%)	6 (20%)	6 (24%)	-
Good	5 (16.7%)	4 (20%)	1 (10%)	9 (30%)	8 (32%)	1 (20%)
Fair	1 (3.3%)	0	1 (10%)	3 (10%)	2 (8%)	1 (40%)
Poor	-	-	-	6 (20%)	4 (16%)	2 (40%)
No response	-	-	-	6 (20%)	5 (20%)	1 (20%)
Relapse	5 (16.7%)			10 (33.3%)		

patients with severe acne in group B, response was rated as good in 1 (20%), fair in 1 (20%), poor in 2 (40%) and nil in 1 (20%) cases. There was a significant difference between group A and group B ($p<0.01$).

In group A, dryness especially on lips and face associated with mild peeling was noted in almost all the cases and controlled easily by liberal use of moisturizers and increased water intake. 3 patients showed a transient rise in serum lipids especially triglycerides but none of the patient had levels enough to warrant stoppage of the drugs. In group B, none of the patient had shown serious side effects except 3 patients complained of mild nausea and abdominal discomfort.

5 (16.7%) patients in group A and 10 (33.3%) in group B experienced relapse during follow up period.

Discussion

In the present study, the mean age of patients in group A was 21.03±4.21 years and in group B 21.5±4.16 years. The age ranged from 15 to 30 years. Out of total 60 patients 27 (45%) were in the age group of 15 to 20 years. The age distribution in the present study is in accordance with an earlier study.[10] There were 33 (55%) males and 27 (45%) females in our study. In group A, 17 (56.7%) cases were males and 13 (43.3%) were females. On the other hand in group B 16 (53.4%) cases were males and 14 (46.7%) were females. So, in both groups male preponderance was found. This differs from earlier studies which showed female preponderance.[7] As our study was hospital-based, less number of female patients usually come to the hospital in our culture for treatment, hence the male preponderance.

In the present study, duration of the disease varied from less than 6 months to more than 12 months. The mean duration of the disease in group A was 9.57±5.52 months and in group B 12.93±6.20 months. The maximum number of patients had acne for 6 to 12 months. This finding is consistent with the study done earlier.[3]

For the treatment of moderate and severe type of acne, topically applied drugs are not effective hence systemic drugs always should be considered.[8,11] The present study compared the efficacy of isotretinoin and weekly pulse dose azithromycin in 60 patients having moderate to severe type of acne. A study by Ghaffarpour *et al.*[11] reported a cure rate of 96.7% with oral isotretinoin. Another study done by Nawaf Al-Mutairi *et al.*[7] found 95.5% improvement with isotretinoin. In our study, cure rate with isotretinoin (group A) was 100%. Kapadia *et al.*[12] with pulse dose azithromycin in the treatment of acne showed a cure rate of 80%. Another study by Singhi *et al.*[13] with pulse dose azithromycin found 77.3% improvement. In this present study, the cure

rate with pulse dose azithromycin in group B was 80%.

Isotretinoin works on all four factors that predispose a person to acne i.e. excess sebum production, clogged skin pores, *P. acne*s and inflammation. On the other hand azithromycin acts by penetrating cells of susceptible bacteria and reversibly binding to the 50-S subunit of the ribosome, inhibiting RNA dependant protein synthesis.[10,14] Side effects of isotretinoin include dryness of skin, chapped lips, increased serum lipid level, bone pain, joint pain, depression, thinning of hair, headache, blurred vision etc.[15] In our study only dryness of skin was found in all cases and transient elevation of serum lipid was found in only 3 cases that did not hamper the study in group A. In group B, no serious side effect was noted. In group A, only 5 (16.7%) cases relapsed mildly and were treated topically. In group B, 10 (33.3%) cases relapsed and those required alternate regime.

Our study concluded that both isotretinoin and azithromycin can be useful for the treatment of moderate and severe type of acne. However, isotretinoin is superior to weekly pulse dose of azithromycin because isotretinoin works on all factors causing acne.

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