Original Research Article

An analytical study on the use of Adapalene and Azithromycin for Acne vulgaris

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Abstract

Introduction: Acne vulgaris is a common dermatological disorder affecting approximately 85 -90% of individuals between 12 and 24 years of age. In this study, the aim is to compare the efficacy of the macrolide: azithromycin given orally as the sole treatment versus a new retinoid adapalene used topically as the sole treatment, versus both given together. The new international consensus guidelines state that, topical retinoids, alone or in combination are regarded today as the first line treatment for both comedogenic and mild inflammatory acne vulgaris.**Methods**: Ninety new patients with inflammatory acne vulgaris attending the Dermatology OPDs at local randomly selected secondary & tertiary medical care centres were incorporated in this study. They were randomly allocated into three groups. Group 1 received topical adapalene (0.01%) gel, group 2 received oral azithromycin, whereas group 3 was given a combination of these two. The patients were treated for a period of 12 weeks, being reviewed every fortnightly. The results obtained were analyzed in detail using statistical methods.**Results:** The combination of adapalene and azithromycin caused the highest reduction in the inflamed lesion count followed by azithromycin given singly. monotherapy with adapalene was also used. This difference in efficacy was small and not statistically significant . Azithromycin lead to a rapid reduction in the inflammatory lesion count, but it had negligible action on non-inflamed lesions.**Conclusion:** The treatment group 3 (combination of topical adapalene and oral azithromycin) showed more improvement in terms of inflammatory lesion count than the other two groups, small number of cases in the present study might have prevented this trend from assuming statistical significance. Topical adapalene has a very good comedolytic effect, while oral azithromycin has a negligible one. The faster reduction in acne lesions when azithromycin was added to the therapeutic regime, suggests that the usage of this drug from the beginning of treatment could lead to a faster clinical response than that achieved by topical therapy alone.

Keywords: Acne vulgaris, analysis, azithromycin, adapalene.

Introduction

Acne vulgaris is a common dermatological disorder affecting approximately 85 -90% of individuals between 12 and 24 years of age. Although acne is most prevalent in this age group, the disease is reported in 8% of adults aged 25 to 34 years and in 3% aged 35 to 44 years [1].Since acne vulgaris occurs mostly on face, the impairment of self-image and self-esteem, clinical depression, social phobia and anxiety factors have been associated with it. Acne is multifactorial in origin. The major factors concerned are: (i) aberrant follicular keratinization,(ii)androgens,(iii)excess sebum and(iv) Propionib-acterium acnes[2].The lesions of acne vulgaris may be inflamed (inflamed papules, nodules, pustules, cysts and abscess) or noninflamed (primary lesions: open and closed comed ones). Most of the patients posses both types of lesions at the same time. Infection with P. acnes plays a major role in the development of inflammatory lesions. Therefore, antibiotics are useful in treatment of inflammatory acne. Topical retinoids are also known to be beneficial in these cases due to their anti-inflammatory action in addition to their comedolytic properties. In this study, the aim is to compare the efficacy of the macrolide: azithromycin given orally as the sole treatment versus a new retinoid adapalene used topically as the sole treatment, versus both given together. The new international consensus guidelines state that, topical retinoids, alone or in combination are regarded today as the first line treatment for both comedogenic and mild inflammatory acne vulgaris.We selected new retinoid adapalene for its highly favourable tolerability profile. Among the available systemic therapies, azithromycin being a broad spectrum antibiotic[4] and since the newer one is less likely to be resistant and has a high affinity for inflammatory tissue, long terminal half-life and good safety profile, its use in treating inflammatory acne vulgaris deserves evaluation. Due to the remarkable pharmacokinetics and efficacy, azithromycin is well established as a potent treatment for skin infections in adult and paediatric patients. In dermatology, clinical uses of azithromycin are not solely limited to infectious diseases. In addition to the antibacterial effects, due to the immunomodulatory and anti-inflammatory potentials of this agent, it appears that azithromycin can be administered to patients with dermatological disorders including intractable rosacea, psoriasis and synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome[3,4]

Methodology

Ninety new patients with inflammatory acne vulgaris attending the Dermatology OPD at local randomly selected secondary & tertiary medical care centres were incorporated in this study. Informed consent was obtained from all the patients before being enrolled into the study. For those below the age of 18 years, the consent of the guardian was taken.

All Patients data had details of standard clinical examinations, routine biochemical and haematological investigations. The study duration was 6 months. This was a study of 90 diagnosed cases of Acne Vulgaris attending OPDs . Information on each patient selected were carefully obtained by using a pre- designed structured proforma. Items related to past history of Presenting Cutaneous lesions & inputs from a detailed clinical / dermatological examination were included. This Performa included data on present age, age of onset, area of residence, personal and family history ,

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seasonal variation, religion of the patient, mile stone development, socio-economic status of the parents, history of relapse etc. Informed consent was obtained from all the patients before being enrolled into the study. For those below the age of 18 years, the consent of the guardian was taken. Exclusion criteria were (i) patients with purely comedonal acne, (ii) history of hypersensitivity to any ingredients of adapalene (0.1%) gel, (iii) patients below the age of 12 years, (iii) patients with known systemic illness, (iv) pregnant women and lactating mothers, and (v) patients who had underwent any treatment for their acne during last 3 months or those with history of any systemic or topical treatments that may affect acne. These patients were randomly categorized into three treatment groups. Group 1 received only topical adapalene (0.1%) gel once daily at bedtime and 1 FTU for the entire face. Group 2 received only oral azithromycin (500 mg) for three consecutive days in a week. Group 3 received both oral azithromycin and topical adapalene (0.1%) gel. Patients of all the groups received general face cleansing advice, which included the washing of face with soap for three to four times a day At the first visit, detailed history and clinical examination (general and dermatological) were undertaken. For the purpose of counting the lesions, the face was divided into four quadrants: upper, lower, right and left. The patients were reviewed fortnightly. At each review, the lesion count was repeated, and we enquired if there were any adverse effects of therapy. Noninflamed (comedones) and inflamed lesions (papules, pustules, cysts or abscesses) were counted separately. The therapy was continued for 12 weeks. After completion of the treatment period, the patients were followed-up every 2 weeks for another 4 weeks and were examined as mentioned before .

Statistical Analysis

The data obtained were analyzed in detail using the statistical software SPSS 20 for Windows. One-way analysis of variance (ANOVA) was used for analyzing the data, considering visit as replication and effects of the three groups of therapy as the sources of variation. In addition to that the determination of differences that exist among the means, we wanted to know the means that differed. For that purpose, in other words, in order to compare the efficacy of different treatments groups, we used the Duncanís multiple range test at 5% significance level (P = 0.05)

Results

The 90 patients, who provided consent to participate, were divided into three groups of 30 members each. Table 1 shows the break up of the study cases in terms of age, sex and duration of illness. Among the patients included in the study, 43.33% was male. Majority (53.33%) of the patients belonged to the age group of 15-20 years. Among them, 47.77% had their illness for more than one year at the time of presentation. The summary of result of counting the facial lesions is shown in Table 2.

Table 1: Break up of subjects

		Group 1 (Adapalene) *n* = 30	Group 2 (Azithromycin) *n* = 30	Group 3 (Combination) *n* = 30
Age	Range	13-28	12-31	14-33
	Mean	18.48	19.17	21.65
Sex	Male	11	16	12
	Female	19	14	18
Duration of illness	>1 year:	16	18	9

Table 2: Summary of mean lesion count at three stages of study

		Average numbers of Lesions		
		Pre-treatment	After 12 weeks	At the end of treatment
Group 1	Inflamed lesions	68.70	53.59	25.90
(Adapalene)	Noninflamed lesions	94.29	76.35	60.17
Group 2	Inflamed lesions	79.44	52.45	18.30
(Azithromycin)	Noninflamed lesions	82.45	72.23	61.63
Group 3	Inflamed lesions	88.13	53.85	15.27
(Combination)	Noninflamed lesions	78.87	64.16	52.16

When ANOVA was performed on the pre-treatment data (at the first attendance of the patient), there was no differences (P = 0.851) in between the groups in terms of the mean number of lesions. On analyzing the data at the second visit by using the same technique to see if the therapies differed in their effect, it was found that group 1 (adapalene) had the greatest mean value; group 2 (azithromycin) had the least mean value, whereas the group 3 (combination) had an intermediate value. These findings suggest that monotherapy with azithromycin was more effective on the inflammatory lesions than other regimes as early as the second visit. However, in this study, this early activity was not significantly different from others (P = 0.252). The analysis of the outcomes at the sixth visit (end of the treatment period) revealed that the reduction in inflammatory lesion count was the maximum in the group with combination therapy, followed by the group that administered azithromycin only, while the group that was given adapalene only showed the minimum reduction However, the means of all the treatment groups fell in the same subset (when Duncanís multiple range test was applied) and again the difference in lesion reduction between the groups failed to be significant (P = 0.616). We may thus infer that at the end of treatment period (12 weeks) that all the groups underwent similar improvement with respect to inflammatory lesions. The effect of three treatment modalities on noninflamed lesions (comedones) at the end of the treatment period was also analyzed by the same techniques. From the DMRT of comedones it was found that the effects of adapalene monotherapy and combination therapy fell in the same subset, implying that both the regimes are relatively similar in effect, whereas drug azithromycin (which formed a different subset) was different from others. The order of effectiveness was: adapalene > combination >> azithromycin. This relationship was highly signifi cant (P < 0.001). From these results, it is safe to conclude that the drug azithromycin had very little comedolytic effect, while other two regimes had good and almost similar effect on noninfl amed lesions. All the treatment regimens were generally well tolerated with a similar, low incidence of adverse events.

Discussion

In this study, a peak in the incidence of acne vulgaris was found to be in the age group of 16-20 years. This finding corroborates with the findings of a pioneer epidemiological study on acne, in which a peak was found in the incidence between 14 and 17 years in the case of females and 16-19 years in case of males.[5] There was no statistical difference amongst the three treatment groups with regard to the reduction in the inflammatory lesion count at the end of the treatment period . In other words, this implies that all the therapies reduced the inflammatory lesions to a similar extent, as measured at the end of the treatment period. This can be attributed to the anti-inflammatory properties of adapalene and some other retinoids, particularly when applied for a long duration. This observation was corroborated by

several previous studies that found significant anti-inflammatory action in the topical usage of adapalene[6-9]. However, the overall quantitative reduction in inflammatory lesion was the greatest in the group treated with combination therapy, as observed in the results of Duncanís multiple range test performed on the results at the end of the treatment period. Although not statistically significant , it shows a trend and effectively correlates with the findings of a previously conducted study[10]. Although the treatment group 3 (combination of topical adapalene and oral azithromycin) showed more improvement in terms of inflammatory lesion count than the other two groups, small number of cases in the present study might have prevented this trend from assuming statistical significance. An improvement in the infl ammatory lesions was observed more rapidly (as early as the second visit, i.e., after 4 weeks of therapy) in the groups of patients treated with azithromycin, alone or in combination. The faster reduction in acne lesions when azithromycin was added to the therapeutic regime, suggests that the usage of this drug from the beginning of treatment could lead to a faster clinical response than that achieved by topical therapy alone. Given the differences in azithromycin dosing and timing of administration, the conclusion on a specific effective therapeutic regimen for acne vulgaris remains indefinite. Nonetheless, most studies applied azithromycin thrice weekly or in 10 days with successful results. With regards to low incidence and mild side effects and also potential anti-inflammatory and immunomodulatory effects of azithromycin, this agent is a good choice for those who cannot tolerate other commonly used oral antibiotics. It is also important to consider that azithromycin is a safe drug for lactating and pregnant women suffering from acne vulgaris, making this drug a promising treatment. Furthermore, no resistance has been yet reported regarding treatment of acne vulgaris with azithromycin. Thus, the addition of azithromycin to the anti-acne regimen may be considered by the dermatologist, particularly when faster reduction is being requested for. However, this observation is statistically was not significant , again may be due to a small number of subjects in the study. Furthermore, the use of adapalene in combination with azithromycin (and other antibiotics as well), may offer the potential to reduce the duration of antibiotic treatment and to possibly reduce the potential for antibiotic resistance, which is an ever increasing clinical problem[11,12] Topical adapalene has a very good comedolytic effect, while oral azithromycin has a negligible one. Therefore, in case of purely comedonal acne, monotherapy with adapalene should be sufficient.

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