COMPARATIVE EVALUATION OF EFFICACY AND TOLERABILITY OF AZITHROMYCIN AND CLINDAMYCIN GEL IN MILD TO MODERATE ACNE VULGARIS

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ABSTRACT

Background: Topical antibiotics are preferred for treatment of mild to moderate acne vulgaris. As there was the lack of studies comparing azithromycin 2% gel and clindamycin 1% gel in acne vulgaris, this study was taken up. **Materials and Methods:** A prospective study was conducted in which patients with mild to moderate acne vulgaris were enrolled. Relevant information on each patient was collected according to the proforma. Patients were advised to apply the test medication over the face, once daily at bedtime. They were followed up every 2 weeks, until 8 weeks. At each visit, efficacy of the test medication was assessed by lesion count, Global Clinical Evaluation (GCE), and Patient's Self-assessment (PSA). Safety of the medications was assessed by Investigator Rated Patient's Tolerability (IRPT) and adverse effects. **Results:** In our study, most of the patients were aged ≤20 years and were females. The malar region was the most common site of involvement. Patients receiving azithromycin 2% gel and clindamycin 1% gel showed significant improvement with respect to lesion count, GCE, and PSA. The difference in the improvement in the above parameters was found to be statistically insignificant between the two groups. Both the medications were found to be equally safe with the pruritus being more common with azithromycin and burning sensation with clindamycin. **Conclusion:** Both azithromycin 2% gel and clindamycin 1% gel are equally efficacious and safe in mild to moderate acne vulgaris.

Key words: Acne vulgaris, Azithromycin, Clindamycin gel

INTRODUCTION

Acne vulgaris is a common skin disorder in adolescence and has a multifactorial etiology. One major factor is the presence of *Propionibacterium acnes*, the suppression of which using topical antibiotics directly correlates with clinical improvement.[1]

Treatment options in acne vulgaris are many including topical and systemic antimicrobials, topical and systemic retinoids, hormonal therapy, and physical modalities. Antibiotics are considered effective in acne. In mild to moderate acne, topical therapy is preferred due to the less severity of the condition and moreover, the use of topical antibiotics has been found over the last decade to be efficacious, more acceptable, and associated with fewer unwanted effects and drug interactions as compared to systemic antibiotics.[2]

Among the topical antibiotics, most commonly used ones are erythromycin and clindamycin in gel form with similar efficacy in patients with acne.[2] Both are effective in reducing the *P. acnes* population in acne vulgaris. But there has been a gradual decrease in the efficacy of erythromycin over the last decade, probably due to antibiotic-resistant propionibacteria.[3] Recently, gel preparation of azithromycin has been introduced with claims of having better efficacy than erythromycin.[4] The newer macrolide-related azalide antibiotic azithromycin has been successfully used by oral route which has the additional advantage of being highly effective in pulse therapy.[4]

As there is a lack of studies comparing topical preparations of azithromycin and clindamycin in acne vulgaris, the present study was carried out.

MATERIALS AND METHODS

A prospective study was conducted from December, 2007 to March, 2010 in patients with mild to moderate acne vulgaris. 67 patients were recruited for the study, of which 60 completed the study. 30 patients received clindamycin gel, and 30 received azithromycin gel. The study was conducted by Department of Pharmacology, Sri Devaraj Urs Medical College, Tamaka, Kolar. A proforma containing detailed information on each patient was prepared according to the protocol designed for the study. Ethical clearance was obtained from Institutional Ethics Committee. Informed consent was taken from all the patients included in the study.

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Patients of either gender, in the age group of 15-30 years diagnosed with mild to moderate acne vulgaris involving face (defined as the presence of at least five inflammatory lesions, mainly erythematous papules and a few comedones on the face above the jaw line) were included. Patients with severe acne vulgaris, drug-induced acneiform eruptions, acne lesions predominantly involving the trunk and those with hypersensitivity to either drug were excluded from the study. Patients with acne vulgaris who had taken systemic antibiotics during the previous 3 months, those who were already on topical therapy for acne or any other topical therapy during the previous 4 weeks, female patients using oral contraceptives, pregnant and lactating women, immunocompromised patients, and those on medication for any chronic illness were also excluded.

Patients were advised to apply clindamycin 1% or azithromycin 2% gel, as a thin layer once daily at bed time, for a period of 2 months. The patients were advised to come for follow-up after 2, 4, 6, and 8 weeks and were assessed.

At baseline, patients were assessed for Lesion count. At each follow-up visit, they were assessed for lesion count, Global Clinical Evaluation (GCE), Patient's Self-assessment (PSA), Investigator Rated Patient's Tolerability (IRPT), and adverse effects.

1. Lesion count: At baseline and each follow-up visit, non-inflammatory lesions (comedones) and inflammatory lesions (papules, pustules and others) were counted. Efficacy was evaluated on the basis of change in the acne lesion number.
2. GCE: At each follow-up visit, the overall clinical evaluation based on the efficacy of the treatment was made by the investigator and was rated as,
   4 = Excellent
   3 = Good
   2 = Satisfactory
   1 = Poor
3. PSA: At each follow-up visit, an overall assessment of the efficacy of the treatment was made by the patient and was rated as,
   4 = Excellent
   3 = Good
   2 = Satisfactory
   1 = Poor
4. IRPT: At each follow-up visit, the investigator rated the patient's tolerability to the given drug as,
   4 = Excellent (no adverse events)
   3 = Good (mild, transient disturbances but no counter measures required)
   2 = Satisfactory (counter measures required)
   1 = Poor (severe adverse events that could not be controlled even by counter measures, possibly interruption of therapy).
5. Adverse effects: Throughout the study period, patients were carefully monitored for clinical adverse events, which were recorded at each follow-up visit. Adverse events included erythema, pruritus, burning, exfoliation, pigmentation, and others. Each adverse effect (if present) was rated as 1 at each follow-up visit, so that if an adverse effect was reported at all the 4 follow-up visits for 1 patient, it was rated as 4 for that patient.

Mean severity scores of lesions were analyzed using ANOVA, Bonferroni adjustment was used for comparing severity scores within the group and unpaired *t*-test was used to compare the lesions between the groups. To assess the overall global assessment scores of treatment by physicians, patients, and tolerability of treatment scores, Kruskal–Wallis test was applied and between the groups, Mann–Whitney U-test was applied.

RESULTS

Sixty patients were included in the study, of which 30 received clindamycin gel once daily, and the other 30 received azithromycin gel once daily. All the patients completed the study.

Table 1 depicts the demographic data of the patients. In the azithromycin group, 33% were males and 67% females with their mean age being 20.67 ± 3.95 years. Among the patients who received clindamycin, 43% were males and 57% females with mean age 21.6 ± 3.45 years.

Table 2 depicts distribution of lesions over the face. All patients in both the groups had their malar region involved with 86.6% patients in the clindamycin group, and 70% of them in the azithromycin group having their forehead involved at baseline.

All the patients in both the groups had both comedones and papules whereas only four of them in the azithromycin group and seven in the clindamycin group had pustules.

Table 3 depicts changes in the mean number of papules and comedones after treatment in both the groups. After initiation of treatment, there was a significant reduction in the mean severity score of papules in both the groups, at 4, 6, and 8 weeks (P = 0.0001 in both groups) and comedones in both the groups, at 6 and 8 weeks (P = 0.0001 in the azithromycin group and 0.035 in the clindamycin group, respectively) as compared to baseline. Between the groups, there was no significant difference in the scores.

There was no significant difference in the severity scores of the lesions between the groups at any visit.

The pustules were seen at baseline, 2 and 4 weeks but subsided and were absent at 6 and 8 weeks in both groups. Hence, there was a reduction in pustules after 4 weeks of treatment [Figure 1].

On global assessment of treatment by physicians, 44% and 31% of the total cases showed good to excellent response to treatment in azithromycin and clindamycin groups, respectively. Fifty-six percent and sixty-nine percent of the total cases in azithromycin and clindamycin groups, respectively, showed poor to a satisfactory response. The scores were significant in both the groups (P < 0.05), at 8 weeks compared to 2 weeks.

On the assessment of tolerability to treatment by physicians, [Figure 2] 98% and 97% of the total cases showed good to excellent tolerance to treatment in azithromycin and clindamycin groups, respectively. Two percent and three percent of the patients in

Table 1: Demographic details of the study groups

	Azithromycin group (n=30)	Clindamycin group (n=30)
Age (years) (%)	20.67±3.95 (16-30)	21.6±3.45 (16-30)
≤20	21 (70)	16 (53)
21-30	9 (30)	14 (47)
Males (%)	10 (33)	13 (43)
Females (%)	20 (67)	17 (57)

Table 2: Distribution of lesions on the face

Area of involvement	Azithromycin group n=30 (%)	Clindamycin group n=30 (%)
Forehead	26 (86.6)	21 (70)
Malar region	30 (100)	30 (100)
Chin	16 (53.3)	18 (60)

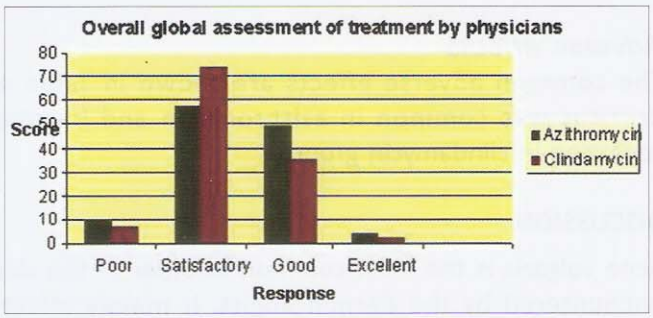

Figure 1: Efficacy of treatment. This figure depicts overall global assessment of treatment by physicians in the azithromycin and clindamycin groups, respectively

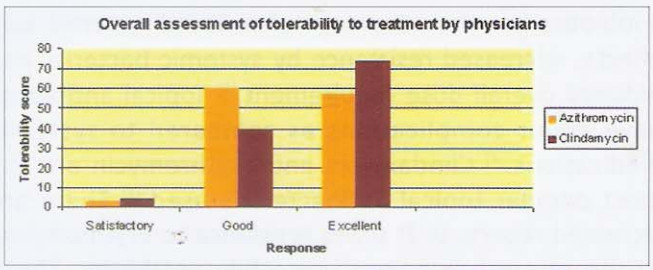

Figure 2: Tolerability to treatment. This figure depicts overall assessment of tolerability to treatment by physicians

Table 3: Changes in the mean number of papules and comedones after treatment

Lesions	Group	Baseline	2 weeks	4 weeks	6 weeks	8 weeks
Papules	Azithromycin					
	Severity score	7.4±2.60	5.8.±2.57	4.7±2.75*	3.9±3.11*	3.48±3.2*
	% change from basal		21.6	36.4	47.2	52.9
	Clindamycin					
	Severity score	6.93±2.28	5.52±2.29	4.6±2.11*	3.8±1.92*	3.6±2.11*
	% change from basal		20.3	33.6	45.1	48.0
Comedones	Azithromycin					
	Severity score	12.2±6.38	9.7±5.50	8.5±4.84	6.8±4.22†	5.6±3.67†
	% change from basal		20.4	30.3	44.2	54.0
	Clindamycin					
	Severity score	11.5±8.5	9.5±6.68	7.8±5.49	6.5±4.37†	6.0±5.49†
	% change from basal		17.3	32.1	43.4	47.8

*P<0.05 as compared to baseline – papules, †P<0.05 as compared to baseline – comedones

azithromycin and clindamycin groups, respectively, showed a satisfactory response. The scores were not significant in both the groups as compared to 2 weeks.

Overall global assessment of treatment by patients

On the assessment of treatment by patients, 54% and 41% of the total cases viewed the treatment as good to excellent in azithromycin and clindamycin groups, respectively. 46% and 59% of the total cases in azithromycin and clindamycin groups, respectively, assessed the treatment as poor to satisfactory. The scores were not significant in clindamycin but in azithromycin there were significant results at 8 weeks as compared to 2 weeks ($P < 0.05$).

Adverse effects

The common adverse effects are shown in Table 4, pruritus was common in azithromycin and burning sensation in clindamycin groups.

DISCUSSION

Acne vulgaris is the most common disorder of the skin encountered by the dermatologist. It mainly affects adolescents. If left untreated, it can lead to serious physical and psychological consequences.[5,6] Antibiotics are considered effective in acne vulgaris.[7] Topical use of antibiotics has the advantage of reduced systemic side effects, decreased resistance by systemic bacteria, and reduced overall dose requirement.[4] Topical antibiotics have minor complications as compared to systemic medications.[4] Clindamycin and erythromycin are the most popular topical antibacterials used.[2] There are increased reports of *P. acnes* resistance to erythromycin. Azithromycin is a newer macrolide antibiotic. There are the lack of studies that compare azithromycin and clindamycin in acne. Hence, we have compared these two drugs in patients suffering from mild to moderate acne vulgaris.

Acne vulgaris mostly appears during the middle to late teenage period.[8] In our study, in both the study groups, majority of the patients were <20 years. In a study on acne vulgaris by Becker *et al.*, the enrolled patients were aged between 12 and 30 years.[9] The incidence of acne is more in males than females.[10] In our study, 67% and 57% of the total cases were females in the azithromycin and clindamycin group, respectively. In another study by RC McHugh, 79% of the enrolled patients were females.[4] Females are more conscious about their physical appearance and, this together with the fact that social customs make women more aware of their attractiveness, may explain the female predominance in our study.

In the present study, the malar region was the most frequent site of involvement. Even the literature says that typical adolescent acne involves the entire face but shows predilection for cheeks.[11]

In our study, azithromycin and clindamycin significantly decreased the papule count at 4, 6, and 8 weeks when compared to baseline. Clindamycin also has an additional anti-inflammatory action by reducing the skin surface levels of free fatty acids.[2] This also may have contributed to the reduction in lesion count. With respect to decrease in papule count, they did not differ significantly from one another. This similarity in response may be attributed to the similarity in the mechanism of action of the two drugs. RC Mc Hugh observed in his study that azithromycin and erythromycin significantly reduced the inflammatory lesion count and that both are comparable.[4] It can be concluded that azithromycin and clindamycin are equally efficacious in reducing the inflammatory lesion count. With respect to change in comedone count, we observed that azithromycin and clindamycin produced a significant response at 6 and 8 weeks. Datta PK's study showed 63% reduction with azithromycin by the end of 8 weeks and the study by Alan R. Shalita showed 30% reduction with clindamycin.[7,12] There was an insignificant difference between azithromycin and clindamycin groups in the comedone count, at baseline and follow-up visits which again may be due to the similarity in mechanism and site of action. Pustules were seen at baseline, 2 and 4 weeks but subsided and were absent at 6 and 8 weeks in both groups. Hence, there was a reduction in pustules after 4 weeks of treatment.

In our study, the overall global assessment of treatment by physicians suggests that 44% and 31% of the total cases showed good to excellent effect in the azithromycin and clindamycin groups, respectively. In a

Table 4: Adverse effects in both the groups

Adverse effects	Azithromycin	Clindamycin
Erythema	17	12
Exfoliation	13	10
Pruritus	32	18
Pigmentary changes	4	3
Burning sensation	11	23

study by Datta PK and Alan R. Shalita, according to the physicians, 57% and 62% of the total cases respectively showed good to excellent response.[7,12] We see here that, azithromycin fared better than Clindamycin, though not significantly, with respect to GCE. In the overall assessment of tolerability to treatment, as assessed by physicians, 97% of the cases in the clindamycin group showed good to excellent tolerance, when compared to the azithromycin (98%) group. When we assessed the adverse effects, we observed that pruritus was more common in the azithromycin group and burning sensation was more common in the clindamycin group.

SUMMARY

A randomized prospective study was conducted on patients with mild to moderate acne vulgaris. Patients were advised to apply the test medication (azithromycin 2% or clindamycin 1% gel) once daily over the face for 8 weeks. The aim of the study was to compare and evaluate the efficacy and safety of the two drugs. Majority of the patients were aged ≤20 years and were females. Malar region was the most common site of involvement.

Efficacy of the treatment was assessed by lesion count, GCE, and Patients' Self-assessment (PSA). Patients in both the study groups showed a significant response at 6 and 8 weeks with regard to Lesion Count, but there was no significant difference in the response between the groups. Both the drugs were found to be equally efficacious with respect to GCE and PSA.

Safety of the medications was analyzed by IRPT and adverse effects. Both the drugs proved to be equally safe with pruritus being more common in the azithromycin group and burning sensation in the clindamycin group.

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