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ORIGINAL ARTICLE

Comparison of Efficacy of Azithromycin and Levamisole in Combination with Azithromycin in Patients of Moderate to Severe Acne

SHABIR HUSSAIN[1], AMJAD MUSTAFA[2], ARIF MUMTAZ[3], MOHAMMAD SOBAN[4], GHAZALA SHAHEEN[5], SHAFIQ AHMAD[6]

[1]*Associate Professor Department of Pharmacology Bannu Medical College, Bannu*
[2]*Assistant Professor Department of Pharmacology Khyber Medical University Institute of Medical Sciences (KMU-IMS), Kohat*
[3]*Assistant Professor Department of Medicine Khyber Medical University Institute of Medical Sciences (KMU-IMS), Kohat*
[4]*Lecturer Khyber Medical University Institute of Medical Sciences (KMU-IMS), Kohat*
[5]*Assistant Professor Department of Pharmacology Khyber Medical University Institute of Dental Sciences (KMU-IDS), Kohat*
[6]*Lecturer Department of Pharmacology Khyber Medical University Institute of Dental Sciences (KMU-IDS), Kohat*
Correspondence to: Dr. Amjad Mustafa; Email: drmustafa670@gmail.com; Cell: +92 333 5132986

ABSTRACT

Objective: To compare the efficacy of azithromycin plus levamisole versus azithromycin in the treatment of moderate to severe acne.

Design: It was a randomized controlled trial.

Study Settings: This study was conducted at Department of Pharmacology over 1 year from March 2020 to March 2021 at Khalifa Gulnawaz Teaching Hospital, Bannu, Khyber Pakhtunkhwa & DHQ Teaching Hospital, Bannu, Khyber Pakhtunkhwa.

Material and Methods: Sixty (120) patients of acne having either gender age between ≤18 to ≥28 years who meet the inclusion criteria were include in this study. Randomly patients were divided into two groups, in group A patients (n=60) were administered azithromycin (500 mg daily for 3 days in a week) plus levamisole (150 mg daily for two days in a week) for 8 weeks. In group B patients (n=60) patients were administered azithromycin 500 mg daily for 3 days for 8 weeks. “Acne Global Severity Score” was used for grading in patients who respond to treatment after 08 weeks therapy.

Results: A total of 120 patients were enrolled in this study In Group-A Azithromycin + Levamisole, 19 males (31.66%) and 41 females (68.33%) and in Group-B (only Azithromycin) 23 males (38.33%) and 37 females (61.66%) were enrolled. Efficacy was noted in 52(86.66%) in patients of group-A receiving azithromycin plus levamisole combination where it was noted in 29(48.33%) in patients of group B receiving azithromycin (p=0.0031).

Conclusion: It is concluded that for treatment of moderate acne vulgaris to severe acne vulgaris combination of azithromycin plus levamisole therapy proved more effective than azithromycin. However, there is need to conduct further comparative studies to measure efficacy in moderate acne vulgaris to severe acne vulgaris.

Keywords: Azithromycin, Levanisole, Acne Vulgaris, Efficacy, Moderate Acne, Efficacy

INTRODUCTION

Acne vulgaris is known as a chronic, inflammatory pilosebaceous unit disease, commonly reveals in adults with polymorphic type of lesions such as papules, nodules, cysts and comedones. If the disease is not properly treated it may result in scaring.[1] This multidimensional disease is affected by genetic, hormonal, microbiological and immunological factors. Although its prevalence is reported very high in adults, but it may influence the patients of all age groups.[2] Generally its severity is directly proportional to time and age.[3]The inflammatory fluctuations in acne patients can be somewhat chronic and may cause to residual scaring severely. Generally in males it is frequency reported problem. The range of age in this disease is 14-17 years in females and 16-19 years in boys. The difference on the basis of gender is not well reported in literature.[4]

On the base of severity of lesion acne vulgaris is graded as mild, moderate and severe. Mild acne shows non-inflammatory lesions which is known as comedones or inflammatory lesions which is known as papulopustular lesions. The appearance of lesions in moderate form is usually more inflammatory, rarely nodule or in some cases both inflammatory & nodule.[5,6,7]

There are several treatment modalities are available for acne vulgaris like topical antibiotics (Erythromycin, Tetracycline and Clindamycin), oxidizing agent like Benzoyl peroxide, topical retinoids, systematic antibiotics (Tetracycline, Erythromycin, Minocycline, Doxycycline and Azithromycin) systematic retinoids like Isotretinoin and therapies of hormones (spironolactone and mixture of oral contraceptive tablets) be contingent on disease severity.[8] Azithromycin is an antibiotic having property to stop synthesis of protein which is RNA dependent. Levamisole have immune modulatory characteristics and also anthelminthic agent. As it stop inflammatory cytokines levasimole applies his immune modulatory influence whereas add with other medicines such as azithromycin.[9]

Waqas et al.[10] reported the efficacy was (67.8% vs. 83.1%; p=0.000) in patients treated with azithromycin + oral levamisole and azithromycin only group respectively.

To the best of our knowledge there is lack of local published data so the purpose of the current study was to repeat this trial to further confirm the results. Current study would help in the choice of more suitable treatment option for patients having acne vulgaris in future.

MATERIAL AND METHODS

The study was conducted after getting approval from the hospital's ethical and research committee. Informed consent in written form was taken from enrolled patients after telling them the protocols of the study. It was a randomized controlled trial conducted at Department of Pharmacology over 1 year from March 2020 to March 2021 at Khalifa Gulnawaz Teaching Hospital, Bannu, Khyber Pakhtunkhwa & DHQ Teaching Hospital, Bannu, Khyber Pakhtunkhwa. Sample size of 120 (60 cases in each group) is calculated with 70% power of test and 85% confidence interval (2-sided) while taking expected efficacy of 83.1% with Azithromycin + oral Levamisole and vs. 67.8% with azithromycin only.[10]

Patients of both genders aged between 15 to 30 years having moderate to severe acne vulgaris were included in this study. Patients with history of allergy, disorders of photosensitivity or dermatitis, lactating mothers, patients on systematic treatment (as per medical record & history), hepatic or renal disease, history of excessive use of alcohol, anticoagulants or anti-convulsant patients were excluded from study. Randomly patients were divided into two groups, in group-A patients (n=60) administered with azithromycin (500 mg daily for 3 days in a week) plus levamisole (150 mg daily for two days in a week) for 8 weeks. In group-B patients (n=60) were administered with azithromycin 500 mg daily for 3 days for 8 weeks. "Acne Global Severity Score" was used for grading in patients who respond to treatment after 08 weeks therapy.

The response of azithromycin + levamisole and azithromycin alone at follow up were noted as (ά) excellent response; when reduction greater than 90% observed, (b) good response; when reduction between 60-90% observed (c) moderate response; when reduction between 30-60% observed (d) mild response; when reduction less than 30% observed. Before therapy at first visit scoring was done then scoring was done after 08 weeks of treatment. By calculating pre and post treatment score efficacy of drugs was determined. Beyond or equivalent to 50 percent reduction in global acne score at baseline was considered as efficacious response while below 50% reduction in global acne score as compare to baseline score was considered as non-efficacious

All collected data was entered then analysed in SPSS version 19.0. Quantitative variables such as age and severity score was given as mean ± SD. Qualitative data such as gender and efficacy of the treatment was given as percentages and frequency . Chi-square test (X^2) was applied to compare the efficacy between two groups. Data was stratified with age, gender and disease severity. The p-value ≤0.05 was set as a statistically significant.

RESULTS

A total of 120 patients were enrolled in this study in Group-A Azithromycin + Levamisole, 19 males (31.66%) and 41 females (68.33%) and in Group-B (only Azithromycin) 23 males (38.33%) and 37 females (61.66%) were enrolled. The age of the patients were ranged from 15– 30 years. In Group a maximum numbers (58.3%) of patients have age less than 18 years in Group B 53.3% patients were less than 18 years as shown in Table 1. According to acne global severity score 32 (53.33%) patients were in group-A with moderate acne and 36(60.0%) in group-B with severe acne. While 28(46.66%) patients were in group-A with moderate acne and 24(40.0%) had severe acne in group-B.

In azithromycin + levamisole group, an excellent response was noted in 17 (28.33%), good response in 22(36.66%), moderate response in 8(13.33%), mild response in 11 (18.33%) and no response was observed in 2 (3.33%) patients. While in only azithromycin group excellent response was noted in 19(31.66%), good response in 26(43.33%), moderate response in 6(10.0%), mild response in 8(13.33%) and no response was noted in 1(1.66%) patients as shown in table 2. The overall response in all grades was observed statistically significant with p-value < 0.05. Efficacy was noted in 52(86.66%) in patients of group-A receiving azithromycin plus levamisole combination where it was noted in 29(48.33%) in patients of group B receiving azithromycin Alone (p=0.0031).

Table 1: Demographic characteristics if the patients

Groups			
Demographics		Azithromycin + Levamisole (%)	Azithromycin (%)
Age	≤18	35(58.3)	32(53.3)
	19-22	13(21.66)	16(26.66)
	23-26	7(11.66)	8(13.33)
	30 plus	5(8.33)	4(6.66)
Gender	Male	19(31.66)	23(38.33)
	Female	41(68.33)	37(61.66)
Global acne scores	Moderate acne	32(53.33)	36(60.0)
	Severe acne	28 (46.66)	24(40.0)

Table 2: Response of patients to treatment in groups

Response	Azithromycin + Levamisole (%)	Azithromycin (%)	Total (%)
Excellent	17(28.33)	19(31.66%)	30.0
Good	22(36.66)	26(43.33%)	40.0
Moderate	8(13.33%)	6(10.0%)	11.66
Mild	11(18.33%)	8(13.33%)	15.83
No response	2(3.33%)	1 (1.66%)	2.5
Total	100%	100	100

Table 3: Efficacy of treatment in both groups

Efficacy	Azithromycin + Levamisole (%)	Azithromycin (%)	P-value
Yes	52(86.66)	29(48.33)	0.0031
No	8(13.33)	31(51.66)	
Total	60	60	

*The observed difference was statistically significant

DISCUSSION

It has been considered since a long time that use of macrolides like azithromycin has anti-inflammatory influence.[12] Ianaro et al. (2000) described that inflammation has been suppressed by stopping growth of pro-inflammatory elements like NOx , PGE_2, and TNF-α. Also it had observed that macrolides down regulate production of ROS, apoptosis and neutrophil migration. There are major evidences available that macrolides specially azithromycin, put immunomodulatory influence by inhibiting the IL-8 cytokines and IL-1α production.[13,14] Further expression in

un-regulated way of proinflammatory factors like TNF-α, IL-1α, IL-8 and PGE-2 had been noted in patients of acne. So, in acne vulgaris patient's beneficial effects of azithromycin can be reconciled by antimicrobial features of this medication.[15]

Majority of our patients 35(58.3%) were aged less than 18 years. Batool et al. (2010)[16] and Ullah et al (2014)[17] reported mean age of the acne vulgaris patients as 17.6±3.6 years and 16.31±2.84 respectively in their researches and Shaukat et al[18] reported that mean age was 21.35±2.17 years which is very close to results of our study. Acne global severity score in our study was 53.33% in group A and 60.0% in group B had moderate acne and 46.66% had severe acne in group A and 40.0% in group B. Hazarika et al. in (2016)[19] also had reported very similar results presenting severe acne prevailing over moderate as reported in our study. Rassai et al. al[11] also performed same research, compared azithromycin plus levamisole and azithromycin alone in patients of acne vulgaris. After 8 weeks therapy there was observed statistically significant difference between both groups.

Efficacy was noted in 52(86.66%) in patients of group-A receiving azithtromycin plus levamisole combination where it was noted in 29(48.33%) in patients of group B receiving azithromycin alone. Rassai et al. al[11] in a randomized controlled trial included 169 acne patients, our study efficacy is very close to findings of his study.[11] Levamisole seems to be very effective as a combination therapy with azithromycin, but further research is prerequisite in this regard.

CONCLUSION

It is concluded that for treatment of moderate acne vulgaris to severe acne vulgaris combination of azithromycin plus levamisole therapy proved more effective than azithromycin alone. However, there is need to conduct further comparative studies to measure efficacy in moderate acne vulgaris to severe acne vulgaris.

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