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EFFICACY AND SAFETY OF ORAL AZITHROMYCIN PULSE VERSUS DOXYCYCLINE IN THE TREATMENT OF ACNE VULGARIS: A HOSPITAL BASED COMPARATIVE STUDY.

Dermatology

Dr. Ratan Singh*
Assistant professor, Department of Dermatology, Veer Chandra Singh Garhwali Government Institute of Medical Sciences and Research, (VCSGGIMS&R) Srinagar Garhwal, Uttarakhand, India. *Corresponding Author

ABSTRACT

Objectives: This present study was to compare the efficacy and safety of oral azithromycin pulse versus doxycycline daily in terms of severity index in patients of acne vulgaris. And also evaluates the incidence and severity of the side effects of azithromycin treated group patients as compared to doxycycline treated patients. **Methods:** Patients were included according to the proposal by the Consensus Conference for the Classification of Acne. Acne lesions were graded according to the severity index described by Michaelsson et al by counting the number of open comedones, closed comedones, papules, pustules, infiltrated lesions and cystic lesions. The acne lesions severity index grading was done as 0.5 for comedones, 1 for papules, 2 for pustules, 3 for infiltrated lesions and 4 for cystic lesions. Total severity score of acne vulgaris was calculated by multiplying the number of each type of acne lesion present in that particular patient with its severity index and then adding them all together. **Results:** Greater mean differences (219.170) of severity score were seen in azithromycin as compared to doxycycline (174.000) group patients. Mean differences was extremely significant ($p<0.0001$) seen in azithromycin group patients as compared to doxycycline treated group patients. **Conclusions:** A significant better improvement was seen in group A patients (combination of oral azithromycin in pulse dose along with topical erythromycin) as compared to group B patients (oral doxycycline daily dose along with topical erythromycin) in the treatment of acne vulgaris. Hence, Oral azithromycin in pulse dose is more convenient, efficacious and safer as compared to oral doxycycline daily for the treatment of acne vulgaris.

KEYWORDS

Acne vulgaris, azithromycin, doxycycline, severity score

INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit of skin which includes the hair follicle and sebaceous glands [1].

It is one of the most common skin disorders treated by dermatologists. The major factors involved in the pathophysiology of acne are obstruction of follicles due to abnormal keratinization of infundibular epithelium, stimulation of sebum secretion by androgensensitive sebaceous glands, and inflammation induced by microbial colonization with Propionibacterium acnes [2].

Though acne vulgaris a benign self-limiting disorder, it can leave behind permanent disfiguring scarring and post inflammatory hyperpigmentation [3]. This has profound impact on the psychological wellbeing of the individual. With its high prevalence in the adolescent population, acne affects the emotional and social development of the individual negatively [4]. Considering the psychosocial ramifications of acne vulgaris, it is pertinent to treat patients effectively in order to improve their quality of life.

Tetracyclines, including tetracycline, doxycycline, minocycline and lymecycline, as well as drugs like erythromycin, clindamycin, co-trimoxazole and trimethoprim have been shown to be effective oral agents [5]. Macrolide antibiotics have a substantial cumulative effect in many tissues especially epithelial lining fluid and host defense cells, such as macrophages and polymorphonuclear

Leukocytes [6]. Macrolides share mild to moderate side effects such as nausea, vomiting, diarrhea, and abdominal pain, which are usually observed in erythromycin administration. Azalides like azithromycin, as a class of macrolides, possess advantageous pharmacokinetic and pharmacodynamic properties compared to other macrolides [7]. Objectives of our study was to compared the efficacy and safety of oral azithromycin pulse versus doxycycline daily in terms of severity index in patients of acne vulgaris.

METHODS

This present study was conducted in the Department of Dermatology, VCSGGIMS &R, Srinagar, Pauri, Garhwal, Uttarakhand, India during a period from July 2020 to April 2021.

A total of 100 acne vulgaris patients who attending in Dermatology OPD, of VCSGGIMS were enrolled in this study. Entire subjects signed an informed consent approved by institutional committee of VCSGGIMS & R was sought.

In accordance to the proposal by the Consensus Conference for the Classification of Acne, those patients having moderate-to-severe acne with lesions like papules, pustules, nodules and cysts and not responding to the conventional treatment were included in this study. Patients suffering from liver diseases, patients taking antibiotics for any other illness and pregnant woman were excluded from this study.

Most of the patients 80(80%) in this study had acne lesions for the past 1 year and a few 20(20%)had for 2 years.

Acne lesions were graded according to the severity index described by Michaelsson et al [8] by counting the number of open comedones, closed comedones, papules, pustules, infiltrated lesions and cystic lesions. The acne lesions severity index grading was done as 0.5 for comedones, 1 for papules, 2 for pustules, 3 for infiltrated lesions and 4 for cystic lesions.

Total severity score of acne vulgaris was calculated by multiplying the number of each type of acne lesion present in that particular patient with its severity index and then adding them all together. Patients participated in this study were divided into two groups.

The group A patients (65 in number) were administered oral azithromycin 500 mg before meals daily for 3 consecutive days in a 10-day cycle with remaining 7-day period as drug free days.

The group B patients (35 in number) were administered oral doxycycline 100 mg after meals daily for 10 days.

For all the patients in both the groups, topical application of erythromycin twice daily was prescribed. Each and every patient in both the groups was clinically assessed at 10-day intervals for a period of 3 months. At each time of clinical assessment of the patient, severity score of acne vulgaris was calculated and recorded by the dermatologists, then the average of their two noted scores was taken for the assessment purpose. At the end of the third month of this study, final clinical assessment of all the patients was done by calculating and recording the severity score of the acne vulgaris lesions.

OBSERVATIONS

In this present study, a total of 100 patients of acne vulgaris were included. Among them, 40(40%) patients were males and 60(60%) were females. Male and female ratio was 2:3.

In this present study, greater mean differences (219.170) of severity score was seen in azithromycin group patients as compared to doxycycline (174.000) group patients. Mean differences was extremely significant seen in azithromycin group patients as compared

to doxycycline.

Antibiotics used in patients	Severity score		Mean differences	t-value	P-value
	Initial at 0 days (Mean ± S.D)	After 3 months (Mean ± S.D)			
Azithromycin (65)	271.43 ±145.65	52.26±124.67	-219.170	-9.217	<0.0001
Doxycycline (35)	262.72±134.27	88.72±122.54	-174.000	-5.663	<0.0001

Table.1. Mean severity score of acne lesions before and after treatment.

% Severity Reduction	Azithromycin	Doxycycline	Total
<40%	5(7.69%)	7(20%)	12(12%)
40%-80%	22(33.85%)	19(54.28%)	41(41%)
>80%	38(58.46%)	9(25.71%)	47(47%)
Total	**65**	**35**	**100**

Table.2. percentage severity reduction

In this present study, greater than 80% severity reduction was seen in most of the patients 38(58.46%) of azithromycin group as compared to doxycycline group 9(25.71%). And 40%-80% severity reduction was seen in 22(33.85%) patients of azithromycin as compared to 9(25.71%) doxycycline group patients.

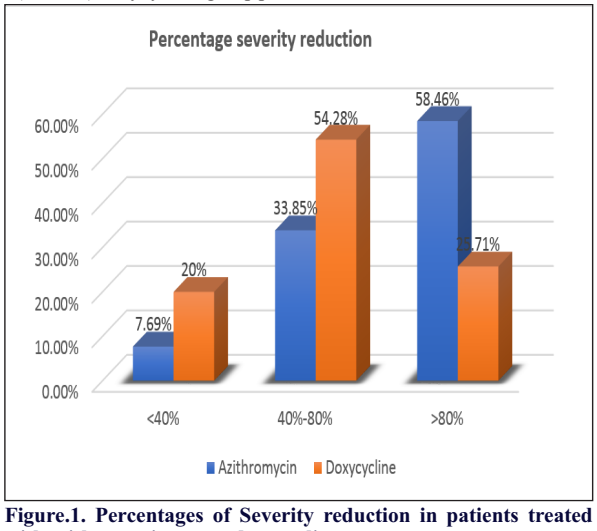

Figure.1. Percentages of Severity reduction in patients treated with azithromycin versus doxycycline.

DISCUSSIONS

Acne Vulgaris is a chronic inflammatory disorder involving the blockage and/or inflammation of pilosebaceous follicles. It is clinically characterized by comedones, papules, pustules, nodules, cysts and scars. It may have an adverse effect on psychosocial and emotional impact in an individual which may lead to social phobias, withdrawal from society and clinical depression [9].

Topical and oral medications can be used for treatment of acne. P. acnes, which is highly sensitive to a number of antimicrobial agents of different classes, including macrolides, tetracyclines, penicillins, clindamycin, aminoglycosides, cephalosporins, trimethoprim, and sulfonamides [10]. Here, we have studied the efficacy of two drugs used routinely in clinical practice worldwide Azithromycin and Doxycycline.

Azithromycin is a broad-spectrum macrolide antibiotic. It prevents bacteria from growing by interfering with their protein synthesis. It binds reversibly to the 50S subunit of the bacterial ribosome, thus inhibiting translation of mRNA. It is used in the treatment of acne due to its anti- bacterial, immunomodulatory and antiinflammatory properties. Common side effects include diarrhea, nausea and abdominal pain, palpitations, angina, dyspepsia, flatus, vomiting, melena, jaundice, vaginal monilia, vaginitis, nephritis, dizziness, headache, vertigo, somnolence and fatigue [11].

Doxycycline is a broad spectrum semisynthetic tetracycline. It inhibits bacterial protein synthesis by reversibly binding to the 30S ribosomal subunit and preventing the association of aminoacyl-tRNA with the bacterial ribosome, thereby giving the immune system time to kill and remove the bacteria. Further inhibition of protein synthesis occurs in mitochondria through binding to the 70S ribosomes. Common side effects include nausea, vomiting, diarrhoea, epigastric burning and oesophagitis. Stevens-Johnson syndrome and toxic epidermal necrolysis may occur with the use of doxycycline. The accumulation of doxycycline in teeth and bones leads to discoloration of teeth. It may also cause enamel dysplasia, bone deformities and impairment in bone growth. It has also been associated with benign intracranial hypertension [12].

In this present study, a total of 100 patients of acne vulgaris were included. Among them, 40(40%) patients were males and 60(60%) were females. Male and female ratio was 2:3. Most of the pateints 70(70%) were belonged in age group of 18 years to 30 years

Babaeinejad et al. concluded that doxycycline is more effective in patients above 18 years old.26 It should also be noted that in both these studies, patients were treated with 4 consecutive days of 500 mg azithromycin per month; while it seems that intermittent higher doses [13,14,15] mainly three times in 10-days or thrice weekly, may be more advantageous. Further, administration of azithromycin in combination with topical erythromycin results in significantly better improvement than doxycycline combined with topical erythromycin [15].

A study by Rafiei et al. found azithromycin to have a slightly higher efficacy in the treatment of inflammatory acne lesions in comparison to tetracycline [16]. On the other hand, retrospective study of patients who could not tolerate tetracycline, erythromycin, minocycline, and doxycycline proved that azithromycin is a significantly better antibiotic regimen for acne [17]. Despite the usefulness of both isotretinoin and azithromycin in the treatment of moderate to severe acne, superior efficacy of isotretinoin is evident [18].

In this present study, greater mean differences of severity score were seen in azithromycin group patients as compared to doxycycline group patients. Improvements were seen, in various parameters assessing lesion severity, in patients with acne receiving both azithromycin and doxycycline separately. The reduction in the percentage in the number of inflammatory lesions post 3 month was better with azithromycin group as compared to Doxycycline, whereas there was improvement with respect to the reduction in number of non-inflammatory lesions and total lesions in both groups.

Greater than 80% severity reduction was seen in most of the patients 38(58.46%) of azithromycin as compared to doxycycline group 9(25.71%). And 40%-80% severity reduction was seen in 22(33.85%) patients of azithromycin as compared to 9(25.71%) doxycycline group patients.

The difference in the degree of improvement was extremely statistically significant ($p<0.05$) for any of the efficacy parameters when compared with the outcome of Azithromycin treated group Vs. Doxycycline treated group for 3 months time. So, the choice of the drug may depend on parameters like cost of drug and side effect profile of the drug rather than its efficacy.

Mable et al, have reported that azithromycin in pulse dosing not only improves patient compliance but is a safe and effective treatment option for all grades of acne vulgaris. The researchers have reported up to 85% clearance in lesions by the 8th week [19]. An open-label noncomparative study conducted by Kapadia et al, in Pakistan found almost 40% improvements in 82% patients by four weeks which increased to 80% clearance by the 12th week [20].

CONCLUSIONS

This study concluded that the acne vulgaris was commonly occurred in young age female patients. The incidence and severity of the side effects was seen minimum in azithromycin treated patients as compared to doxycycline treated patients. A significant better improvement was seen in group A patients (combination of oral azithromycin in pulse dose along with topical erythromycin) as compared to group B patients (oral doxycycline daily dose along with topical erythromycin) in the treatment of acne vulgaris. Hence, Oral azithromycin in pulse dose is more convenient, efficacious and safer as compared to oral doxycycline daily for the treatment of acne vulgaris.

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