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Original Research Article.

A Comparative Study Between the Efficacy of Oral Azithromycin Versus the Efficacy of Oral Doxycycline Over 6 Months in Patients of Meibomian Gland Dysfunction

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ABSTRACT

Background: Meibomian Gland Dysfunction (MGD) is a chronic, diffuse abnormality of the Meibomian Glands (MG), commonly characterized by obstruction of the terminal duct and/or quantitative/qualitative changes in the secretions of the meibomian glands. These cases usually require conservative management in the form of lubrication and warm compresses; however, severe cases may require anti-inflammatory and topical or systemic antibiotics.

Materials and Methods: This was a prospective, randomized, interventional, parallel-group, open-label study that included 100 patients diagnosed with MGD. Patients fulfilling the inclusion and exclusion criteria were enrolled and randomized into 2 groups of 50 patients each: Group 1 administered Azithromycin tablet 500 mg/day for 5 days and Group 2 given Doxycycline tablet 200 mg/day for 4 weeks. Follow-up was done at 7 days, 4 weeks, 3 months and 6 months.

Results: The mean age of patients was 59.83±12.89 years. The most common symptom was itching. The most common sign was altered MG secretion. The symptom and sign scores were comparable at baseline in the two groups. Azithromycin was significantly better at controlling bulbar redness scores at 3 and 6 months. The side effects like nausea, diarrhoea, abdominal cramps were similar in both drugs but were prolonged in doxycycline group.

Conclusion: Azithromycin and Doxycycline significantly improved the symptoms, signs and OSDI score in MGD patients, but the systemic side effects lasted longer with Doxycycline. Therefore, a 5-day course of oral Azithromycin is recommended based on equivalent clinical improvement with shorter duration of treatment and lesser side effects as compared to oral Doxycycline.

Keywords: MGD, Azithromycin, Doxycycline.

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INTRODUCTION

According to the International Workshop on MGD and the TOFS DEWS II, both held in 2011, Meibomian Gland Dysfunction (MGD) is a chronic, diffuse abnormality of the Meibomian Glands, commonly characterized by obstruction of the terminal duct and/or quantitative/qualitative changes in the secretions of the meibomian glands. This may result in alteration of the tear film, clinically apparent inflammation, symptoms of eye irritation, and ocular surface disease.[1,2]

MGD occurs as a result of terminal duct obstruction by thickened meibum that contains keratinized cell material formed by hyperkeratinization of the ductal epithelium. The obstruction of the Meibomian Glands may lead to intra-glandular cystic dilatation, gland dropout, meibocyte atrophy and low secretion, leading to increased evaporation of the tear film causing evaporative dry eye, increased bacterial growth and ocular surface inflammation and damage.[1] Alterations in the lipid phase of tear film points towards MGD, hence, it may, thus, be accepted that MGD is important, underestimated, and probably, the most common cause of dry eye disease due to increased evaporation of the tears.[3]

The symptomatic MGD patients usually present with dry eye symptoms like foreign body sensation or itching, burning sensation etc. the common signs of MGD seen in patients are alteration of tear film, frothy discharge at eyelid margin, meibomian gland plugging or drop out, thickening and opacification of meibum. Most of these cases usually require conservative management in the form of lubrication and warm

compresses; however, severe cases may require anti-inflammatory topical or systemic antibiotics. Antibiotics such as Doxycycline and Azithromycin have shown anti-inflammatory properties. Although, the previous studies have shown the efficacy of both oral Doxycycline and oral Azithromycin in the treatment of MGD, to the best of our knowledge there has been no study in India comparing their effects over extended period of 6 months. Therefore, this study was conducted to compare the efficacy of oral Azithromycin versus the efficacy of oral Doxycycline over 6 months in patients of MGD.

MATERIALS & METHODS

This study was conducted to compare the efficacy of oral Azithromycin versus the efficacy of oral Doxycycline over 6 months in patients of MGD.

Data was collected from the patients of MGD attending Ophthalmology outpatient department, Government Medical College, Patiala willing to participate in the study. All participants signed an informed consent. Patient data was collected according to the proforma. All MGD patients of age 18 years and above were included. Exclusion criteria were therapy with systemic or topical antibiotics within 1 month before selection, contact lens wear, ocular diseases (such as keratitis, episcleritis, scleritis), punctal occlusion, liver disease, pregnancy and breast feeding, allergy to Azithromycin or Cyclins, Allergic Keratoconjunctivitis, ocular and orbital surgery of any kind, altered lid anatomy and patients allergic to any component of procedural medication such as stains. A prospective, Randomized Trial on 100 patients was conducted. Randomization was done by using closed envelopes for allocation to both the groups. The Meibomian gland assessment was done by a masked observer. The participants were divided into two groups: Group 1: Azithromycin tablet 500 mg per day for 5 days and Group 2: Doxycycline tablet 200 mg per day for 4 weeks, along with conservative management to all patients throughout the study. Follow-up was done at 7 days, 4 weeks, 3 months and 6 months. A detailed history was taken including age, sex, ocular symptoms, detailed history of diabetes, allergy, smoking, drug intake, joint pain, chemical injury. The presence of any systemic disease, history of ocular surgeries, trauma or contact lens use and ocular medications was noted.

Severity of five main symptoms was measured on a 4-point categorical scale (0–3) according to patients' response to questions: itching, burning, foreign body sensation, dryness and eyelid swelling. (Table 1.)

After recording visual acuity with Snellen's chart, Slit lamp examination was performed to assess and record the severity of seven signs on a 4-point categorical scale: MG secretion, number of plugged gland orifices, conjunctival injection, lid margin redness, lid margin debris, tear break up time (TBUT), and ocular surface staining with fluorescein. (Table 2).

MGD was diagnosed based on having at least two symptoms and two signs (one must be the presence of meibomian gland signs) with a minimum severity score of 2 for each.

Ocular Surface Disease Index was calculated by asking 12 questions: questions 1–5 refer to ocular pain or visual difficulties; questions 6–9 are about visual functionality in daily life such as reading or driving at night; and questions 10–12 analyze environmental factors such as air conditioning or wind. The number in the box that best represents each answer was circled. The OSDI score was assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease.

Schirmer's Test was performed with a strip of commercially available pre-sterilized Whatman 41 filter paper measuring 5mm x 35mm without anaesthesia. A value less than 10 mm was taken as dry eye.

Tear Break Up Time (TBUT) was tested by instilling a 2% fluorescein dye into the inferior conjunctival fornix and measuring the time taken for the appearance of the first randomly distributed dark spot in the pre-corneal tear film under broad beam of cobalt blue light of slit lamp biomicroscope. A value less than 10 seconds was taken as abnormal.

Ocular Surface Staining

The ocular surface staining score was adapted as a modification of panels in the Oxford scale and was performed before assessment of TBUT. The panel most similar to the pattern and the number of dots on the cornea and conjunctiva was chosen, and the corresponding grade was applied. (Figure 1)

Statistical Analysis

The data was noted in excel format. Data was subjected to statistical analysis using SPSS version 22. Student t test and Chi Square test was used for assessment of level of significance. p-value less than 0.05 was taken as significant.

Table 1: Grading of five symptoms in 100 patients with Meibomian gland disease.

Symptom	Grade 0	Grade 1	Grade 2	Grade 3
1. Itching	None	Awareness	Desire to rub	Frequent rub
2. Foreign body sensation	None	Awareness	Desire to rub	Desire to close eyelids
3. Dryness	None	Awareness	Need drops	Frequent drops
4. Burning	None	Awareness	Desire to rub	Frequent rub
5. Eyelid Swelling	None	Noticeable	Obvious	Decrease in palpebral fissure

Table 2: Grading of seven signs in 100 patients with Meibomian gland disease.

Signs	Grade 0	Grade 1	Grade 2	Grade 3
1. MG secretion (central lower eyelid)	Clear	Cloudy	Turbid with clumps	Solid with paste
2. Plugged MG orifice (middle lower eyelid)	None	Less than 1/3	1/3-2/3	More than 2/3
3. Bulbar conjunctival redness	None	Pink	Light red	Bright red
4. Eyelid margin redness	None	Pink	Light red	Bright red
5. Eyelid margin debris	None	1-5	6-10	More than 10
6. Tear film breakup time (in seconds)	>10	8-10	5-7	<5
7. Ocular surface staining	4-point categorical panels (figure 1)			

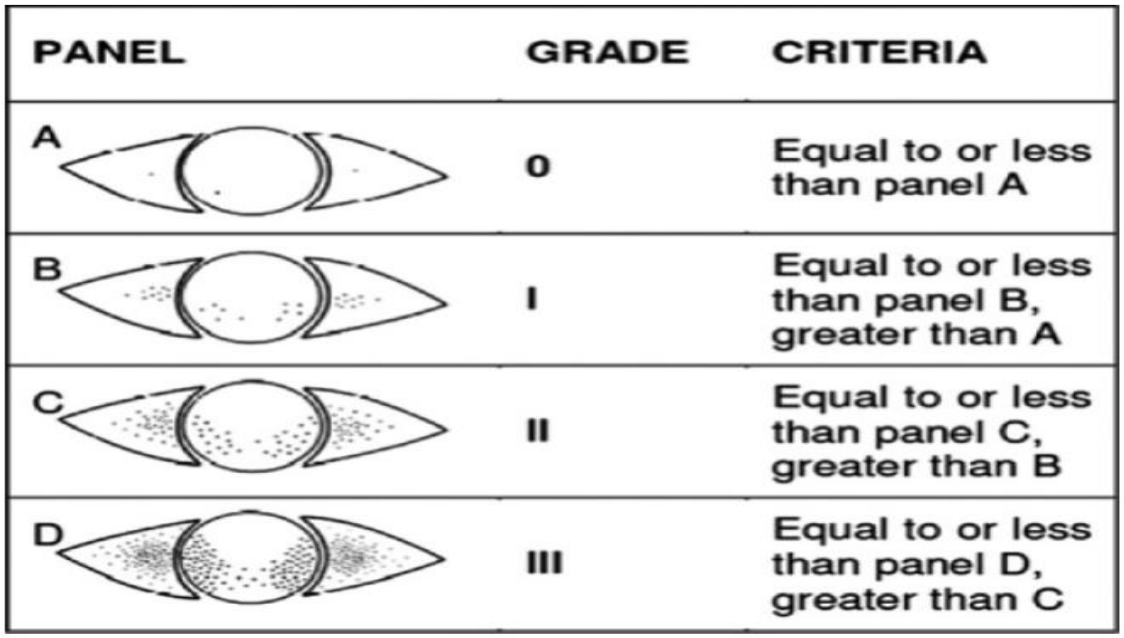

Figure 1: Ocular Surface Staining

RESULTS

There were 138 patients, of whom 38 did not complete the study according to the protocol (figure 2). Therefore, included for analysis were 100 patients. The two groups were matched for demographics.

Demography

The majority of patients, 59% were ≥60 years of age. Eight percent patients belonged to age group of <40 years of age. The age distribution among azithromycin and doxycycline was comparable; p=0.8. (Figure-3).

The symptom score at baseline was 10.62±3.07 years, which was comparable in azithromycin and doxycycline groups. The most common symptom was itching of eyes with maximum score at baseline, followed by dryness, foreign body sensation and ocular burning. The symptom score decreased significantly over six months in both groups, without a significant difference between any symptoms at each visit. (Table-4. Figure 4)

The signs score was 15.24±4.18 in all patients at baseline and the total score was 25.86±7.0. Both sign score and total score were comparable in Azithromycin and Doxycycline groups at baseline and at each visit. The most common sign was altered MG secretion in central lower eyelid followed by plugged MG orifices and bulbar conjunctival redness. Bulbar conjunctival redness score was significantly lower in azithromycin group at 3 months (p=0.03) and at 6 months (p=0.01) as compared to doxycycline group. (Table-5,6. Figure 4)

The Schirmer's Test score and OSDI scores were also comparable at baseline as well as at each visit between two groups. (Table-7)

The common side effects were nausea, abdominal cramps, diarrhea and decreased appetite. The side effects were more common and prolonged in the doxycycline group as compared to azithromycin group. (Table 8)

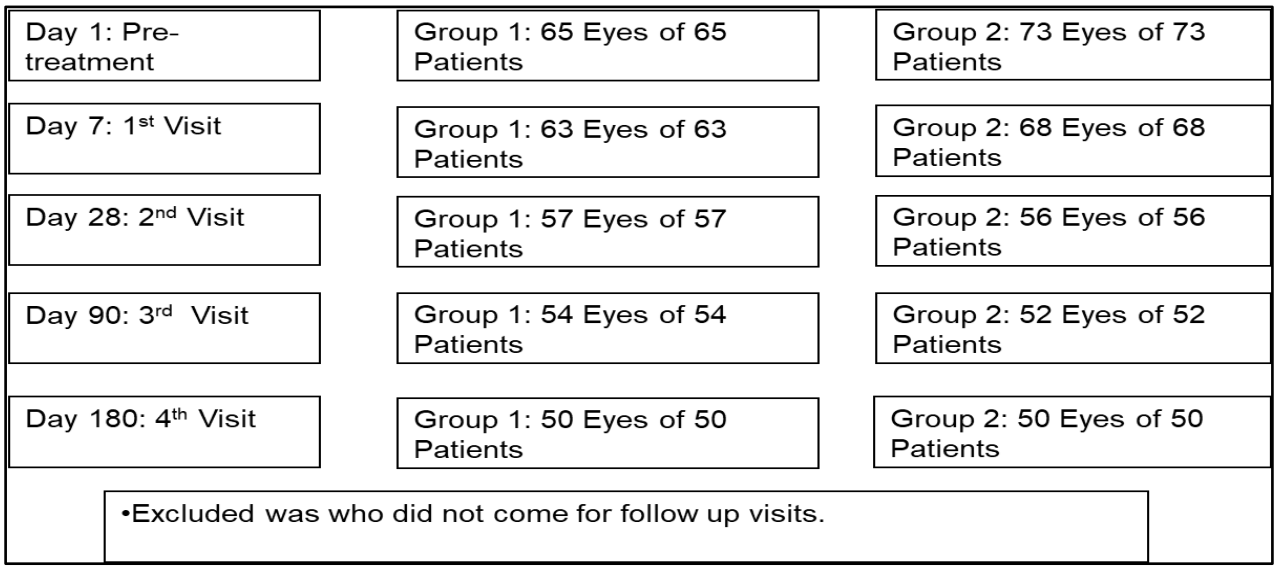

Figure 2: Flow diagram of participants: Trial of 5-day oral azithromycin (group 1) versus 1-month oral doxycycline (group 2) for treatment of MGD at different stages: pre-treatment and first (day 7), second (day28), third (day 90) and forth (day 180) post-treatment visits.

Table 3: Baseline data of all the patients comparing the Azithromycin and Doxycycline groups.

	All Patients	Azithromycin	Doxycycline	P-Value
Age (Mean±SD)	59.83±12.89	59.8±13.7	59.9±12.2	0.51
Gender (number)	F=40; M=60	F=21; M=29	F=19; M=31	0.68
Symptoms Score (Mean±SD)	10.62±3.07	10.32±2.75	10.92±3.36	0.33
Signs Score (Mean±SD)	15.24±4.18	15.48±4.04	15.00±4.34	0.56
Total Score (Mean±SD)	25.86±7.0	25.8±6.54	25.92±7.5	0.93

Table 4: Comparison of symptoms of MGD between azithromycin and doxycycline groups.

Itching	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	2.36(0.56)	2.16(0.65)	1.4(0.53)	0.94(0.65)	0.92(0.49)
Doxycycline	2.40(0.67)	2.26(0.66)	1.34(0.59)	1.04(0.53)	0.76(0.59)
p-value	0.74	0.44	0.59	0.4	0.14
FB scores	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	2.24(0.62)	2.18(0.63)	1.26(0.56)	0.78(0.71)	0.60(0.67)
Doxycycline	2.30(0.71)	2.12(0.69)	1.32(0.65)	0.78(0.79)	0.52(0.68)
p-value	0.65	0.65	0.62	1	0.55
Dryness score	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	2.26(0.66)	2.14(0.67)	1.46(0.65)	1.08(0.53)	0.92(0.57)
Doxycycline	2.40(0.67)	2.32(0.71)	1.42(0.61)	0.92(0.49)	0.80(0.57)
p-value	0.29	0.19	0.75	0.11	0.29
Burning Score	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	1.78(0.68)	1.72(0.64)	0.98(0.71)	0.62(0.72)	0.40(0.61)
Doxycycline	1.98(0.77)	1.7(0.68)	0.78(0.68)	0.58(0.57)	0.24(0.52)
p-value	0.17	0.87	0.15	0.38	0.15
Symptoms Score	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	10.32(2.75)	9.8(2.66)	5.94(2.61)	3.88(2.65)	3.18(2.26)
Doxycycline	10.92 (3.36)	9.82(3.09)	5.56(2.6)	3.58(2.2)	2.52(2.26)
p-value	0.33	0.97	0.46	0.54	0.14

Table 5: Comparison of signs of MGD between azithromycin and doxycycline groups

Eyelid Swelling	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	1.68(0.68)	1.6(0.73)	0.84(0.77)	0.46(0.68)	0.34(0.59)
Doxycycline	1.84(0.93)	1.42(0.84)	0.7(0.61)	0.26(0.56)	0.20(0.53)
p-value	0.33	0.25	0.31	0.11	0.21
MG Secretion	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	2.46(0.54)	2.38(0.53)	1.58(0.54)	0.94(0.74)	0.72(0.76)
Doxycycline	2.4(0.61)	2.32(0.62)	1.38(0.64)	0.82(0.56)	0.68(0.59)
p-value	0.6	0.6	0.09	0.36	0.38
Plugged MG Orifice	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	2.36(0.63)	2.34(0.63)	1.54(0.58)	1.20(0.53)	1.20(0.45)
Doxycycline	2.32(0.62)	2.2(0.64)	1.4(0.61)	1.08(0.49)	1.12(0.43)
p-value	0.75	0.27	0.24	0.24	0.18
Bulbar Conjunctival Redness	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	2.22(0.76)	2.02(0.68)	1.1(0.71)	0.54(0.73)	0.42(0.64)
Doxycycline	2.16(0.77)	1.88(0.72)	1.04(0.75)	0.82(0.56)	0.70(0.46)
p-value	0.69	0.32	0.68	**0.03**	**0.01**
Eyelid Margin Redness	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	2.42(0.73)	1.92(0.67)	1.06(0.79)	0.56(0.79)	0.46(0.76)
Doxycycline	2.20(0.64)	1.84(0.68)	0.96(0.64)	0.38(0.53)	0.42(0.24)
p-value	0.11	0.55	0.48	0.18	0.38
Eyelid Margin Debris	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	2(0.61)	1.88(0.66)	1.22(0.65)	0.84(0.71)	0.74(0.69)
Doxycycline	1.98(0.8)	1.86(0.7)	1.16(0.65)	0.56(0.57)	0.70(0.54)
p-value	0.88	0.88	0.64	0.01	0.75
Signs Score	**Baseline**	**7 Days**	**4 Weeks**	**3 Months**	**6 Months**
Azithromycin	15.48(4.04)	14.18(3.73)	8.58(3.69)	5.36(3.41)	4.28(3.33)
Doxycycline	15.00(4.34)	13.50(3.79)	7.52(3.47)	4.66(2.65)	4.18(2.42)
p-value	0.56	0.36	0.14	0.25	0.86

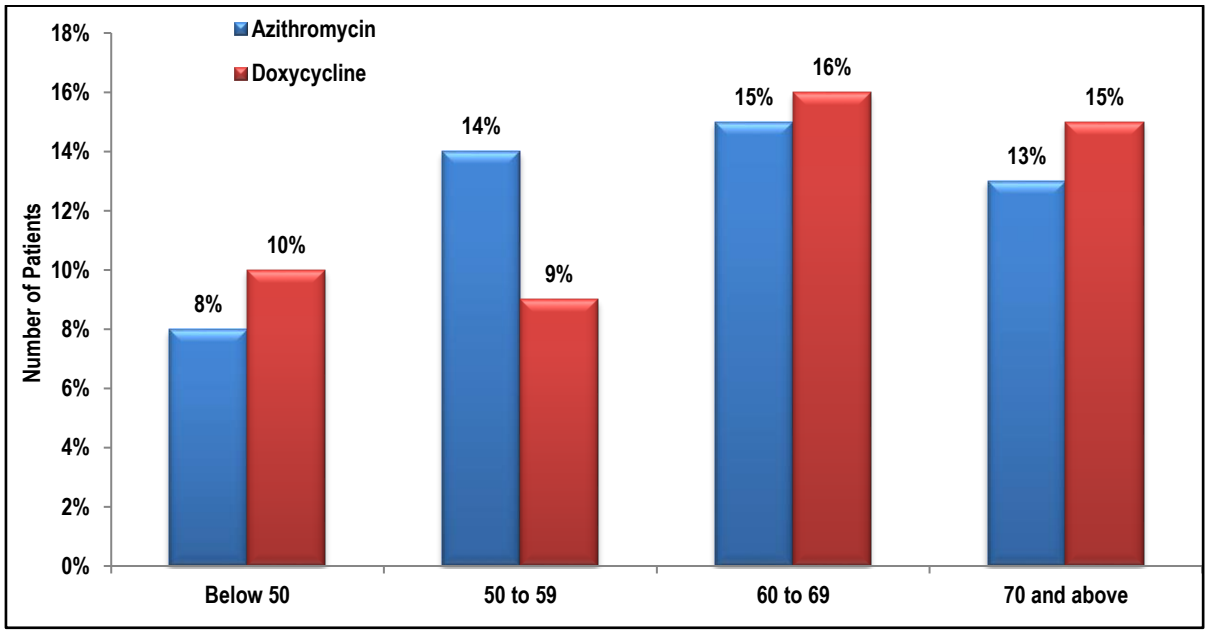

Figure 3: Age-wise distribution of patients.

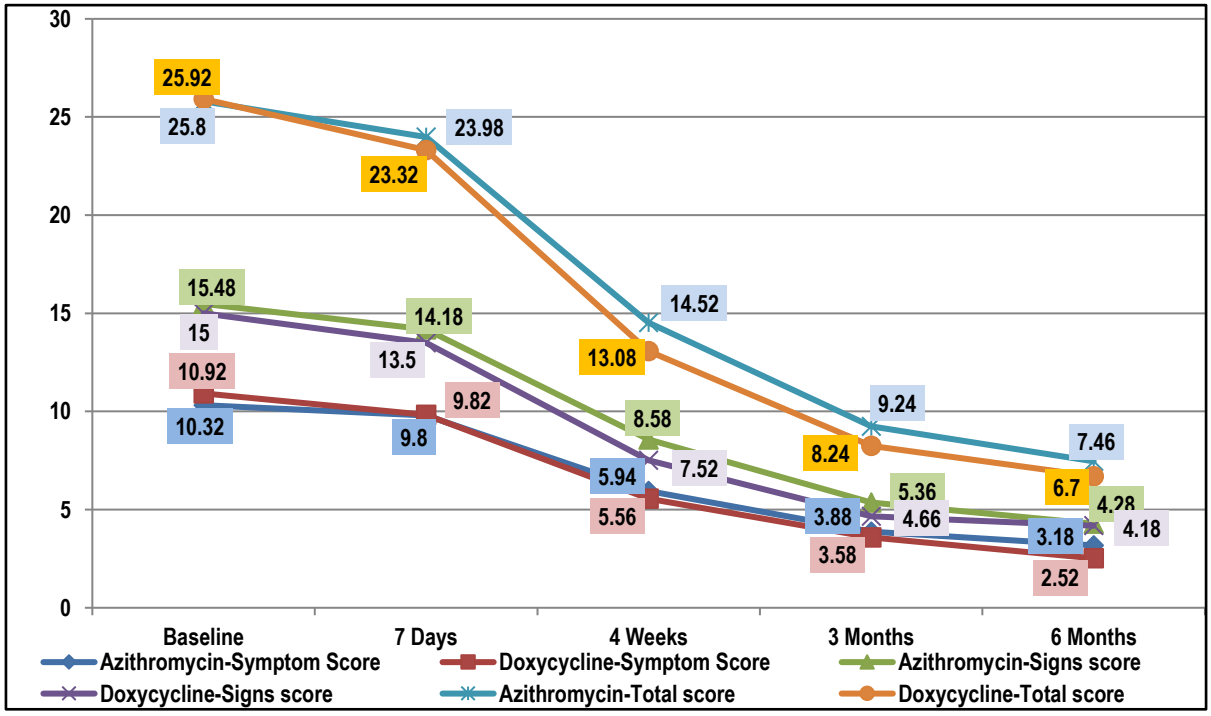

Figure 4: Comparison of signs, symptoms score and total score between azithromycin and doxycycline groups.

Table 6: Comparison of Total score of MGD between azithromycin and doxycycline groups.

Total score	Baseline	7 Days	4 Weeks	3 Months	6 Months
Azithromycin	25.8±6.54	23.98±5.89	14.52±5.97	9.24±5.79	7.46±5.42
Doxycycline	25.92±7.5	23.32±6.63	13.08±5.63	8.24±4.56	6.70±4.51
P value	0.93	0.59	0.2	0.34	0.45

Table 7: The comparison of Schirmer's Test score and OSDI scores between azithromycin and doxycycline groups.

	Schirmer's Test score			OSDI SCORE		
Score	Azithromycin	Doxycycline	p-value ttest	Azithromycin	Doxycycline	p-value ttest
Baseline	9.31(2.34)	9.84(2.37)	0.17	56.55(19.88)	59.07(18.16)	0.50
7 Days	10.23(2.35)	10.56(2.68)	0.51	51.19(19.01)	49.67(16.89)	0.67
4 Weeks	11.77(1.96)	12.06(2.46)	0.52	37.83(18.61)	34.17(14.68)	0.27
3 Months	13.33(2.1)	13.34(2.6)	0.97	25.49(18.91)	21.43(14.4)	0.22
6 Months	14.35(1.94)	14.74(2.41)	0.38	20.35(18.59)	14.64(15.05)	0.09

Table 8: Side effect profile of azithromycin versus doxycycline

Follow up Visit	Group	Nausea	Abdominal cramp	Diarrhea	Decreased appetite	p Value
7 days	**Doxycycline**	6(12%)	5(10%)	4(8%)	7(14%)	0.08
	Azithromycin	4(8%)	3(6%)	2(4%)	3(6%)	
4 weeks	**Doxycycline**	8(16%)	4(8%)	3(6%)	6(12%)	0.002
	Azithromycin	0(0%)	0(0%)	0(0%)	0(0%)	
3 months	**Doxycycline**	0(0%)	0(0%)	0(0%)	0(0%)	--
	Azithromycin	0(0%)	0(0%)	0(0%)	0(0%)	--
6 months	**Doxycycline**	0(0%)	0(0%)	0(0%)	0(0%)	--
	Azithromycin	0(0%)	0(0%)	0(0%)	0(0%)	--

DISCUSSION

Azithromycin and Doxycycline have been used in MGD in human eyes. While Azithromycin is available in both oral and topical formulations, Doxycycline is available in oral form only, for human use. Doxycycline inhibits the microbial Lipases produced by bacteria like Staphylococcus epidermidis, thus, reducing the free fatty acids at the lid margin and inhibits phospholipase-A2, MMPs, IL1α and β associated inflammation.[4] Azithromycin exerts immunomodulatory and anti-inflammatory action by inhibiting cytokine release – IL8, IL6, TNFα and also acts upon the human Meibomian Gland epithelial cells and promotes their differentiation and maturation.[5,6] There is no study in Indian population comparing the effect of oral Doxycycline to oral Azithromycin in symptomatic MGD. Therefore, we studied the effect of oral Doxycycline versus oral Azithromycin on MGD. This was a hospital-based prospective randomized trial on a minimum 100 patients of ≥18 years with MGD to evaluate the effect of treatment with oral Azithromycin as compared to oral Doxycycline. The presentation of MGD can be hypersecretory, hyposecretory, non-obvious due to gland loss or obstructive type.[7] The hyposecretory or obstructive type of MGD usually presents with dry eye state and worse ocular symptoms.[7] In order to include symptomatic MGD patients in our study, we used symptom and sign score grading of MGD for establishing the diagnosis as used in a previous clinical trial by Kashkouli at al. and Benedetti et al.[8,9] Furthermore, the signs and symptoms score was used to assess the severity of MGD. The assessment of the dry eye disease related to MGD was made using the OSDI questionnaire.

The mean symptom score in our study was 10.62±3.07 in all patients which was comparable in Azithromycin and Doxycycline group. Kashkouli et al. reported the baseline symptom score of 7.2±2.3 in Azithromycin group and 6.8±2 in Doxycycline group.[8] This suggests that our study had slightly severe grade of MGD as compared to the above study. However, Benedetti et al. had similar symptom scores to our study in both Azithromycin as well as Doxycycline group.[9] It has been described that MGD contributes to worse severity of symptoms in dry eye disease.[12] The most common symptoms of MGD were itching, dryness and foreign body sensation in most studies.[8,9,13,14] The signs score in MGD in our study at baseline was found to be 15.24±4.17 in all patients with no significant difference in Azithromycin and Doxycycline group at baseline. Kashkouli et al reported lower sign scores at baseline as compared to our study.[8] The most prominent signs were Meibomian gland secretion and plugging in our study, because it was mandatory to include one of these two in diagnosis of MGD. There was significant improvement at each follow-up, in our study, in mean symptom scores and sign scores post-treatment with both Doxycycline and Azithromycin with no significant difference between two groups. Bulbar conjunctival redness was significantly better for Azithromycin group at 3 months (p=0.03) and 6 months (p=0.01) as compared to Doxycycline group. Kashkouli et al reported significant improvement in symptoms in both groups at 2 months; while the sign scores, esp. bulbar conjunctival redness and ocular surface staining, were significantly better in azithromycin group.[8] Benedetti at al also reported significant decrease in symptoms from baseline, in both oral Azithromycin and oral Doxycycline groups at 9 months, while sign score was better with azithromycin at end of treatment.[9] Mehdi et al also compared topical Azithromycin versus oral Doxycycline for MGD at 3 weeks from baseline and reported a significant decrease in peripheral injection score and Meibomian gland plugging with use of topical Azithromycin as compared to oral Doxycycline.[15] Therefore, all the previous studies with Doxycycline as well as Azithromycin have shown an improvement in symptoms scores and sign score from baseline. Azithromycin use has been found to be better for signs improvement like bulbar conjunctival redness and ocular surface staining. The Schirmer's test, done to evaluate dry eye disease associated with MGD, showed reduced values, around 9, in both Azithromycin group and Doxycycline group; both improved to above 14 levels at 6 months. Mehdi et al compared the effect of topical Azithromycin versus oral Doxycycline on Schirmer's test and found minimal but non-significant improvement in both groups. OSDI score has been shown to be severe in dry eye disease associated with MGD.[16] The overall OSDI scoring reduced significantly at 6 months after treatment without significant difference between the two groups in our study. Yildiz et al and Ciloglu et al evaluated patients for MGD also found significant improvement in OSDI scoring after treatment of MGD.[14,17] The mean age of the patients in our study was 59.83±12.90 years, which was comparable in Doxycycline (59.88±12.21 years) and Azithromycin (59.78±13.66 years). A hospital-based study, done in central India, screened 3410 subjects >20 years age attending the outpatient department and found MGD in 272 (71 symptomatic) subjects with a mean age of 53.3±15.2 (20–84) years.[18] The patients who were symptomatic for MGD were 47.8±15 years, 60% below 60 years of age. A study by Gao et al showed that the prevalence of MGD increases with age, significantly and is most prevalent in 50-59 year age group.[19] There was a predominant male distribution in our study as 60% of patients in our study were males, although there was no significant difference in gender distribution across age groups. A few studies have previously found higher MGD prevalence in males.[20] Hassanzadeh et al studied the global prevalence of MGD and found found that men were more prone to having MGD than women.[21] Therefore, the results of this may be translated to the general population.

The common side effects of oral medications are nausea, abdominal cramps, diarrhoea or decreased appetite. None of the patients in our study had any serious side effects following the drug administration. 22% of patients on Doxycycline had one or more side effects as compared to 10% in Azithromycin during first week of administration. Kashkouli et al also reported that 26% of patients on Doxycycline had one or more systemic side effects, which were not significantly different in oral Azithromycin or Doxycycline at 7 days. However, at 4 weeks the systemic side effects were much higher in oral Doxycycline group as Azithromycin had been discontinued at 7 days.[11] This finding was similar in our study. Therefore, prolonged course of Doxycycline is associated with prolonged side effects.

The strengths of this study are that it is a randomized prospective trial with an adequate sample size. The follow-up of this study is 6 months, which is more than most of the previously performed studies. Also, we observed that at 6 months there is no difference between oral Azithromycin and oral Doxycycline, in terms of MGD improvement. Oral Doxycycline has a prolonged course of medication for 4 weeks whereas similar effect can be achieved by a short course of oral Azithromycin. The limitation of this study is fixed dosage regimen used for a short period of time, especially in oral Azithromycin. We did not include the patients with any systemic illness in our study, may be another limitation for practical application of these results to general population.

From this study, it was concluded that both drugs significantly improved the symptoms, signs and OSDI score in MGD patients. There was no significant difference between the effects of two drugs at 6 months. As Doxycycline was given for a longer period of time, the systemic side effects lasted longer with Doxycycline. Therefore, a 5-day course of oral Azithromycin is recommended based on equivalent clinical improvement with shorter duration of treatment and lesser side effects as compared to oral Doxycycline.

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