Original Article
DOI: https://doi.org/10.70749/ijbr.v3i6.1709

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Efficacy of Topical Azithromycin 1% Ophthalmic Solution in the Treatment of Posterior Blepharitis

Samreen Sohail[1], Ubaidullah Yasin[2], Amina Shabbir[1], Iqra Saleem[1], Sheena Liaquat[1], Haziq Zaman[1]

[1]Department of Eye, Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan
[2]Department of Oculoplastic, Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan

ARTICLE INFO

Keywords: blepharitis, azithromycin, meibomian gland dysfuction, tear film breakup- time.

Correspondence to: Samreen Sohail, Department of Eye, Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan.
Email: Samreensohail98@yahoo.com

Declaration
Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History
Received: 13-03-2025 Revised: 26-05-2025
Accepted: 13-06-2025 Published: 30-06-2025

ABSTRACT

Objective: This study aims to address this gap by investigating the efficacy of topical azithromycin in infectious posterior blepharitis. **Design of study:** Descriptive study. **Place and duration of study:** AFIO, Rawalpindi between July, 2024 to January, 2025. **Methodology:** Individuals with posterior blepharitis who have been diagnosed, regardless of gender. Each participant was only allowed to participate in the study with one eye; if both eyes qualified, the left eye was chosen. Patients with a history of pregnancy, ocular infections, conjunctivitis, keratitis, or any ocular inflammations other than posterior blepharitis, as well as known allergies to azithromycin were excluded. Patients with a history of recent eye injuries or ocular surgery were also not included. For two days, 1% azithromycin eyedrops (Zithrosan) were given twice a day in the morning and evening. After that, they were given once a day in the evening for twelve days. Twice daily, each patient was told to apply a warm compress to the study eye. At baseline and following the two-week treatment period, all individuals had their ocular symptoms and MGD-related indicators assessed. **Results:** The prevalence of all four symptoms showed a significant reduction after treatment compared to before: sensitivity to light ($p=0.0253$), eyes grittiness ($p<0.0001$), burning sensation ($p=0.0039$) and blurred vision ($p=0.0082$). Significant improvements were observed in lid vascularity, lid plugging, and meibum grade on Day 14 ($p=0.0001$, 0.0001, and 0.0001, respectively). **Conclusion:** In summary, the current study shows that AZM treatment for blepharitis in MGD patients was effective when administered for 14 days.

INTRODUCTION

A persistent inflammatory disease that affects the meibomian glands and the posterior edge of the eyelids is called posterior blepharitis. Hyperemia and/or redness of the eyelid edge are the hallmarks of blepharitis, which can be either infected or non-infectious. Bacterial infections are the primary source of the inflammation linked to infectious blepharitis, which is known to have recurrent flare-ups and remissions. It frequently results in eye pain and has a major effect on a patient's quality of life.[1,2] Despite its prevalence, the management of posterior blepharitis remains challenging due to its multifactorial etiology, including bacterial colonization, inflammation, and meibomian gland dysfunction.[3] Meibomian gland dysfunction (MGD), a key component of posterior blepharitis, involves hyperkeratinization of the duct epithelium and obstruction of the gland, leading to inflammation and increased bacterial colonization of the lid margins. MGD frequently results in tear film instability, evaporative dry eye, and ocular surface damage. Symptoms of posterior blepharitis often include itching, redness, photophobia, foreign body sensation, and lacrimation, while clinical signs range from thickened eyelid margins and plugged gland orifices to gland dropout observed via meibography.[4,5]

Azithromycin ophthalmic drug (zithrosan USP 200mg/5ML) is specifically approved for use in posterior blepharitis. While systemic azithromycin has shown efficacy in managing various ocular and systemic infections, its use is often limited by systemic side effects such as gastrointestinal disturbances, drug interactions, and the potential for antibiotic resistance.[6,7] In this context, topical azithromycin presents a promising alternative, offering localized treatment with potentially fewer

systemic risks.[8]

Despite these potential advantages, there is limited data specifically evaluating the efficacy of topical azithromycin in treating posterior blepharitis. Current therapeutic guidelines often rely on generalized management strategies or extrapolate findings from studies focused on anterior blepharitis or meibomian gland dysfunction, leaving a significant gap in evidence-based treatment options tailored to posterior blepharitis.[9,10]

This study aims to address this gap by investigating the efficacy of topical azithromycin in infectious posterior blepharitis. Furthermore, diagnostic methods for associated conditions like dry eye disease, including tear osmolarity measurements and OSDI scoring, highlight the complexity of assessing treatment efficacy comprehensively. The findings could contribute to improving treatment protocols and reducing reliance on systemic therapies, thus minimizing associated systemic side effects while effectively managing this challenging condition.

METHODOLOGY

This descriptive study was conducted at the Armed Forces Institute of Ophthalmology in Rawalpindi from July, 2024 to January, 2025. Individuals with posterior blepharitis who have been diagnosed, regardless of gender. Each participant was only allowed to participate in the study with one eye; if both eyes qualified, the left eye was chosen. The WHO Sample Size Calculator was used to determine the sample size.[10] In this research, which included 31 patients with posterior blepharitis, the following calculations were made: confidence level = 95%, population mean = 16.28, population standard deviation = 4.5, and absolute precision = d = 1. They were selected using a non-probability consecutive sampling technique. Patients with a history of pregnancy, ocular infections, conjunctivitis, keratitis, or any ocular inflammations other than posterior blepharitis, as well as known allergies to azithromycin were not included. Patients with a history of recent eye injuries or ocular surgery were also excluded.

Written informed consent was given by each patient. A complete medical history was acquired. A clinical evaluation was carried out and properly recorded. For two days, 1% azithromycin eyedrops (Zithrosan) were given twice a day in the morning and evening. After that, they were given once a day in the evening for twelve days. Twice daily, each patient was told to apply a warm compress to the study eye. It has been established that MGD can be effectively treated with a warm compress and artifical tears free of preservatives. At baseline and following the two-week treatment period, all individuals had their ocular symptoms and MGD-related indicators assessed. Following the baseline assessment, the study treatment was started right away. The individuals were instructed to apply the warm compress and eyedrops until the night before the two-week appointment, but not on the day of the visit.

The Ocular Surface Diseased Index Questionnaire was used to measure ocular symptoms. Slit lamp microscopy revealed anomalies in the lid margin, such as clogging (scale of 0–3) and vascularity (scale of 0–3). Redness in the lid margin conjunctiva, telangiectasia distribution across meibomian gland orifices, eyelid swelling, quality of meibomian gland secretions (scale of 0-3), and eyelid debris were all taken into consideration when grading the lid margin vascularity. The fluorescein-based break-up time of the tear film (TBUT) was evaluated using slit lamp microscopy. TBUT scores were interpreted as follows: less than 5 seconds indicated low (abnormal), 5–10 seconds indicated medium (borderline), and greater than 10 seconds indicated high (normal) tear film stability.

We used version 23.0 of the Statistical Package for Social Sciences to look at the data. We utilized frequencies and percentages to show qualitative data and mean ± SD to show quantitative data. The independent sample t-test was used to look at the inferential statistics. We compared the outcomes before and after therapy using the Wilcoxon signed-rank test. A p-value below 0.05 was considered significant.

RESULTS

The study participants were 53.32 ± 6.89 years old on average. The age range was 30 to 70 years old. The female to male ratio among these patients was 8:1, with 40 (88.89%) being female and 05 (11.11%) being males.

The prevalence of all four symptoms listed in Table 1 shows a significant reduction after treatment compared to before: sensitivity to light (p=0.0253), eyes grittiness (p<0.0001), burning sensation (p=0.0039) and blurred vision (p=0.0082).

Table 2 demonstrated the grade of meibum, lid plugging, and lid vascularity. There were big changes on Days 14 (p=0.0001, 0.0001, and 0.0001, respectively). Table 3 also showed the TBUT. Significant improvement in the score was observed on Day 14 (0.0001). The remaining findings did not show any significant differences.

Table 1

Presence of symptoms pre- and post-treatment (n=31).

Parameters	Pre-treatment	Post- treatment	Significant improvement in symptoms after azithromycin treatment
Eye(s) feel sensitive to light	Yes n=12 (38.7%) No n=19 (61.3%)	Yes n=7 (22.6%) No n=24 (77.4%)	Yes (McNemar's Chi Sq= 5.00, p=0.0253)
Eye(s) feel gritty	Yes n=29 (93.6%) No n=2 (6.5%)	Yes n=11 (35.5%) No n=20 (64.5%)	Yes (McNemar's Chi Sq= 18.00, p<0.0001)
Burning sensation in eye(s)	Yes n=17 (54.8%) No n=14 (45.2%)	Yes n=7 (22.6%) No n=24 (77.4%)	Yes (McNemar's Chi Sq=8.33, p=0.0039)
Blurred vision	Yes n=18 (58.1%) No n=13 (41.9%)	Yes n=11 (35.5%) No n=20 (64.5%)	Yes (McNemar's Chi Sq=7.00, p=0.0082)

Table 2

Outcome before and after 2 Weeks of Therapy.

Parameters	Before	After 2 weeks	P-value
	Mean ± SD	Mean ± SD	
Lid vascularity	2.0 ± 0.78	1.23 ± 0.45	0.0001
Lid plugging	2.4 ± 0.78	1.67 ± 0.52	0.0001
Meibum grade	2.0 ± 0.46	1.31 ± 0.27	0.0001
TBUT	4.25 ± 2.62	5.67 ± 3.18	0.0001

DISCUSSION

The anatomical position of blepharitis determines its classification: anterior blepharitis affects the area of the eyelids that exposes the lashes, whereas posterior blepharitis, commonly referred to as meibomian gland dysfunction (MGD), affects the meibomian glands (MG).[11,12] Changes to the MGs structure and secretions frequently result in obstructed MG in cases of posterior blepharitis.[13] Once the MGs are blocked, bacterial colonization and inflammatory mediators are released, which exacerbates patient symptoms and clinical indicators. Most blepharitis patients will have mixed anterior-posterior blepharitis, even though anterior and posterior blepharitis are described differently. Blepharitis is typically chronic in nature, with inflammation and bacterial proliferation contributing to symptoms.[14]

Because blepharitis has several causes, several phase 4 clinical trials were done to see how well azithromycin 1.0% worked. We discovered six trials that, taken together, recruited close to 300 patients to examine the effectiveness of 1.0% azithromycin in treating blepharitis. The first experiment to be published was a prospective, open-label study with 75 participants and 150 eyes that administered topical ophthalmic erythromycin or topical azithromycin 1.0% to patients with a diagnosis of chronic mixed anterior blepharitis.[15] Following 4 weeks of therapy, the clinical improvement for the azithromycin was 98.5%, while that of the erythromycin was 37.5%. At 8 weeks, the erythromycin and azithromycin concentrations were 50% and 98.5%, respectively. Within a month or so of receiving 1.0% azithromycin ophthalmic solution, subjects demonstrated improvement ($P = 0.0237$).[15]

Participants with posterior blepharitis were examined in a second trial. In this open-label trial, 21 patients were randomly assigned to receive either warm compresses alone or azithromycin 1.0% with warm compresses.[16] One drop was applied to each eye in the azithromycin group 2 times a day for two days, and then one time for the next twelve. The quality of meibomian gland secretions, meibomian gland clogging, and eyelid redness all significantly improved in individuals in the azithromycin group ($P < 0.001$).[16]

A multicenter open-label research evaluating 26 participants with blepharitis was conducted in a third study.[17] After treatment with azithromycin 1.0%, ocular symptoms as MG plugging, redness at the eyelid margin, redness in the palpebral conjunctiva, and ocular discharge were greatly reduced ($P < 0.002$). Additionally, there was significant improvement in eyelid itching, burning, dryness, swollen or heavy eyelids, and foreign body sensation/grittiness. Notably, these signs and symptoms significantly decreased and continued to do so for four weeks after treatment. Eyelid margin bacterial cultures were conducted both before and after therapy, and tears were collected for cytokine analysis in the same investigation. Remarkably, there were no variations in the levels of tear cytokines.[17] This outcome contradicts a study that was conducted using a mouse model.[18] Since hyperemia, a defining feature of inflammation, significantly improved from baseline, this study indicates that there was a decrease in inflammation even if there was no statistical change.[17]

Azithromycin 1.0% ophthalmic solution was administered to 33 patients twice daily for two days, followed by every evening for 28 days, in a fourth open-label research assessing individuals with meibomian gland dysfunction.[18] After treatment, both objective and subjective findings got better. The TBUT and Schirmer scores rose up after treatment, whereas the lid margin scores went down ($P < 0.0001$). The OSDI shows that azithromycin 1.0% is a good treatment for posterior blepharitis since it improved by 57.9% after 2 weeks and 61.8% after 4 weeks from the start. At baseline, the patient's symptoms were 2.73; after 30 days of treatment, they were 2.21 ($P < 0.01$).[18]

A fifth study compared the clinical manifestations of MGD before and after a 4-week course of 1.0% azithromycin treatment. It also used spectroscopy to assess the lipids in the meibomian gland.[19] In the 17 patients who finished the 4-week trial, all eyelid indications were looked at. These included the number of blocked meibomian glands, the amount of redness on the lid margin, how easy it was to express the meibomian glands, and the sort of secretions that came from them. The findings indicated a statistically significant improvement in symptoms ($P < 0.001$).[19] By lowering the transition temperature, the meibomian gland secretions were more mobile and easier to express, which enhanced the meibomian gland lipids' phase transition and statistically lengthened the tear breakup time ($P < 0.001$).[19]

Another study[20] compared the effectiveness of 0.3%/0.5% tobramycin/dexamethasone ophthalmic suspension versus 1.0% azithromycin in the treatment of blepharitis in a multicenter, randomized study with adult participants over the age of 19 (n = 122). Forty patients were randomly assigned to receive either one drop of AzaSite® twice a day for two days, followed by once a day for twelve days, or one drop of Tobradex ST® four times a day for fourteen days. On days 1, 8, and 15, the study examined global scores for ocular discharge, irritation, grittiness, lid swelling, bulbar and palpebral conjunctival redness, and lid margin redness. 96.7% of the recruited participants finished the study. At day 8, participants treated with Tobradex ST® had a significantly lower score for ocular signs and symptoms overall than those treated with azithromycin ($P = 0.0002$). Neither group experienced any significant adverse events.[20]

Two Phase II, randomized, prospective, multi-center studies looked at how DuraSite® topical azithromycin 1% affected anterior blepharitis at the same time.[21] Two weeks were allotted for treatment in one trial, and four weeks in the other. While

blepharitis indications and symptoms at different time points improved during the four-week experiment ($P < 0.05$). The primary outcome of lid debris did not significantly improve for the AzaSite-treated group over the two-week experiment. For all assessed blepharitis symptoms and indicators, statistically significant improvements were noted in both trials.[21]

There were various restrictions on this investigation. Initially, the trial was open-label and assessed the effectiveness of AZM by comparing each evaluation measure before and after therapy. Randomized clinical trials are necessary to elucidate the more conclusive effectiveness of AZM monotherapy for treating blepharitis associated with MGD. Second, because hypersecretory MGD has no widely recognized definition, it was unable to identify MGD types in every individual.

CONCLUSION

In summary, the current study shows that AZM treatment for blepharitis in MGD patients was effective when administered for 14 days. Additionally, AZM's effectiveness lasted for a while after treatment ended.

REFERENCES

1. Vernhardsdottir RR, Magno MS, Hynnekleiv L. Antibiotic treatment for dry eye disease related to meibomian gland dysfunction and blepharitis - a review. Ocul Surf. 2022;26:211-21. https://doi.org/10.1016/j.jtos.2022.08.010
2. Morthen MK, Magno MS, Utheim TP, Snieder H, Hammond CJ, Vehof J. The physical and mental burden of dry eye disease: a large population-based study investigating the relationship with health-related quality of life and its determinants. Ocul Surf. 2021;21:107–17.
3. Vernhardsdottir RR, Magno MS, Leif H, Neil L Dartt DA, Vehof J, et al. Antibiotic treatment for dry eye disease related to meibomian gland dysfunction and blepharitis. Ocular Surface. 2022;26:211-21. https://doi.org/10.1016/j.jtos.2022.08.010
4. Ahmad A, Rehman M. Comparison of efficacy of 1-week oral azithromycin with 2-week topical 1% azithromycin eye drops in the treatment of Posterior Blepharitis. J Postgrad Med Inst. 2022;36(3):145-9. https://doi.org/10.47391/jpma.6732
5. Nejima R, Eguchi H, Todokoro D, Inoue T, Kaji Y, Suzuki T, et al. Analysis of treatment protocols using azithromycin eye drops for bacterial blepharitis: second report-bacteriological investigation. Jpn J Ophthalmol. 2022;66:579–89. https://doi.org/10.1007/s10384-022-00947-8
6. Amano S, Shimazaki J, Yokoi N, Hori Y, Arita R. Committee for Meibomian Gland Dysfunction Clinical Practice Guidelines. Meibomian Gland Dysfunction Clinical Practice guidelines. Jpn J Ophthalmol. 2023;67:448–539. https://doi.org/10.1007/s10384-023-00995-8
7. Nejima R, Inoue T, Kaji Y, Suzuki T, Hattori T, Hoshi S, et al. Analysis of treatment protocols using azithromycin eye drops for bacterial blepharitis-first report: study of clinical course. J Eye. 2022;39:999–1004. https://doi.org/10.1007/s10384-022-00947-8
8. Jarvis I, McCullough S, Jarvis J. The topical azithromycin meibomian gland dysfunction survey: The effect of topical azithromycin on signs and symptoms of meibomian gland dysfunction. Ophthalmic Physiological Optics. 2024;44(5):910-6. https://doi.org/10.1111/opo.13330
9. Arita R, Fukuoka S. Efficacy of azithromycin eyedrops for individuals with meibomian gland dysfunction-associated posterior blepharitis. Eye Contact Lens. 2021;47:54–9. https://doi.org/10.1097/icl.0000000000000729
10. Shimazaki J, Kito G, Kamoi M, Satake Y. Efficacy and safety of topical azithromycin therapy in patients with blepharitis and meibomian gland dysfunction. Japanese J Ophthalmol. 2024;68:472–81. https://doi.org/10.1007/s10384-024-01079-x
11. Onghanseng N, Ng SM, Halim MS, Nguyen QD. Oral antibiotics for chronic blepharitis. Cochrane Database Syst Rev. 2021;6(6):CD013697. https://doi.org/10.1002/14651858.cd013697.pub2
12. Reiko A, Shima F. Efficacy of azithromycin eyedrops for individuals with meibomian gland dysfunction–associated posterior blepharitis. Eye and Contact Lens: Sci Clin Prac. 2021;47:54-9. https://doi.org/10.1097/icl.0000000000000729
13. Tauber J, Berdy GJ, Wirta DL. NOV03 for dry eye disease associated with meibomian gland dysfunction: Results of the randomized phase 3 GOBI study. Ophthalmol. 2023;130:516-524. https://doi.org/10.1016/j.ophtha.2022.12.021
14. Onghanseng N, Ng SM, Halim MS, Nguyen QD. Oral antibiotics for chronic blepharitis. Cochrane Database Syst Rev. 2021;6:CD013697. https://doi.org/10.1002/14651858.cd013697.pub2
15. John T. Use of azithromycin ophthalmic solution in the treatment of chronic mixed anterior blepharitis. Ann Ophthalmol. 2008;40(2): 68–74.
16. Luchs J. Efficacy of topical azithromycin ophthalmic solution 1% in the treatment of posterior blepharitis. Adv Ther. 2008;25(9):858–70. https://doi.org/10.1007/s12325-008-0096-9
17. Haque RM, Torkildsen GL, Brubaker K. Multicenter open-label study evaluating the efficacy of azithromycin ophthalmic solution 1% on the signs and symptoms of subjects with blepharitis. Cornea. 2010;29:871–7. https://doi.org/10.1097/ico.0b013e3181ca38a0
18. Opitz DL, Tyler KF. Efficacy of azithromycin ophthalmic solution for treatment of ocular surface disease from posterior blepharitis. Clin Exp Optom. 2011;94(2):200–6. https://doi.org/10.1111/j.1444-0938.2010.00540.x
19. Foulks GN, Borchman D, Yappert M. Topical azithromycin therapy for meibomian gland dysfunction: clinical response and lipid alterations. Cornea. 2010;29:781–8. https://doi.org/10.1097/ico.0b013e3181cda38f
20. Torkildsen GL, Cockrum P, Meier E. Evaluation of clinical efficacy and safety of tobramycin/dexamethasone ophthalmic suspension 0.3%/0.05% compared to azithromycin ophthalmic solution 1% in the treatment of moderate to severe acute blepharitis/blepharoconjunctivitis. Curr Med Res Opin. 2011;27(1):171–8. https://doi.org/10.1185/03007995.2010.539603
21. Utine CA. Update and critical appraisal of the use of topical azithromycin ophthalmic 1% (AzaSite®) solution in the treatment of ocular infections. Clin Ophthalmol. 2011;5:801–9. https://doi.org/10.2147/opth.s13785