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ORIGINAL RESEARCH

Exploratory Pilot Study on the Tolerability and Ocular Surface Effects of Liposomal Ozonated Oil Compared with Standard Prophylaxis in Cataract Surgery. The CAREST Study

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Purpose: To obtain preliminary data on the tolerability and ocular surface outcomes of liposomal ozonated oil compared with standard prophylaxis in cataract surgery.

Patients and Methods: This open-label, prospective, contralateral-eye controlled pilot study included 60 eyes from 33 adult patients undergoing bilateral cataract surgery. For each patient, one eye was treated with liposomal ozonated oil (one drop, four times daily) from 3 days before surgery until 21 days postoperatively, while the contralateral eye received standard treatment. The study outcomes included treatment tolerability, postoperative infectious complications, ocular signs and symptoms, Tear Break-Up Time (TBUT), Ocular Surface Disease Index (OSDI), visual acuity, anterior chamber reaction (Tyndall effect), and patient-reported discomfort. Assessments were performed at postoperative day 21, with exploratory follow-up evaluations at month 3.

Results: No postoperative infectious complications were observed in either treatment group. No significant between-group differences were observed in most evaluated ocular surface parameters at postoperative day 21 and month 3. At postoperative day 21, fewer patients in the liposomal ozonated oil group reported foreign body sensation and a higher proportion had TBUT > 10 seconds, although these differences were not statistically significant. At month 3, foreign body sensation was reported more frequently in the liposomal ozonated oil group, whereas no other significant between-group differences were observed. The majority of patients showed no anterior chamber reaction at postoperative day 21 (96.67%), and all patients reported good tolerability and no discomfort.

Conclusion: Liposomal ozonated oil was well tolerated and showed comparable clinical outcomes to standard prophylaxis following cataract surgery. The findings of this pilot study suggest potential benefits for ocular surface outcomes that warrant confirmation in adequately powered studies with larger sample sizes and longer follow-up. No infectious complications occurred in either treatment group; however, the absence of events and the limited sample size preclude conclusions regarding its potential role in infection prevention.

Clinical Trial Registration: The study was registered in the Spanish Registry for Post-Marketing Clinical Investigations with Medical Devices (NEOPS; Spanish Agency of Medicines and Medical Devices, AEMPS) under registration code 22–0061.e (September 6, 2022).

Plain Language Summary: Preventing eye infections is an important part of care before and after cataract surgery. This is usually achieved using antibiotic-based treatments, but concerns about increasing antibiotic resistance have encouraged the exploration of alternative options. Liposomal ozonated oil is an eye drop formulation with antimicrobial activity that may also help support the ocular surface.

This pilot study evaluated whether liposomal ozonated oil is well tolerated and how it affects the ocular surface when used around the time of cataract surgery, compared with standard preventive treatment. Patients undergoing cataract surgery in both eyes received liposomal ozonated oil in one eye and standard treatment in the other eye. Clinical assessments were performed after 21 days of treatment, with an additional exploratory follow-up at 3 months. Liposomal ozonated oil was well tolerated, and overall clinical outcomes were comparable between treatments. No postoperative infectious complications occurred in either treatment group. At 21

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days, fewer patients treated with liposomal ozonated oil reported a foreign body sensation, and a higher proportion showed Tear Break-Up time values above 10 seconds, suggesting a possible benefit for ocular surface protection and comfort. At the exploratory 3-month follow-up, no relevant differences were observed between treatments in most ocular surface parameters. Because this was a small pilot study, the results should be interpreted with caution. Larger studies are needed to confirm the potential benefits of liposomal ozonated oil for ocular surface outcomes and to evaluate its possible role in preventing postoperative ocular infections.

Keywords: cataract surgery, liposomal ozonated oil, ocular infections, OSDI, TBUT

Introduction

Antibiotic resistance has increased markedly in recent years and is now recognized by the World Health Organization (WHO) as one of the most serious threats to global public health.[1] In ophthalmic surgery, infection prophylaxis is essential to reduce the conjunctival and periocular bacterial load,[2,3] thereby maintaining a low incidence of post-surgical ocular infection. Nevertheless, a considerable incidence of ocular infections and related complications, including endophthalmitis, continues to be reported, with rates reaching up to 2.4% depending on the type of intervention.[4] In this context, there is increasing interest in optimizing perioperative prophylactic strategies and reassessing the routine use of topical antibiotics, particularly in light of their limited additional benefit and the global challenge of antimicrobial resistance, as reflected in recent expert discussions and emerging consensus within the ophthalmic community.

Given this context, there is growing interest in new antiseptic agents that are well tolerated by ocular tissues and compatible with existing therapies. One such innovation is a recently marketed medical device (Ozonest®, Esteve Pharmaceuticals S.A.), which contains ozonated oil encapsulated in liposomes. This formulation exhibits a distinctive mechanism of action and represents a novel approach to ocular surface disinfection even including multidrug resistant bacteria.[5–7]

The use of ozonated oil in ophthalmology is relatively recent. Antiseptics are increasingly recognized for their broad-spectrum antimicrobial efficacy, either as monotherapy or in combination with other antimicrobials.[5,6,8] The advantages of antiseptics include their ability to act against a wide range of pathogens, the absence of antibiotic resistance induction, and a generally favorable safety profile.[5,6,8,9]

Liposomal ozonated oil exerts its antimicrobial activity through a dual mechanism involving direct oxidation of the microbial surface and the intracellular release of reactive oxygen species and lipid peroxides. These oxidative compounds disrupt membrane phospholipids, proteins, enzymes, and nucleic acids, leading to irreversible microbial damage. This mechanism provides broad-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria, fungi, and viruses, including multidrug-resistant bacterial strains, without evidence of inducing antimicrobial resistance.[10–13] Preclinical studies support its potential role in the prophylaxis and treatment of ocular surface infections.[14,15] In contrast to conventional antiseptics such as povidone-iodine, whose primary effect relies on rapid broad-spectrum antimicrobial activity, liposomal ozonated oil has also been associated with reported anti-inflammatory and ocular surface restorative properties that may promote epithelial recovery and indirectly support tear film stability.[12,15] Moreover, liposomal ozonated oil has been shown to reduce ocular surface bacterial load to an extent comparable to that achieved with 5% povidone iodine, while maintaining good ocular tolerability.[16] Clinically, liposomal ozonated oil has shown promising results in several ophthalmic settings. In a large Phase IV study, liposomal ozonated oil achieved a significant reduction in conjunctival bacterial load (>90%) prior to cataract surgery, supporting its use as a well-tolerated adjunct to preoperative antiseptic protocols.[5] In the OPERA study, liposomal ozonated oil combined with ozonated liposomal foam significantly reduced the ocular surface microbial burden before intravitreal injections compared with 5% povidone-iodine alone.[6] It has also demonstrated favorable outcomes in the treatment of viral conjunctivitis.[17]

The aim of this pilot study was to obtain preliminary data on tolerability and ocular surface effects of liposomal ozonated oil compared with standard prophylaxis in cataract surgery.

Methods

Study Design and Patients

This was an open-label, prospective, contralateral-eye controlled, pilot study designed to include 60 eyes from 30 adult patients undergoing bilateral cataract surgery, with protocol-defined postoperative follow-up through day 21. An additional month 3 assessment was performed as part of routine clinical follow-up and is reported as an exploratory outcome. Initially, the study was planned for 30 patients contributing both eyes; however, in the final sample, 27 patients contributed both eyes (one per treatment group), while 6 patients contributed only one eye each (three per group), resulting in a partially paired design. Eligible patients met all the inclusion criteria and none of the exclusion criteria. The study was conducted at the Hospital General Universitario Morales Meseguer following approval by the Ethics Committee from the same hospital (internal code: ENS 13/22), and in accordance with the Declaration of Helsinki and the Good Clinical Practice Guidelines. All participants provided written informed consent prior to any study-related procedure. The study was registered in the Spanish Registry for Post-Marketing Clinical Investigations with Medical Devices (NEOPS; Spanish Agency of Medicines and Medical Devices, AEMPS) under registration code 22–0061.e (September 6, 2022).

Eligible patients were adults ≥18 years scheduled for bilateral cataract surgery. The exclusion criteria included the use of systemic or topical antibiotics, topical ocular antiseptics, or other eye treatments that could not be discontinued; presence of ocular or systemic inflammatory diseases; active infections; and allergy or hypersensitivity to fluorescein, lysamine green, or any component of the liposomal ozonated oil.

Treatment

For each patient, one eye received liposomal ozonated oil (one drop, four times daily), starting 3 days prior to surgery and continuing for 21 days postoperatively, in accordance with the manufacturer's instructions. The contralateral eye also followed a 21-day treatment protocol according to standard clinical practice, beginning with ciprofloxacin or moxifloxacin three times daily for the first week, starting 3 days before surgery, followed by a regimen of tobramycin/dexamethasone, six times daily during the first postoperative week, three times daily in the second week, and twice daily in the third week. The antibiotic-corticosteroid suspension used in the standard treatment group contained benzalkonium chloride (0.1 mg/mL) as a preservative. Treatment was assigned per protocol. All patients performed daily eyelid hygiene using antiseptic wipes in both eyes. All mandatory anti-infective procedures, including those routinely applied in the operating room during the intervention, were followed. These included the institution's standard perioperative prophylaxis, with 5% povidone-iodine instilled into the conjunctival sac and applied to the ocular surface before surgery, 10% povidone-iodine applied to the eyelids and periocular skin, and intracameral cefuroxime during surgery. All surgeries were performed by the same surgeon. The use of artificial tears or other topical ocular lubricants during the follow-up period was not permitted.

Outcome Measurements

Study outcomes included the assessment of treatment tolerability, safety, and ocular surface effects, as well as the occurrence of postoperative ocular infectious complications. Outcome assessments were performed at baseline and postoperative day 21, according to the study protocol. Additional postoperative assessments performed at month 3 as part of routine clinical follow-up, and not prespecified in the study protocol, were included as exploratory outcomes. Clinical assessments, including TBUT measurements, were performed according to the routine clinical practice of the Ophthalmology Department.

The evaluated outcomes measures were:

- Occurrence of postoperative ocular infectious complications during the 21-day treatment period.
- Comparison of postoperative ocular infectious complications between groups during the 21-day treatment period, according to age, gender, history of prior cataract surgery, cataract classification (Lens Opacities Classification System III [LOCS III]), presence of concomitant ocular disease (none, diabetic retinopathy, glaucoma, macular

degeneration, other-specify), and ocular comorbidities (none, prior corneal refractive surgery, white cataract requiring trypan blue, pseudoexfoliation, previous vitrectomy, corneal opacities, small pupil requiring mechanical dilation, other-specify), type of surgery (phacoemulsification, other-specify), and intraocular lens (IOL) characteristics (type, material, etc).

- Visual acuity (reported as corrected distance) at postoperative day 21 and month 3.
- Postoperative ocular surface findings at postoperative day 21 and month 3: presence/absence of conjunctival or mixed hyperemia, changes in bulbar redness, superficial keratitis, and mean change in fluorescein staining using the Oxford scale.
- Presence or absence of anterior chamber reaction (Tyndall effect) at postoperative day 21 and month 3. Anterior chamber inflammation was assessed via slit-lamp biomicroscopy using Tyndall evaluation (aqueous flare), and signs of endophthalmitis were specifically ruled out at each postoperative visit.
- Physician-assessed ocular symptoms and signs (itching, stinging, dryness, and foreign body sensation).
- Tear Break-Up Time (TBUT) and Ocular Surface Disease Index (OSDI) score changes at postoperative day 21 and month 3.
- Patient-reported discomfort using Visual Analogue Scale (VAS: 1 = none, 2 = mild, 3 = moderate, 4 = severe) at postoperative day 21.
- Safety and tolerability of liposomal ozonated oil at postoperative day 21.

Statistical Analysis

Quantitative variables were compared using the Student's *t*-test. For non-normally distributed variables, the Mann–Whitney *U*-test was used. Qualitative variables were compared using the chi-square test with Yates continuity correction or Fisher's exact test when appropriate. A p value < 0.05 was considered statistically significant. Continuous variables were reported as mean ± standard deviation (SD) and/or median (95% confidence interval [CI], minimum to maximum). Categorical variables were presented as absolute frequencies and percentages.

Because some patients contributed both eyes and others only one, analyses were conducted at the eye level treating observations as independent. This approach does not account for within-patient correlation, so p-values should be interpreted as exploratory. All statistical analyses were exploratory and conducted using two-sided hypothesis tests. The null hypothesis assumed no difference between the treatment groups, and statistical significance was defined as $p < 0.05$.

Results

A total of 60 eyes from 33 patients were included in the study. Of these, 27 patients contributed both eyes (one per treatment group), while 6 patients contributed only one eye each (three per group), resulting in a partially paired design. In the liposomal ozonated oil group, the mean age was 66.53 years, and 50.00% of patients were males, while in the standard treatment group, the mean age was 67.20 years and 53.33% of patients were males. Baseline characteristics are summarized in Table 1. No significant differences were observed between the treatment groups at baseline.

All surgeries were performed using phacoemulsification with IOL implantation.

Changes in ocular signs and symptoms at baseline, postoperative day 21, and month 3 are shown in Table 2. No statistically significant differences between groups were observed for itching, stinging, conjunctival hyperemia, superficial keratitis, or dryness at any study visit. Foreign body sensation tended to be less frequent in the liposomal ozonated oil group at day 21 (20.0% vs 40.0%; $p = 0.091$), although the difference did not reach statistical significance. At month 3, foreign body sensation was reported more frequently in the liposomal ozonated oil group than in the standard treatment group (46.7% vs 20.0%; $p = 0.028$).

Changes in TBUT and OSDI are shown in Table 3. No significant differences were observed between liposomal ozonated oil and standard treatment. However, the number of patients with TBUT > 10 seconds increased from 56.67% at baseline to 66.67% at day 21 and 76.67% at month 3 in the liposomal ozonated oil group and from 56.67% at baseline to 63.33% at day 21 and 63.33% at month 3 in the standard treatment group. OSDI scores were numerically lower at day 21 than at baseline in both groups, whereas values at month 3 were similar to baseline.

Table 1 Demographic Characteristics

	Liposomal Ozonated Oil (n = 30)	Standard Treatment (n = 30)	*p* value
Age, years	66.53 ± 9.50	67.20 ± 10.03	0.7924
Gender			0.7961
Male	15 (50.00%)	16 (53.33%)	
Female	15 (50.00%)	14 (46.67%)	
Cataract classification (LOCS3)			1.0000
N2	2 (6.67%)	2 (6.67%)	
N3	11 (36.67%)	10 (33.33%)	
N4	8 (26.67%)	9 (30.00%)	
N5	8 (26.67%)	8 (26.67%)	
N5 PSX	1 (3.33%)	1 (3.33%)	
Ocular comorbidity			
No	30 (100.00%)	30 (100.00%)	1.0000
Treated eye			0.7961
Right eye	15 (50.00%)	14 (46.67%)	
Left eye	15 (50.00%)	16 (53.33%)	
Previous treatments			1.0000
Refractive surgery myopia	2 (6.67%)	2 (6.67%)	
PVD both eyes	1 (3.33%)	1 (3.33%)	
No	27 (90.00%)	27 (90.00%)	
Previous cataract surgery			1.0000
No	15 (50.00%)	15 (50.00%)	
Yes	15 (50.00%)	15 (50.00%)	
Concomitant ocular disease			1.0000
No	30 (100.00%)	30 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	

Notes: Data are presented as the mean ± standard deviation (SD) or *n* (%). All *p* values correspond to between-group comparisons. Categorical variables were compared using the chi-square test with Yates' continuity correction or Fisher's exact test, as appropriate, and continuous variables were compared using Student's *t*-test.
Abbreviations: LOCS3, lens opacities classification system III; N, nuclear; PVD, posterior vitreous detachment.

Corrected distance visual acuity remained similar between groups at postoperative day 21 (0.88 ± 0.15 in the liposomal ozonated oil group vs 0.87 ± 0.15 in the standard treatment group; p = 0.7348) and month 3 (0.89 ± 0.14 in the liposomal ozonated oil group vs 0.87 ± 0.14 in the standard treatment group; p = 0.7107). Anterior chamber reaction revealed that 96.67% of eyes in both groups showed no anterior chamber reaction at postoperative day 21 increasing to 100.00% of eyes in both groups at month 3, with no differences between treatment groups.

Table 2 Changes in Ocular Signs and Symptoms from Baseline to day 21 and month 3

	Baseline			Day 21			Month 3		
	Liposomal Ozonated Oil (n = 30)	Standard (n = 30)	*p* value	Liposomal Ozonated Oil (n = 30)	Standard g(n = 30)	*p* value	Liposomal Ozonated Oil (n = 30)	Standard (n = 30)	*p* value
Foreign body sensation			0.3169			0.0910			0.0285
No	23 (76.67%)	26 (86.67%)		24 (80.00%)	18 (60.00%)		16 (53.33%)	24 (80.00%)	
Yes	7 (23.33%)	4 (13.33%)		6 (20.00%)	12 (40.00%)		14 (46.67%)	6 (20.00%)	
Itching			0.7065			0.7386			0.3169
No	27 (90.00%)	25 (83.33%)		25 (83.33%)	24 (80.00%)		26 (86.67%)	23 (76.67%)	
Yes	3 (10.00%)	5 (16.67%)		5 (16.67%)	6 (20.00%)		4 (13.33%)	7 (23.33%)	
Stinging			0.4884			0.7656			0.0953
No	26 (86.67%)	24 (80.00%)		23 (76.67%)	22 (73.33%)		27 (90.00%)	22 (73.33%)	
Yes	4 (13.33%)	6 (20.00%)		7 (23.33%)	8 (26.67%)		3 (10.00%)	8 (26.67%)	
Conjunctiva hyperemia			0.6707			1.0000			1.0000
No	26 (86.67%)	28 (93.33%)		28 (93.33%)	28 (93.33%)		30 (100.00%)	30 (100.00%)	
Yes	4 (13.33%)	2 (6.67%)		2 (6.67%)	2 (6.67%)		0 (0.00%)	0 (0.00%)	
Superficial keratitis			1.0000			1.0000			1.0000
No	28 (93.33%)	29 (96.67%)		30 (100.00%)	30 (100.00%)		30 (100.00%)	30 (100.00%)	
Yes	2 (6.67%)	1 (3.33%)		0 (0.00%)	0 (0.00%)		0 (0.00%)	0 (0.00%)	
Dryness			1.0000			1.0000			0.5186
No	29 (96.67%)	28 (93.33%)		25 (83.33%)	25 (83.33%)		23 (76.67%)	25 (83.33%)	
Yes	1 (3.33%)	2 (6.67%)		5 (16.67%)	5 (16.67%)		7 (23.33%)	5 (16.67%)	

Notes: Data are presented as *n* (%). All *p* values correspond to between-group comparisons at each study visit; no within-group comparisons over time were performed. Categorical variables were compared using the chi-square test with Yates' continuity correction or Fisher's exact test, as appropriate.

Table 3 Changes in TBUT and OSDI from Baseline to day 21 and month 3

	Baseline			Day 21			Month 3		
	Liposomal Ozonated Oil (n = 30)	Standard (n = 30)	*p* value	Liposomal Ozonated Oil (n = 30)	Standard (n = 30)	*p* value	Liposomal Ozonated Oil (n = 30)	Standard (n = 30)	*p* value
TBUT			1.0000			0.7866			0.2598
>10	17 (56.67%)	17 (56.67%)		20 (66.67%)	19 (63.33%)		23 (76.67%)	19 (63.33%)	
<10	13 (43.33%)	12 (40.00%)		10 (33.33%)	11 (36.67%)		7 (23.33%)	11 (36.67%)	
<5	0 (0.00%)	1 (3.33%)		0 (0.00%)	0 (0.00%)		0 (0.00%)	0 (0.00%)	
OSDI	16.35 ± 14.15	19.15 ± 18.90	0.5185	14.91 ± 14.31	15.85 ± 18.94	0.8288	16.63 ± 12.92	18.45 ± 19.08	0.6677

Notes: Data are presented as the mean ± standard deviation (SD) or *n* (%). All *p* values correspond to between-group comparisons at each study visit; no within-group comparisons over time were performed. TBUT categories were compared using the chi-square test with Yates' continuity correction or Fisher's exact test, as appropriate, and OSDI values were compared using Student's *t*-test.
Abbreviations: OSDI, ocular surface disease index; TBUT, tear break-up time.

Regarding patient-reported outcomes, all patients (100.00%) in both groups reported no discomfort on the VAS after 21 days of treatment. Similarly, all patients (100.00%) in both groups reported good tolerability after 21 days of treatment.

No intraoperative complications and no postoperative infectious or non-infectious complications were reported in either treatment group during the 21-day treatment period.

Discussion

The aim of this pilot study was to obtain preliminary data on tolerability and ocular surface effects of liposomal ozonated oil, compared with standard medical practice, when used in the perioperative management of cataract surgery.

Liposomal ozonated oil was well tolerated by all patients, consistent with prior studies reporting a favorable safety profile and good biocompatibility with corneoconjunctival tissues.[5,9,17,18] Furthermore, no patients reported discomfort on the VAS evaluation, and all patients rated the treatment as well tolerated.

Notably, almost all patients reported no anterior chamber inflammation (Tyndall effect), suggesting good postoperative inflammatory control with both treatment protocols. Foreign body sensation tended to be less frequent in the liposomal ozonated oil group at postoperative day 21, although the difference did not reach statistical significance. Interestingly, this pattern was not maintained at month 3, when foreign body sensation was reported more frequently in the liposomal ozonated oil group. Given the exploratory nature of the study, the small sample size, and the absence of within-group longitudinal analyses, this isolated finding should be interpreted with caution.

On the other hand, TBUT values showed a modest improvement, with a greater increase in the proportion of eyes achieving TBUT > 10 seconds in the liposomal ozonated oil group at both postoperative day 21 and month 3. Although these differences were not statistically significant, they may suggest a favorable effect of liposomal ozonated oil on tear film stability.

Liposomal ozonated oil has previously demonstrated antimicrobial and restorative properties in clinical studies involving viral conjunctivitis,[17] complicated corneal diseases,[19,20] blepharitis,[18] and in intravitreal injection preintervention asepsis.[6] Favorable results have also been reported in cataract preoperative asepsis, where a previous study showed a > 90% reduction in microbial load following administration of 2 drops 4 times daily for 3 days in 174 patients.[5] The findings of the present study, although exploratory, are broadly consistent with previous reports, as no post-surgical infections were observed in either treatment group during the 21-day treatment period. In particular, these findings should be interpreted in the context of previous clinical evidence showing a marked reduction in conjunctival bacterial load prior to cataract surgery following perioperative use of liposomal ozonated oil.[5] However, the small sample size precludes any conclusions regarding infection prevention.

This study has several strengths, including its prospective, controlled design and the fact that most patients contributed both eyes, allowing partial within-subject comparison and reducing inter-individual variability. The inclusion of both objective (eg, TBUT, visual acuity) and subjective (eg, discomfort, symptoms) outcome measures further strengthens the clinical relevance of the findings. An additional strength is the inclusion of exploratory 3-month postoperative assessments, which provided preliminary information regarding the persistence of ocular surface findings beyond the treatment period.

The antibiotic-corticosteroid suspension used in the standard treatment group contained benzalkonium chloride (0.1 mg/mL) as a preservative. Benzalkonium chloride has been associated with ocular surface toxicity and tear film instability after repeated topical administration.[21] Therefore, its potential influence on ocular surface parameters, including TBUT and patient-reported symptoms, cannot be excluded and should be considered when interpreting the ocular surface findings observed in this study.

However, several limitations must be acknowledged. The small sample size limits statistical power, particularly for rare outcomes such as postoperative infections. The open-label design may introduce observer or reporting bias. Although exploratory postoperative assessments at month 3 were available, this follow-up remained limited for evaluating long-term outcomes. In addition, although most patients contributed both eyes, a partially paired design was used, and statistical analyses were performed at the eye level without adjustment for intra-patient correlation, which may underestimate variability. Therefore, the results should be interpreted as preliminary and exploratory.

Despite these limitations, the favorable tolerability profile and comparable clinical outcomes observed with liposomal ozonated oil suggest that it may represent a promising option for further clinical evaluation, including future studies exploring its potential to reduce reliance on antibiotics. However, this was a pilot study, and larger, randomized, controlled trials are warranted to confirm these preliminary findings and to further explore its potential benefits for ocular surface stability and infection prevention.

Conclusion

Liposomal ozonated oil was well tolerated and showed comparable clinical outcomes to standard prophylaxis following cataract surgery. The findings of this pilot study suggest potential benefits for ocular surface outcomes that warrant confirmation in adequately powered studies with larger sample sizes and longer follow-up. No infectious complications occurred in either treatment group; while the absence of events and the limited sample size preclude conclusions regarding the prophylactic role of liposomal ozonated oil in this pilot study, this finding is consistent with its previously reported antimicrobial profile.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

The study was approved by the Ethics Committee from Hospital General Universitario Morales Meseguer (internal code: ENS 13/22), and the procedures were performed in accordance with the guidelines of the Declaration of Helsinki of 1964, and its later amendments. Written informed consent was obtained from all participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare that they have no competing interest.

References

1. Munita JM, Arias CA. Mechanisms of antibiotic resistance. *Microbiol Spectr*. 2016;4(2). doi:10.1128/microbiolspec.VMBF-0016-2015
2. Halachmi-Eyal O, Lang Y, Keness Y, Miron D. Preoperative topical moxifloxacin 0.5% and povidone-iodine 5.0% versus povidone-iodine 5.0% alone to reduce bacterial colonization in the conjunctival sac. *J Cataract Refract Surg*. 2009;35(12):2109–2114. doi:10.1016/j.jcrs.2009.06.038
3. Oakley CL, Vote BJ. Aqueous chlorhexidine (0.1%) is an effective alternative to povidone-iodine for intravitreal injection prophylaxis. *Acta Ophthalmol*. 2016;94(8):e808–e809. doi:10.1111/aos.12981
4. Vaziri K, Schwartz SG, Kishor K, Flynn HW. Endophthalmitis: state of the art. *Clin Ophthalmol*. 2015;9:95–108. doi:10.2147/OPTH.S76406
5. Spadea L, Zanotto E, Cavallo R, et al. Effectiveness of liposomal ozonised oil in reducing ocular microbial flora in patients undergoing cataract surgery. *J Cataract Refract Surg*. 2021;47(12):1548–1555. doi:10.1097/j.jcrs.0000000000000672
6. Grassi MO, Boscia G, Alessio G, et al. Liposomal ozonated oil ensures a further reduction in the microbial load before intravitreal injection: the "OPERA" Study. *Ophthalmol Ther*. 2024;13(10):2771–2788. doi:10.1007/s40123-024-01006-w
7. Grandi G, Cavallo R, Zanotto E, et al. In vitro antimicrobial activity of ozonated oil in liposome eyedrop against multidrug-resistant bacteria. *Open Med*. 2022;17(1):1057–1063. doi:10.1515/med-2022-0495
8. Ugazio E, Tullio V, Binello A, Tagliapietra S, Dosio F. Ozonated oils as antimicrobial systems in topical applications. Their characterization, current applications, and advances in improved delivery techniques. *Molecules*. 2020;25(2):334. doi:10.3390/molecules25020334
9. Cutarelli A, Carlini G, Sarno F, et al. The role of ozone carried by liposomes in the therapy of infectious and skin-regenerating ocular surface. *J Biomed Sci Eng*. 2019;12:347–353. doi:10.4236/jbise.2019.127026

10. Travagli V, Zanardi I, Bocci V. Topical applications of ozone and ozonated oils as anti-infective agents: an insight into the patent claims. *Recent Pat Antiinfect Drug Discov*. 2009;4(2):130–142. doi:10.2174/157489109788490271
11. Spadea L, Tonti E, Spaterna A, Marchegiani A. Use of ozone-based eye drops: a series of cases in veterinary and human spontaneous ocular pathologies. *Case Rep Ophthalmol*. 2018;9(2):287–298. doi:10.1159/000488846
12. Pérez-Santonja JJ, Güell JL, Gris O, et al. Liposomal ozonated oil in ocular infections: a review of preclinical and clinical studies, focusing on its antiseptic and regenerative properties. *Clin Ophthalmol*. 2022;16:1953–1962. doi:10.2147/OPTH.S360929
13. Ozodrop [Internet]. FB Vision; 2021. Available from: https://www.fb-vision.it/prodotto/ozodrop/. Accessed August 20, 2026.
14. Marchegiani A, Spaterna A. Ozone-based eye drops in anterior segment pathologies: rationale and pre-clinical data. *Ozone Ther*. 2017;2(1):6743. doi:10.4081/ozone.2017.6743
15. Basile AA, Cendali M, Mandelli G, Fioretto G. Anti-inflammatory effect of an eye drops solution based on liposomal ozonated oil in different corneal and anterior segment human diseases. *Ozone Ther*. 2019;4(2):8377. doi:10.4081/ozone.2019.8377
16. Marchegiani A, Magagnini M, Cerquetella M, et al. Preoperative topical liposomal ozone dispersion to reduce bacterial colonization in conjunctival sac and periocular skin: preliminary study in dogs. *Exp Eye Res*. 2019;189:107848. doi:10.1016/j.exer.2019.107848
17. Cagini C, Mariniello M, Messina M, et al. The role of ozonized oil and a combination of tobramycin/dexamethasone eye drops in the treatment of viral conjunctivitis: a randomized clinical trial. *Int Ophthalmol*. 2020;40(12):3209–3215. doi:10.1007/s10792-020-01503-4
18. Benítez-Del-Castillo JM. Liposomal ozonated oil effectiveness in the signs and symptoms of blepharitis in usual clinical practice. *Eur J Ophthalmol*. 2024;34(3):678–682. doi:10.1177/11206721231207116
19. Passidomo F, Pignatelli F, Addabbo G, Costagliola C. Topical liposomal ozonated oil in complicated corneal disease: a report on three clinical cases. *Int Med Case Rep J*. 2021;14:327–332. doi:10.2147/IMCRJ.S311839
20. Giralt IM, de Los Bueis AB, Ucero AM, Colomo PV. Management of neurotrophic corneal ulcer with a topical liposomal ozonated oil: a report on three clinical cases. *Am J Ophthalmol Case Rep*. 2025;38:102344. doi:10.1016/j.ajoc.2025.102344
21. Eraslan N, Bahar A. Evaluation of corneal epithelial thickness by anterior segment optical coherence tomography in glaucoma patients receiving topical prostaglandin and dry eye treatment. *Int Ophthalmol*. 2025;45(1):481. doi:10.1007/s10792-025-03859-x

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