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# Hypochlorous acid in ophthalmology: a narrative review

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## Abstract

**Background:** Hypochlorous acid (HOCl) is a naturally occurring molecule that plays a key role in host defence, exhibiting broad-spectrum antimicrobial activity against bacteria, viruses and fungi while maintaining an excellent safety profile for human tissues. Its utility has been demonstrated in numerous studies in wound care, perioperative antisepsis and more recently in nasopharyngeal sprays and inhalation applications.
**Aim:** The purpose of this study was to provide an overview of the current and potential uses of hypochlorous acid in ophthalmic practice.
**Materials and methods:** A comprehensive narrative review of the literature was conducted using the PubMed, Web of Science, ResearchGate, Google Scholar, Scopus and Embase databases. The search strategy was based on the following combination of key terms: ("hypochlorous acid" OR HOCl) AND (ophthalmology OR keratitis OR "ocular surgery" OR "meibomian gland dysfunction" OR "dry eye" OR blepharitis OR ocular OR "ocular surface" OR "eye infections" OR conjunctivitis).
**Results:** HOCl demonstrated broad antimicrobial activity in several studies, with meaningful reductions in bacterial load, rapid in vitro fungicidal effects and improvement in clinical parameters of blepharitis, dry eye disease and meibomian gland dysfunction. Antiseptic efficacy relative to povidone-iodine varied, with some studies showing inferior perioperative performance. Across all reports, HOCl was well tolerated, with no serious adverse events and consistently better patient comfort than povidone-iodine.
**Conclusions:** Hypochlorous acid is a safe, well-tolerated antiseptic with potential benefits in eyelid hygiene, dry eye disease, blepharitis and as an adjunct in ocular infections. While its antimicrobial efficacy is promising, it is inconsistent compared with povidone-iodine and it should currently be viewed as a complementary rather than a replacement agent. Further standardized clinical studies are needed to clarify its optimal role.

**Keywords:** hypochlorous acid; ocular surface; blepharitis; dry eye disease; ophthalmic surgery; antiseptic agents;

## 1. Introduction

Hypochlorous acid (HOCl) is a naturally occurring molecule formed by neutrophils as a part of the antimicrobial oxidative burst pathway to destroy pathogens. It plays a crucial role in host defence by exhibiting broad-spectrum antimicrobial activity against bacteria, viruses and fungi, while maintaining an excellent safety profile for human tissues. Hypochlorous acid exhibits antimicrobial, anti-inflammatory and antipruritic effects, as well as the capacity to disrupt biofilms. By reducing bacterial burden and local inflammation, it also helps create a more favourable oxygen environment at the wound site. Stabilized HOCl solutions function as well-tolerated antiseptic oxidizing agents with both antimicrobial and wound-healing properties and show no evidence of cytotoxicity. (1)(2)

Hypochlorous acid induces microbial death through multiple biochemical mechanisms, including oxidation of sulfhydryl-containing enzymes and amino acids, disruption of membrane integrity with leakage of intracellular contents, amino acids ring chlorination, impaired nutrient and oxygen uptake, suppression of protein synthesis, respiratory components oxidation, reduction in ATP production and fragmentation of DNA or inhibition of DNA synthesis. In viral pathogens, HOCl additionally targets structural proteins, such as capsid and surface components, as well as lipid envelopes and nucleic acids, compromising their integrity and function. (3)

At concentrations within the authorized range, topical HOCl solutions have not been associated with documented adverse effects. (3) In vitro biocompatibility assessments indicate that HOCl solutions are safe for both skin and ocular surface. (4)

Numerous investigations demonstrate its utility in perioperative antisepsis, wound management and more recently in nasopharyngeal sprays and inhalation applications. The use of HOCl in wound care is already established as an accepted clinical practice. (3)

These well-documented properties make HOCl a compelling agent for potential applications within ophthalmology. Therefore, this review aimed to summarize current evidence regarding the clinical applications, effectiveness and tolerability of hypochlorous acid in ophthalmology, in order to clarify its potential role in routine ocular care and peri-operative practice.

## 2. Research materials and methods

A comprehensive narrative review of the literature was conducted using the PubMed, Web of Science, ResearchGate, Google Scholar, Scopus and Embase databases. The search strategy was based on the following combination of key terms: ("hypochlorous acid" OR HOCl) AND (ophthalmology OR keratitis OR "ocular surgery" OR "meibomian gland dysfunction" OR "dry eye" OR blepharitis OR ocular OR "ocular surface" OR "eye infections" OR conjunctivitis). Studies were screened by title and abstract. Letters to the editor, single case reports, conference abstracts, animal studies and articles not published in English were excluded from the analysis. References of included articles were also manually screened to identify additional relevant studies.

## 3. Research results

Once the literature search and preliminary screening were completed, the eligible studies were classified into subcategories according to their clinical applications in ophthalmology. Consequently, this section is organised into thematic groups covering the major uses of hypochlorous acid, including eyelid hygiene, dry eye management, antimicrobial activity, perioperative antisepsis, treatment of ocular infections and safety considerations.

### 3.1 The role of hypochlorous acid in eyelid hygiene, dry eye disease, ocular surface inflammation, blepharitis management and its antimicrobial and antibiofilm properties in ophthalmic settings.

Maintaining good eyelid hygiene is absolutely crucial for ocular surface health. Its lack or inefficiency can lead to meibomian gland dysfunction, dry eye disease and blepharitis. Products such as facial cleanser, baby shampoo, soap, low concentration tea tree oil, low concentration of Terpine-4-ol, boric acid solution with a concentration of 3%, low concentration okra oil, alongside low concentration hypochlorous acid are commercially available for at-home eyelid cleaning. Common domestic cleaning methods include finger massage cleaning and use of lid brushes, cotton swabs, sponge pads and cleaning wipes. In hospital eyelid cleansing, substances such as iodophor, povidone-iodine, medicinal alcohol, hydrogen peroxide and highly concentrated tea tree oil are commonly used. (5)

Blepharitis is a frequent inflammatory disorder affecting the eyelid margin and is often linked to ocular surface disturbances and a reduction in patients' quality of life. The condition may involve either the front or back portion of the eyelid. Anterior blepharitis primarily impacts the skin of the lid, the bases of the eyelashes and the lash follicles, whereas posterior blepharitis is characterized by abnormal function of the meibomian glands situated on the posterior eyelid margin. Dysfunction of these glands contributes to instability of the tear film and represents a major underlying factor in the development of dry eye disease. The origin of blepharitis is complex and not fully understood. It encompasses a range of infectious and non-infectious pathways. The term primary blepharitis typically includes presentations associated with conditions such as rosacea, seborrheic disease or hypersensitivity responses to staphylococcal exotoxins. Secondary blepharitis, in contrast, refers to cases driven by microbial overgrowth, bacterial or viral, or by parasitic infestations, including phthiriasis or Demodex mites. (6) Demodex is a mandatory skin parasite that normally resides on the human skin surface, but excessive proliferation can trigger pathological reactions. Only two species, Demodex folliculorum and Demodex brevis, are found on the human face and eyelids. (7)

In a scoping review about eyelid hygiene products, sprays containing 0.01% HOCl are presented as a well-tolerated and user-friendly alternative to traditional wipes or gels. They may be applied to a cotton pad and wiped along the lash margins and do not require rinsing after use. They are generally well tolerated, offering a comfort level comparable to saline. (8)

In a study assessing the effectiveness of bacterial load reduction on ocular skin 20 minutes after application of a 0.01% pure hypochlorous acid saline hygiene solution, it has proved its utility.

Samples for microbiological analysis were obtained from the skin below the eyelid at baseline and again 20 minutes after the product was applied. The authors stated that staphylococci constituted for about 61% of all strains originating from the skin under the lower eyelid with S. epidermidis strains comprising 60% of all staphylococcal strains identified. The HOCl hygiene solution achieved a rapid and profound antibacterial effect, reducing overall staphylococcal load on the skin by 99.6% within 20 minutes, including a 99.5% reduction in S. epidermidis. Notably, its efficacy was comparable against both antibiotic resistant and antibiotic susceptible strains. HOCl treatment did not preferentially eliminate susceptible strains, but it effectively reduced potentially clinically relevant bacterial overgrowth, lowering the overall bacterial load by more than 90%. Lowering the bacterial burden may aid in the management of blepharitis, meibomian gland dysfunction, dry eye disease and other causes of ocular surface irritation. (9) In contrast to the findings of Stroman et al., who demonstrated a significant reduction in periocular bacterial load after in vivo application of a 0.01% HOCl solution, the in vitro evaluation of eye drops containing 0.011% HOCl showed no antimicrobial activity against Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa and Candida albicans across increasing dilutions. The impact of the eye drops on bacterial growth was evaluated beginning with a 1:2 dilution in Mueller-Hinton or Sabouraud broth, followed by additional dilutions (1:8, 1:32, 1:128, 1:512, 1:2048) prepared in 100 µl volumes. When used at high concentrations, the HOCl formulation demonstrated only a growth-suppressing effect on bacteria. These differing results likely reflect variations in experimental conditions, including the use of ophthalmic formulations, the in vitro setting and the assessment of efficacy at various dilution levels. (10) Another recent in vitro study by Fernández-Engroba et al. was performed to assess the bactericidal effectiveness of various agents employed in the management of chronic staphylococcal anterior blepharitis. Cultures of standard Staphylococcus aureus and coagulase-negative Staphylococcus (CoNS) strains were prepared, and their susceptibility to vancomycin 30 µg, netilmicin 30 µg, 0.01% hypochlorous acid, Melaleuca alternifolia leaf oil and 1% chlorhexidine digluconate was evaluated using the agar disk diffusion method. After 24 hours of exposure, the halos produced by each agent against both S. aureus and CoNS were measured in millimetres. The inhibition zones produced by the antiseptic agents, excluding antibiotics, were analysed quantitatively, since no established reference standards exist in the literature. When an agent generates a measurable halo, it indicates some degree of bactericidal action, but the actual strength and clinical significance of this effect remain uncertain, as the halo measurement also includes the diameter of the test discs. The halo induced by 0.01% HOCL against S. aureus was small (under 15 mm). However, because no sensitivity guidelines exist for this agent, its activity cannot be formally classified as "sensitive" or "resistant." Although 0.01% HOCl showed weaker activity against CoNS than the other tested substances (excluding Melaleuca alternifolia leaf oil), it still produced a larger inhibition zone for CoNS than for S. aureus. Both netilmicin and vancomycin effectively inhibited the growth of the two staphylococcal strains, supporting their use as potential second-line treatments in chronic staphylococcal blepharitis. Chlorhexidine digluconate showed a level of antimicrobial activity similar to these antibiotics, whereas hypochlorous acid and Melaleuca alternifolia leaf oil exhibited noticeably weaker bactericidal effects. (11)

On the other hand, an in vitro study assessing the bactericidal activity of a hypochlorous acid hygiene solution against biofilms formed by ocular clinical isolates demonstrated partial efficacy. The authors evaluated the effect of HOCl solution on biofilms generated by blepharitis-derived isolates of Staphylococcus aureus, coagulase negative staphylococci and a keratitis-associated Pseudomonas aeruginosa strain after introducing them into contact lens cases and incubating them at 37 °C for 24 hours. The study shows that HOCl effectively eradicates biofilm-associated Staphylococcus species isolated from blepharitis cases, though the response differs among strains. S. capitis and S. aureus were more sensitive to HOCl than S. epidermidis. (12) Given that S. epidermidis represents normal skin microbiota whereas S. aureus is a more pathogenic, transiently colonizing species, the selective reduction of S. aureus while preserving S. epidermidis may offer a clinical advantage. (9,12) The 0.01% hypochlorous acid hygiene solution demonstrated bactericidal activity against bacteria embedded in biofilms, although it did not compromise the structural integrity of the biofilm itself. Consequently, physical cleaning methods, such as washing or scrubbing, are likely necessary to eliminate the dead bacteria from treated surfaces. In clinical practice, this role is commonly fulfilled by eyelid scrubs, which are routinely recommended for patients with blepharitis and effectively aid in mechanically clearing away the dead microorganisms. (12)

A prospective randomised study was conducted by Mencucci et al. to evaluate the therapeutic effects and antimicrobial performance of a hypochlorous acid hygiene solution in comparison with hyaluronic acid wipes for managing blepharitis in individuals with dry eye disease. The clinical evaluation included a series of measurements taken at baseline and after completing a 4-week treatment period, during which one group used a hypochlorous acid hygiene solution and the second group (HYAL) used hyaluronic acid wipes twice daily. These assessments comprised Non-Invasive Keratograph Break-Up Time (NIK-BUT), tear film break-up time (TF-BUT), Tear Meniscus Height (TMH), Keratograph meibography, Meibomian Gland Yield Secretion Score (MGYSS), Corneal Staining Score (CSS), Schirmer test I, Keratograph conjunctival redness score and Ocular Surface Disease Index (OSDI). Furthermore, at the beginning of the study, microbiological assessments of the upper and lower eyelid margins were carried out both prior to treatment and 5 minutes following its application. The HOCl group demonstrated significant improvements in NIK-BUT, TF-BUT, TMH, and OSDI scores, whereas the HYAL group showed meaningful changes only in TMH and OSDI. Based on these findings, the enhanced tear film stability observed in the HOCl group may stem from its ability to reduce bacterial load and the subsequent lipolytic exoenzyme activity with the improvement of meibomian secretion, which likely contributed to superior symptomatic relief. Microbiological testing aligned with the clinical outcomes, revealing a notable decrease in bacterial presence in both groups, though the reduction was more substantial with HOCl (approximately 90%) compared with hyaluronic acid wipes (62%). Both treatments demonstrated broad activity across the eyelid microbial flora, without selective effects on specific bacterial species. In the HOCl group, the enhanced reduction in bacterial load appeared to result from the dual action of the product, its mechanical cleansing effect provided by the sterile wipe and the chemical activity of hypochlorous acid. Based on these results, wipes containing hypochlorous acid appear to be a safe option for managing blepharitis, offering favourable clinical and microbiological outcomes with no adverse reactions observed in the study. (6)

Further evidence supporting the usefulness of hypochlorous acid in blepharitis management comes from a randomized clinical trial by Zhang et al., evaluating the effect of HOCl delivered through ultrasonic atomization. Ultrasonic atomization breaks the liquid into fine droplets, allowing them to permeate and spread uniformly across the ocular surface. Participants were assigned either to the HOCl atomization group or to a control group performing traditional eyelid scrubs. Both groups received the same adjunctive therapy consisting of warm compresses twice daily and topical 0.5% levofloxacin three times a day. Assessments of clinical parameters were carried out at the start of the study and on day 14 of treatment. After a two-week treatment period, the study evaluated primary outcomes including a mean reduction in clinical symptoms measured by Ocular Surface Disease Index scores (OSDI), lid margin redness, lid margin abnormalities, meibum expressibility, meibum quality and non-invasive breakup time. Secondary outcomes comprising changes in conjunctival redness, corneal epitheliopathy as assessed by Corneal Fluorescein Staining (CFS) and Tear Meniscus Height (TMH) were also assessed. This study shows that, compared with conventional eyelid scrubs, ultrasonic atomization of 0.01% HOCl for eyelid hygiene leads to significant improvements in OSDI scores, accompanied by reductions in lid margin redness and abnormalities, as well as enhanced meibum expressibility and quality. Furthermore, patients treated with HOCl demonstrated greater improvement in CFS scores compared with the control group ($p < 0.05$), which may be attributed to HOCl's ability to manage biofilms, stabilize the tear film and support ocular epithelial healing. Moreover, the treatment was well tolerated, with no reported drug-related discomfort or adverse events. Overall, two weeks of 0.01% HOCl applied by ultrasonic atomization for five minutes per eye was effective and well tolerated in managing blepharitis, supporting its potential role as an adjunctive treatment alongside topical levofloxacin and warm compresses. (13)

Another study assessing effectiveness of HOCl delivered through ultrasonic atomization was performed by Li et al. This double-blind, placebo-controlled randomized study aimed to investigate how hypochlorous acid applied through ultrasonic atomization influences meibomian gland dysfunction dry eye. The study group received a commercially available 0.01% hypochlorous acid solution, while the control group was treated with a placebo containing 0.1% purified sodium hyaluronate. Data were collected on days 1, 15, 30, and 55. Patients' complains, Schirmer's I test, the meibum analysis, conjunctive congestion, corneal staining and Non-Invasive Keratograph Break-Up Time (NIK-BUT) were assessed using Keratograph 5M, while tear levels of MMP-9 and IL-2 were measured with a commercially available inflammation kit and Demodex mites amount, morphology and survival time were evaluated via microscopy. The study demonstrated that hypochlorous acid (HOCl) provided greater improvement in patient-reported symptoms compared with the placebo group. HOCl significantly reduced ocular inflammatory markers, including IL-2 and MMP-9. Additionally, HOCl outperformed the control in improving tear production as measured by the Schirmer test. The treatment also shortened the survival time of Demodex mites in vivo, supporting its potential as an effective therapy for Demodex-associated blepharitis. (14) In opposition to these promising results regarding Demodex mites, an in vitro study by Kabat showed that demodicidal activity of 0.01% HOCl was minimal as compared to 4% terpinen-4-ol (T4O) solution with mineral oil (MO) as negative control. Live Demodex mites collected from volunteers were exposed to small volumes of the tested substances including 0.01% HOCl, 4% T4O or pure MO. The specimens were examined microscopically at 10-minute intervals for up to 90 minutes. The "kill time" was defined as the period from application of the solution to the point at which the mites showed no movement of the body, legs, mouthparts or pedipalps for at least 60 seconds. The study showed that Demodex mites were eliminated much quicker by T4O, which killed all mites in about 40 minutes. In comparison, exposure to HOCl resulted in substantially slower mite death (mean kill time of 87.86±4.23 mins), with most mites (79%) still alive at the end of the 90-

minute observation period. Mineral oil showed no acaricidal activity at all. Statistically, T4O was significantly more effective than HOCl, while HOCl did not differ meaningfully from mineral oil in its ability to kill Demodex. Additionally, a subset of mites exposed to HOCl monitored beyond the main observation window remained alive for as long as 3.5 hours. A possible limitation of the study was the limited stability of 0.01% HOCl. Being a saline-based solution, it evaporated from the test slides much faster than the lipid-based 4% T4O or 100% mineral oil. (7)

Yang et al. conducted a study to analyse the microbial profiles of meibomian gland secretions in patients with internal hordeolum before and following therapy with hypochlorous acid eyelid wipes, with the aim of clarifying the mechanism by which this treatment exerts its therapeutic effect. Meibomian gland secretions were obtained from patients prior to therapy and from those who had recovered after using hypochlorous acid eyelid wipes for seven days. The samples underwent 16S rRNA high-throughput sequencing, and the resulting datasets were analysed to identify changes in the microbial composition and community structure of the glandular secretions before and after treatment of internal hordeolum. The analysis showed no meaningful differences in microbial composition at the phylum level before and after treatment. However, from the class level onward, significant shifts in the microbial population structure were observed following hypochlorous acid eyelid cleansing. Although overall microbial diversity remained unchanged, the treatment appeared to influence the balance of specific bacteria. Hypochlorous acid eyelid wipes reduced the relative abundance of symbiotic pathogens, such as Staphylococcus, Neisseria, Actinomycetes and Ruminococcus, while increasing levels of beneficial, anti-inflammatory symbionts like Faecalibacterium prausnitzii. These findings suggest that the therapeutic effect in internal hordeolum may stem from broad-spectrum antibacterial action combined with a shift towards more favourable, anti-inflammatory microbial profiles. (15)

### 3.2 Hypochlorous acid in the treatment of ocular infections.

Most of previously cited studies already provided information about antimicrobial and antibiofilm properties of hypochlorous acid in ophthalmology. (6,9–12,14,15) This subchapter will mainly focus on its use in fighting eye infections and preventing them.

Bertone et al. made a case series describing practical clinical experiences with an HOCl ophthalmic spray as the adjuvant treatment in the management of eye infections, providing additional insight into its potential roles in ophthalmic care. In this series, ten cases of blepharitis accompanied by additional ocular complications were reviewed. All patients showed improvement of blepharitis after incorporating HOCl ophthalmic spray as adjunctive therapy. The mean treatment time was 20 days, during which patients typically applied the HOCl ophthalmic spray twice daily. In every case, the combination of antibiotics, topical in 8 patients and systemic in 2, together with HOCl spray led to a noticeably faster resolution of the ocular conditions associated with blepharitis. A 78-year-old patient who had been receiving low-dose oral tetracycline for over a month to manage blepharitis linked to meibomian gland dysfunction experienced full resolution within just one week after HOCl ophthalmic spray was added to the regimen. A comparable outcome was observed in another case involving chronic blepharitis with concomitant conjunctival redness and meibomitis. The patient received a 14-day course of topical corticosteroids and antibiotics along with the HOCl ophthalmic spray twice daily. After one week, the patient noted symptomatic improvement, accompanied by a marked reduction in conjunctival hyperaemia and meibomitis. A 55-year-old patient with rosacea-related chronic blepharitis discontinued oral tetracycline due to intolerance but continued using the HOCl ophthalmic spray, which resulted in full symptom resolution within 15 days, demonstrating that HOCl was effective even without systemic antibiotic therapy. A 78-year-old patient with severe blepharitis and catarrhal conjunctivitis was treated with topical antibiotics, corticosteroids and HOCl spray. After two weeks, symptoms improved and by 40 days the eyelid inflammation, conjunctivitis and ulcerations had resolved, with a marked reduction in discomfort such as burning, tearing and foreign-body sensation. Two cases were described in which patients with herpes zoster received adjunctive treatment with the HOCl ophthalmic spray. The first patient, diagnosed with hypertensive herpetic uveitis due to herpes zoster, initially discontinued systemic antivirals after three days without improvement. At follow-up, he showed extensive facial lesions and significant ocular inflammation. A full antiviral and anti-inflammatory regimen with topical antiviral, systemic antiviral, along with topical dexamethasone, tropicamide, dorzolamide was initiated and twice-daily HOCl ophthalmic spray was added. Within three days, facial scabs and pustules had resolved and the herpetic uveitis showed clear signs of improvement. In a second case, an 83-year-old patient developed a herpes zoster rash along the first left trigeminal branch. He received systemic antivirals and HOCl ophthalmic spray applied to the face, eyelids and eye surface. After three days, vesicles and edema decreased, and by 10 days only minor crusts remained. The patient continued HOCl spray for one month, leading to complete resolution of the lesions. (16)

These clinical cases indicate that using HOCl ophthalmic spray as an adjunct therapy can shorten the duration of antibiotic, corticosteroid and antiviral treatments, even in severe ocular conditions. Its anti-inflammatory properties help reduce infection, alleviate symptoms such as itching and pain, prevent scarring and limit harmful inflammatory responses. Overall, HOCl spray improved clinical outcomes and accelerated recovery when combined with conventional therapies. Additionally, HOCl ophthalmic spray was well tolerated, with no reported adverse effects and high patient compliance. (16)

Two articles addressing antifungal activity of hypochlorous acid and its use in the treatment of fungal ocular infections were found. (17,18) Odorcic et al. published a study, which aim was to summarize current literature about fungal keratitis and endophthalmitis after Boston Keratoprosthesis (KPro) implantation and to assess the antifungal effects of 0.01% hypochlorous acid against representative mold and yeast species known to cause ocular infections. The Boston Keratoprosthesis is used in patients with advanced corneal disease who are unlikely to benefit from standard corneal transplantation. Although long-term use of broad-spectrum antibiotics has greatly lowered bacterial endophthalmitis rates, it has simultaneously increased susceptibility to fungal colonization and infection. Fungal growth on the contact lens typically appears as small, white deposits and active fungal keratitis or endophthalmitis requires prompt topical and systemic or intravitreal antifungal therapy based on culture findings. Despite the persistent risk of fungal infection in KPro recipients, no clear guidelines for effective antifungal prophylaxis currently exist. In this study, five molds (Acremonium kiliense, Aspergillus flavus, Aspergillus fumigatus, Fusarium solani, Mucor indicus) and two yeasts (Candida albicans, Candida parapsilosis) were tested. For the time kill assay, 2 µl of each fungal suspension was mixed with either 18 µl of normal saline (control) or 18 µl of 0.01% hypochlorous acid to evaluate antifungal activity. Initial testing showed that 0.01% hypochlorous acid rapidly reduced viable conidia of Acremonium kiliense, Aspergillus flavus, Aspergillus fumigatus, Fusarium solani and Mucor indicus by over 99% within 15 seconds. After 1 minute, fungal reduction reached at least 99.9%, with no further improvement at longer exposure times. Based on these findings, all fungal isolates were subsequently assessed using a 1-minute contact time with 0.01% hypochlorous acid. At inoculum levels of $5 \times 10^6$–$5 \times 10^7$ CFU/ml, 0.01% hypochlorous acid achieved at least a 99.99% reduction in viable fungal cells or conidia across all tested molds and yeasts, with some species reaching ≥99.999% kill rates. This demonstrates a rapid and broad-spectrum fungicidal effect within just 60 seconds, outperforming many conventional antifungal treatments that act slowly or show limited activity against spores. Importantly, hypochlorous acid was consistently effective against all evaluated genera, including Acremonium, Aspergillus, Fusarium, Mucor and Candida. The authors noted that confirming hypochlorous acid as a potential topical antifungal prophylaxis requires evaluating its safety on the ocular surface and within the eye. However, because HOCl is highly reactive, short-lived and becomes further diluted by the tear film, they consider the likelihood of ocular or intraocular toxicity to be minimal. (17) Wang et al. conducted a randomized controlled trial to assess how effective and safe 0.01% hypochlorous acid (HOCl) eye drops are for managing fungal keratitis. Infectious keratitis is a major cause of corneal blindness in China, with fungal cases rising steadily. Fungal ulcers are often harder to manage than bacterial ones due to poor penetration of many antifungal agents. In this study, patients in the control group received standard therapy consisting of frequent topical natamycin, oral itraconazole, atropine gel and prophylactic levofloxacin, with pressure-lowering drops added if needed. In the HOCl group, patients were treated with the same regimen but with the addition of hourly hypochlorous acid eye drops. Key clinical indicators included visual acuity, ulcer size and depth, hypopyon changes, epithelial defect area and overall treatment success. Both in mild (grade I) and more severe (grade II) fungal keratitis, the addition of HOCl to standard therapy accelerated clinical improvement. Patients in the HOCl group showed a significantly shorter healing time and faster hypopyon resolution compared with controls, while final visual acuity and complication rates remained similar between groups. In more advanced cases, treatment failure rates did not differ significantly, but the overall recovery was still faster with adjunctive HOCl. The study also showed that antifungal therapy, being invasive, can cause complications such as cataracts or corneal neovascularization and HOCl did not lower their frequency. This may be because HOCl effectively kills fungi but has limited impact on mycotoxins. Unlike some antifungal drugs that trigger corneal irritation, such as photophobia, tearing or increased pain, these adverse symptoms were not observed with topical HOCl. (18)

Siktberg and Mawn presented a case series at the intersection of surgery and ophthalmology, describing the use of locally administered hypochlorous acid in the treatment of periorbital necrotizing fasciitis. Periorbital necrotizing fasciitis is a rapidly progressive soft-tissue infection that can lead to extensive necrosis and even death. Although the immune system normally uses reactive oxygen species like hypochlorous acid to combat bacteria, pathogens in necrotizing fasciitis neutralize these defences. Applying hypochlorous acid externally may help restore antimicrobial activity in heavily infected tissues. Standard periorbital necrotizing fasciitis management relies on intravenous antibiotics and repeated surgical debridement. However, outcomes can be poor, with reported exenteration rates of 6.7-15.1% and mortality rates of 8.5-14.4%. In this case series 18 orbits from 15 patients with periorbital necrotizing fasciitis were treated with local hypochlorous acid alongside standard surgical debridement and intravenous antibiotics. HOCl was delivered through an orbital catheter and Penrose drain to flush toxins.

All patients responded well to HOCl irrigation, with no cases of irritation, allergic reactions or orbital compartment syndrome. Additionally, no patient required exenteration or died. The authors concluded that HOCl was incorporated into the periorbital necrotizing fasciitis protocol because it is safe, replaces a key reactive oxygen species involved in natural antimicrobial defence and, based on their clinical experience, appears to accelerate patient improvement. (19)
Romanowski et al. conducted an in vitro study assessing a potential disinfection method for multi-use contact lens trial sets by testing the in-vitro antimicrobial activity of 0.01% hypochlorous acid on hybrid rigid gas-permeable contact lenses fitted with silicone hydrogel skirts and single-well contact lens cases. Proper disinfection of contact lenses and their storage cases is crucial for maintaining ocular hygiene, particularly for reusable trial lens sets used in fittings. Surfaces were contaminated with a range of common ocular pathogens, including Staphylococcus aureus, Coagulase-negative Staphylococcus, Streptococcus pneumoniae, Pseudomonas aeruginosa, Serratia marcescens, Achromobacter xylosoxidans, Candida albicans, adenovirus type 19/64 and HSV-1. After spraying the lenses and cases with HOCl or control solution and allowing a 1-minute exposure, they were sonicated to detach any remaining microbes, which were then quantified. A 1-minute exposure to 0.01% hypochlorous acid effectively eliminated nearly all tested pathogens from contact lenses. All bacterial and Candida albicans strains were completely removed from hybrid lenses except S. aureus, which persisted on one lens. Among viruses, adenovirus type 19/64 was fully eradicated, while HSV-1 showed resistance. The cause of 0.01% hypochlorous acid's ineffectiveness against HSV-1 on the lenses remains unclear. In contrast, all microorganisms, including bacteria, yeast and viruses, were entirely eliminated from the single-well cases after 1 minute of HOCl exposure. (20)

### 3.3 HOCl in preoperative and perioperative antisepsis

Current prophylaxis before intravitreal injections and other ocular surgeries relies on 5% povidone-iodine (PI) applied to the ocular surface, along with clearing the eyelids and lashes. PI provides broad-spectrum antimicrobial activity through free iodine but it can cause irritation, including stinging and burning. Because many patients undergo repeated procedures, clinicians have increasingly looked for alternative antiseptic options that are both effective and better tolerated. (21)
In the literature search, four studies were identified that directly compared HOCl with povidone-iodine in the context of ophthalmic preoperative antisepsis. (21–24)

Kowalski et al. evaluated whether 2.5% povidone-iodine and 0.01% HOCl, potentially better tolerated by patients, are as effective as standard 5% povidone-iodine. Using corneoscleral tissue as a model of the ocular surface, the authors tested the three antiseptics against bacterial endophthalmitis isolates from 20 cases, assessing their efficacy after a 3-minute exposure. Corneal tissue was seeded with $10^3$ CFU of bacteria, exposed to antiseptics for 3 minutes, then transferred to liquid culture and observed for three days. Absence of microbial growth was considered successful disinfection. In this study, 5% and 2.5% povidone-iodine outperformed HOCl in preventing bacterial growth on corneoscleral tissue. Although HOCl showed weaker antiseptic efficacy, it may still serve as an option for patients unable to tolerate PI. Overall, 5% PI remains the most effective preoperative prophylactic agent. (21)

Gonzalez-Gonzalez et al. performed randomized, single-masked, controlled fellow eye study comparing the antibacterial effect of 0.01% hypochlorous acid with 5% povidone-iodine on the eyelid margins of 20 healthy volunteers. Each participant received HOCl on one eye and PI on the other, with both eyelid margins swabbed before treatment for baseline cultures. After applying the solutions to the eyelid margin and lash bases, repeat swabs were taken 10 minutes later. All bacterial counts and culture analyses were performed in a masked fashion. All cultures were observed for bacterial growth over a 5-day period. The primary outcome was the decrease in colony-forming units on the eyelid margin. Secondary outcomes included the reduction in the percentage of culture-positive swabs and any adverse reactions reported within the first hour after application. The trial demonstrated that both 0.01% hypochlorous acid (HA) and 5% povidone-iodine (PI) significantly lowered eyelid margin bacterial colony-forming units compared with baseline samples. PI produced a greater numerical reduction in bacterial load, but the difference between the two groups was not statistically significant. Over half of the volunteers showed decreased flora with both agents, while some improved only with PI and very few showed no improvement. Mild, short-lived irritation occurred only in PI-treated eyes, whereas HA caused no adverse effects. Overall, both HA and PI effectively reduced common pathogens associated with postoperative endophthalmitis, with PI remaining the stronger and preferred antiseptic. Hypochlorous acid could serve as an adjunctive treatment for blepharitis in the days leading up to surgery or other ophthalmic procedures, helping to reduce the natural bacterial load on the eyelids and surrounding ocular tissues. (22)

Hejkal et al. conducted a study which aimed to compare the antimicrobial efficacy of 0.01% hypochlorous acid (HA) with 5% povidone-iodine (PI) used topically on the ocular surface. This single-center study enrolled 40 healthy volunteers without ocular diseases or medications. Each participant had baseline swabs taken from the inferior conjunctiva and lower lid margin of both eyes. Depending on participant number, one eye was treated with 0.5 ml of 0.01% hypochlorous acid and the second eye with 0.5 ml of 5% povidone-iodine. After a 1-minute exposure, both eyes were swabbed again for culture. Eyes treated with PI were additionally rinsed with sterile saline and swabbed a third time, whereas HA-treated eyes required no rinse and no third swab. All cultures were processed by masked laboratory personnel. In this study, only eyes with more than one baseline colony-forming unit (CFU) were included, yielding 21 HA-treated eyes and 17 PI-treated eyes. Both antiseptics produced substantial bacterial reduction: HA reduced CFUs by an average of 86%, while PI reduced them by 82%. Many samples reached zero CFU after treatment, indicating that the true reductions were likely even greater. One PI-treated eye showed a slight increase in CFUs. Additionally, after the mandatory saline rinse of PI-treated eyes, 42% of those eyes had higher CFU counts compared to their post-treatment swabs. This included several eyes not considered in the main analysis due to very low baseline counts. These findings suggest that rinsing PI with saline may reintroduce or spread bacteria and that HA, being both antimicrobial and non-irritating, might be a better rinse alternative. No participants experienced discomfort in the eyes treated with HA, whereas 31 out of 40 individuals (78%) reported noticeably greater stinging, burning or irritation in the eyes that received PI compared with the HA-treated eyes. Although no statistically significant difference between the agents was found, partly due to limited sample size and many baseline-negative swabs, both HA and PI effectively lowered bacterial load. Even though this study lacked sufficient statistical power to determine whether HA is genuinely comparable to PI, these findings suggest that HA may serve as a suitable antiseptic option for patients who are unable to tolerate PI. (23)

Kanclerz et al. performed a study which purpose was to evaluate how effectively prepared diluted hypochlorous acid solution (Microdacyn®) (HA) compares with a 10% povidone-iodine solution (PI) in providing antisepsis in phacoemulsification cataract surgery. A total of 110 patients completed the study (59 PI, 51 HA). The PI group received periocular skin disinfection and conjunctival lavage with 10% PI, while the HA group underwent the same steps using HA. Before surgery, a baseline conjunctival swab was taken from the eye to be operated on. Patients were then assigned to receive either PI or HA irrigation and a second swab was collected three minutes later. During cataract surgery, both groups received standard Ringer's lactate irrigation and a final swab was taken before removing the speculum. All patients were monitored for 3 months for signs of postoperative inflammation or endophthalmitis. In this study, conjunctival lavage with 10% PI significantly reduced bacterial load immediately after application, whereas hypochlorous acid solution (HA) did not significantly decrease positive conjunctival cultures immediately after lavage. In the HA group, the number of positive cultures was significantly lower at the end of surgery compared to immediately after HA lavage. Conjunctival irrigation with Ringer's lactate during surgery probably contributed to a reduction in bacterial load. A significant difference in bacterial presence between the PI and HA groups was observed both immediately after lavage and at the end of surgery. Patients receiving HA reported significantly less discomfort during lavage compared with PI. No cases of postoperative endophthalmitis or ocular inflammation occurred in either group. The authors stated that these results indicate that while HA is better tolerated, its antimicrobial efficacy is substantially lower than PI and therefore HA should not be used for perioperative antisepsis in cataract surgery. (24) Hejkal et al. stated that the differing results likely stem from study design differences: Kanclerz et al. only recorded positive or negative cultures without quantifying bacterial load and the hypochlorous acid concentration was not specified. In contrast, study by Hejkal et al. measured colony-forming units reductions, providing quantitative evidence of hypochlorous acid's in vivo bactericidal effect. (23)

Kanclerz and Myers in their review of comparative studies about alternatives for povidone–iodine in ophthalmic surgery describe hypochlorous acid as a clear, odorless, pH-neutral liquid that is nonirritating and exhibits antimicrobial effects due to its oxidizing action. They find it important to note that continuous irrigation is necessary with this agent, as it quickly becomes inactive upon contact with organic matter. Although some guidelines suggest using hypochlorous acid in patients intolerant to PI, they found no supporting evidence for this practice. (25) Grzybowski et al. in their article about the rising importance of antiseptics in ophthalmology added that HOCl has demonstrated the ability to manage biofilms and support the healing of the ocular epithelial tissue. The authors believe that HOCl may have limited antiseptic effectiveness in surgical contexts according to some studies. However, there is some evidence supporting its use as an adjunct for managing eye infections and for periocular cleansing before and after ocular procedures. Additionally, they stated that further studies are needed to clarify the effects of HOCl disinfection on ocular flora. (26)

### 3.4 Safety and tolerability of hypochlorous acid on the ocular surface

Previously cited studies support the view that HOCl is a safe and well-tolerated agent. None of the studies reported any serious adverse effects or significant hypersensitivity or intolerance to HOCl.

Fam et al. carried out a patient reported outcomes study to evaluate how hypochlorous acid antiseptic washout affects patient comfort following intravitreal injections. Povidone–iodine is the standard antiseptic used before intravitreal injections, typically at concentrations of 5–10%. However, patients frequently report that povidone-iodine application is the most uncomfortable part of the procedure and topical anaesthesia often does not prevent this discomfort. With injections being performed monthly, this pain can become a significant issue, potentially affecting treatment adherence. Patients were eligible if they had previously undergone at least three intravitreal injections using only 5% povidone-iodine for antisepsis. They then received three additional injections in which povidone-iodine was applied first, followed by multiple sprays of 0.01% hypochlorous acid to wash out most of the povidone–iodine staining. After completing all six injections (three with povidone-iodine alone and three with povidone-iodine plus HOCl), 37 participants completed a questionnaire evaluating five patient-reported outcomes: duration of post-injection discomfort, use of pain medication, use of artificial tears, impact on quality of life and vision and the frequency of sleep disturbance. With povidone-iodine 5% alone, only 13.5% of patients reported discomfort lasting just seconds, whereas after adding 0.01% HOCl, this proportion increased to 54.1%. This shift reflects a statistically significant reduction in post-injection discomfort duration (P = 0.001). Nearly half of the patients (48.6%) needed artificial tears after injections prepared with povidone-iodine 5% alone, whereas after adding a 0.01% HOCl washout, most patients (73%) no longer required them. This reduction in artificial tear use was statistically significant (P = 0.003). Over half of the patients (54.1%) reported a decline in quality of life after injections using povidone-iodine 5% alone, whereas with the addition of a 0.01% HOCl washout, most (64.9%) reported no impact on quality of life. This improvement with HOCl use was statistically significant (P = 0.04). Following povidone-iodine 5% alone, 40.5% of patients reported changes in sleep quality after injections, whereas with the addition of a 0.01% HOCl washout, 86.5% reported no changes in sleep quality. This improvement with HOCl was statistically significant (P = 0.01). After povidone-iodine 5% alone, 70.3% of patients reported never using pain medication following injections, compared with 75.5% after adding HOCl 0.01%. This difference was not statistically significant (P = 0.20). In conclusion, adding HOCl 0.01% spray after povidone-iodine 5% significantly reduced postinjection discomfort and the need for artificial tears, while improving patients' reported quality of life and sleep. (27)

## 4. Discussion

Interest in antiseptics within ophthalmology has grown, as they are used both to prevent postoperative endophthalmitis and to treat infections of the anterior segment. Their broad antimicrobial activity and lack of resistance development make them especially valuable, particularly as concerns continue to rise about antibiotic resistance and the emergence of multidrug-resistant ocular pathogens. (6) Hypochlorous acid is an endogenous antimicrobial molecule generated by neutrophils as part of the innate immune response. It demonstrates broad activity against bacteria, viruses and fungi, while maintaining an excellent safety profile for human tissues. Stabilized formulations provide a well-tolerated antiseptic option with both antimicrobial and wound-healing properties. (1,2) The purpose of this study was to summarize the current state of the literature on the use of hypochlorous acid in ophthalmology.

Some studies support HOCl's ability to kill common ocular pathogens. (6,9,12) In a study by Stroman et al., HOCl reduced the overall bacterial load on ocular skin by more than 90%, with a 99.6% reduction in staphylococcal load and a 99.5% reduction in S. epidermidis within 20 minutes. Importantly, it did not alter the diversity of bacterial species. (9) The 0.01% hypochlorous acid hygiene solution showed the in vitro ability to kill bacteria (blepharitis-derived isolates of Staphylococcus aureus, coagulase negative staphylococci and a keratitis-associated Pseudomonas aeruginosa) residing within biofilms, but it did not disrupt the biofilm structure. Mechanical cleaning, such as rinsing or scrubbing, is still required to remove the non-viable bacteria remaining on the surface. (12) Both studies showed weaker bactericidal activity against S. epidermidis as compared to other staphylococci. Since S. epidermidis is part of the normal skin flora, while S. aureus is a more pathogenic organism, the preferential reduction of S. aureus with preservation of S. epidermidis could be clinically beneficial. (9,12) HOCl demonstrated superior efficacy to hyaluronic acid wipes in reducing bacterial load in patients with blepharitis and dry eye, achieving a 90% reduction compared with the 62% reduction observed with hyaluronic acid wipes. (6) In contrast, some in vitro studies indicate that HOCl exhibits limited activity against common ocular pathogens, particularly when compared with established antiseptics and antibiotic agents. (10,11) These inconsistencies are likely attributable to differences in study methodologies, underscoring the need for further research in this area.

HOCl may serve as a valuable adjunct to standard treatment regimens for blepharitis, dry eye disease and meibomian gland dysfunction or may even represent an alternative to some commonly used approaches, such as hyaluronic acid wipes. When compared to hyaluronic acid wipes, HOCl use resulted the enhanced tear film stability and stronger bacterial load reduction. (6) Compared with standard eyelid scrubs, ultrasonic atomisation of 0.01% HOCl produced greater improvements in Ocular Surface Disease Index (OSDI) scores, reduced lid margin redness and abnormalities and enhanced meibum quality and expressibility. Patients receiving HOCl also showed superior Corneal Fluorescein Staining (CFS) improvement, likely reflecting its biofilm-disrupting, tear-film-stabilizing and epithelial-healing effects. (13) HOCl delivered via ultrasonic atomisation led to more pronounced improvements in patient-reported symptoms than placebo. It also significantly lowered ocular inflammatory markers such as IL-2 and MMP-9 and produced superior enhancement of tear secretion as demonstrated by the Schirmer test. (14) Ultrasonic atomization, which converts the solution into fine, evenly dispersing droplets that can better cover the ocular surface, may represent an effective approach for delivering hypochlorous acid in ophthalmic applications.

Regarding the demodicidal activity of HOCl, study findings remain inconclusive. Li et al. reported that HOCl may enhance Demodex eradication by reducing the mites' average survival time, (14) whereas Kabat noted that HOCl demonstrates minimal in vitro demodicidal activity compared with a 4% terpinen-4-ol solution, with mineral oil serving as the negative control. (7) Using HOCl as an adjunct treatment in ophthalmic infections (such as conjunctivitis, herpes zoster uveitis, fungal keratitis, periorbital necrotizing fasciitis) may shorten the course of antibiotic, corticosteroid and antiviral therapy, while reducing inflammation and associated symptoms. Overall, it appears to enhance clinical outcomes and speed recovery when added to standard care. (16,18,19) HOCl shows fast, broad-spectrum in vitro fungicidal activity, making it a promising candidate for topical antifungal prophylaxis. (17,20) 0.01% hypochlorous acid proved highly effective in rapidly eliminating bacteria, yeast and viruses from contact lens cases, though its failure to fully eradicate HSV-1 on lenses suggests a limitation. These findings support its potential as a fast disinfectant for reusable trial lenses and cases, while highlighting the need to investigate longer exposure times for HSV-1 on lens surfaces. (20)

Taken together, the comparative studies show that while hypochlorous acid is consistently better tolerated than povidone-iodine, its antiseptic efficacy varies across studies. In some investigations HOCl performs comparably to PI (22,23), whereas others demonstrate clearly inferior antimicrobial activity (21,24), particularly in surgical settings. At present, HOCl may be considered a useful adjunct or an option for patients unable to tolerate PI, but it cannot yet be regarded as a reliable replacement for standard povidone-iodine prophylaxis. (21–26)

Further standardized, adequately powered studies are needed to clarify its role in ophthalmic antisepsis.

Overall, the available evidence consistently indicates that hypochlorous acid is a safe and well-tolerated antiseptic. Across all reviewed studies, spanning preoperative antisepsis, eyelid hygiene, blepharitis management and intravitreal injection preparation, no serious adverse events, hypersensitivity reactions or clinically significant intolerance to HOCl were reported. In direct comparisons with povidone-iodine, HOCl demonstrated a markedly superior tolerability profile, with patients consistently reporting less stinging, burning and ocular surface irritation. The study by Fam et al. further highlights that integrating HOCl into the intravitreal injection protocol significantly improves patient comfort, reduces post-injection discomfort and dryness and positively affects sleep and quality of life. (27) These findings reinforce HOCl as a patient-friendly option, suitable particularly for individuals who experience discomfort with traditional antiseptics. While its antimicrobial efficacy varies across studies, its excellent safety and tolerability make HOCl a valuable adjunct in ophthalmic care.

Current evidence is limited by small sample sizes, heterogeneous study designs and variable HOCl concentrations. Many in vitro findings may not fully translate to clinical outcomes. Further randomized, adequately powered clinical trials are needed to determine the optimal concentration, exposure time and delivery method of HOCl for different ophthalmic indications. Comparative studies focusing on surgical prophylaxis, biofilm management and demodicidal activity are particularly warranted. Additionally, long-term safety and efficacy data are needed to support broader clinical adoption.

## 5. Conclusions

Hypochlorous acid represents a well-tolerated antiseptic with promising applications in ophthalmology. Current evidence supports its value in eyelid hygiene, blepharitis, dry eye disease and as an adjunct in managing ocular infections. While several studies demonstrate meaningful antimicrobial effects, including activity against bacteria, fungi and biofilm-associated isolates, its efficacy remains inconsistent when compared with established antiseptics, particularly povidone-iodine in perioperative settings. At present, HOCl should be considered a safe and patient-friendly complementary agent rather than a substitute for povidone-iodine in routine surgical prophylaxis. Further standardized, adequately powered clinical studies are needed to define its optimal role and to clarify the circumstances in which HOCl may provide equal or superior benefit.

**Disclosure**

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