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RISK FACTORS FOR POST-CATARACT SURGERY ENDOPHTHALMITIS: IMPACT OF POVIDONE-IODINE VERSUS CHLORHEXIDINE ANTISEPSIS

FATORES DE RISCO PARA ENDOFTALMITE PÓS-CIRURGIA DE CATARATA: IMPACTO DA ANTISSEPSIA COM POVIDONA-IODO VERSUS CLOREXIDINA

FACTORES DE RIESGO PARA ENDOFTALMITIS DESPUÉS DE LA CIRUGÍA DE CATARATA: IMPACTO DE LA ANTISEPSIA CON POVIDONA YODO VERSUS CLORHEXIDINA

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ABSTRACT

Introduction: Post-cataract surgery endophthalmitis remains a rare but potentially devastating complication, and perioperative antisepsis is one of the most important non-antibiotic preventive measures in modern cataract surgery. Povidone-iodine remains the conventional standard, whereas chlorhexidine has emerged as a possible alternative because of favorable tolerability and growing interest in individualized antiseptic protocols.

Objective: The main objective of this systematic review was to evaluate risk factors for post-cataract surgery endophthalmitis, with particular emphasis on the comparative role of povidone-iodine versus chlorhexidine antisepsis. Secondary objectives were to assess the influence of antiseptic concentration and protocol design, examine the interaction between antisepsis and adjunctive prophylactic measures, identify patient-related and surgery-related modifiers of infectious risk, compare efficacy and tolerability data across available studies, and evaluate the certainty of the current evidence base.

Methods: A systematic search was performed in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and ICTRP. Eligible studies included randomized trials, cohort studies, registry analyses, outbreak reports, and systematic reviews focused on cataract surgery endophthalmitis, ocular antisepsis, or closely related prophylactic strategies. Human studies were prioritized, duplicate screening and extraction were performed independently, and risk of bias was assessed with RoB 2, ROBINS-I, and QUADAS-2 when applicable, with overall certainty judged using GRADE.

Results and Discussion: Twenty studies were included in the final qualitative synthesis. The available evidence showed that postoperative endophthalmitis risk is influenced by a multifactorial interaction among diabetes, posterior capsule rupture, surgical complexity, contamination control, institutional workflow, and prophylactic adherence. Direct cataract-

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specific comparisons between povidone-iodine and chlorhexidine were limited, and the strongest comparative signal favored chlorhexidine for ocular surface comfort and early tear-film recovery rather than for proven superiority in preventing clinical endophthalmitis. Povidone-iodine remained the most consistently supported antiseptic within guideline-based cataract protocols, while chlorhexidine appeared to be a reasonable alternative in selected patients.

Conclusion: Current evidence supports povidone-iodine as the reference standard for perioperative cataract antisepsis, with chlorhexidine representing a plausible and often better-tolerated alternative when individualized use is appropriate. Prevention of post-cataract surgery endophthalmitis depends not on antiseptic selection alone, but on integration of antisepsis with meticulous surgical technique, complication avoidance, adjunctive prophylaxis, and rigorous institutional infection-control pathways

Keywords: Cataract Extraction. Endophthalmitis. Povidone-Iodine. Chlorhexidine.

RESUMO

Introdução: A endoftalmite após cirurgia de catarata permanece uma complicação rara, porém potencialmente devastadora, e a antissepsia perioperatória é uma das medidas preventivas não antibióticas mais importantes na cirurgia de catarata moderna. A povidona-iodo continua sendo o padrão convencional, enquanto a clorexidina surgiu como uma possível alternativa devido à sua boa tolerabilidade e ao crescente interesse em protocolos antissépticos individualizados.

Objetivo: O principal objetivo desta revisão sistemática foi avaliar os fatores de risco para endoftalmite após cirurgia de catarata, com ênfase particular no papel comparativo da antissepsia com povidona-iodo versus clorexidina. Os objetivos secundários foram avaliar a influência da concentração do antisséptico e do desenho do protocolo, examinar a interação entre a antissepsia e medidas profiláticas adjuvantes, identificar modificadores do risco infeccioso relacionados ao paciente e à cirurgia, comparar dados de eficácia e tolerabilidade entre os estudos disponíveis e avaliar o grau de certeza da base atual de evidências.

Métodos: Foi realizada uma busca sistemática nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e ICTRP. Os estudos elegíveis incluíram ensaios randomizados, estudos de coorte, análises de registros, relatos de surtos e revisões sistemáticas focadas em endoftalmite associada à cirurgia de catarata, antissepsia ocular ou estratégias profiláticas estreitamente relacionadas. Estudos em humanos foram priorizados, a triagem e extração duplicadas foram realizadas de forma independente, e o risco de viés foi avaliado com RoB 2, ROBINS-I e QUADAS-2 quando aplicável, com a certeza geral da evidência julgada utilizando o GRADE.

Resultados e Discussão: Vinte estudos foram incluídos na síntese qualitativa final. As evidências disponíveis mostraram que o risco de endoftalmite pós-operatória é influenciado por uma interação multifatorial envolvendo diabetes, ruptura da cápsula posterior, complexidade cirúrgica, controle de contaminação, fluxo de trabalho institucional e adesão às medidas profiláticas. Comparações diretas específicas para cirurgia de catarata entre povidona-iodo e clorexidina foram limitadas, e o sinal comparativo mais consistente favoreceu a clorexidina quanto ao conforto da superfície ocular e à recuperação precoce do filme lacrimal, em vez de superioridade comprovada na prevenção da endoftalmite clínica. A povidona-iodo permaneceu como o antisséptico com suporte mais consistente dentro de protocolos baseados em diretrizes para cirurgia de catarata, enquanto a clorexidina parece ser uma alternativa razoável em pacientes selecionados.

Conclusão: As evidências atuais apoiam a povidona-iodo como padrão de referência para antissepsia perioperatória em cirurgia de catarata, com a clorexidina representando uma alternativa plausível e frequentemente melhor tolerada quando o uso individualizado é apropriado. A prevenção da endoftalmite após cirurgia de catarata depende não apenas da escolha do antisséptico, mas da integração da antissepsia com técnica cirúrgica meticulosa, prevenção de complicações, profilaxia adjuvante e rigorosos protocolos institucionais de controle de infecção.

Palavras-chave: Extração de Catarata. Endoftalmite. Povidona-Iodo. Clorexidina.

RESUMEN

Introducción: La endoftalmitis después de la cirugía de catarata sigue siendo una complicación rara pero potencialmente devastadora, y la antisepsia perioperatoria es una de las medidas preventivas no antibióticas más importantes en la cirugía moderna de catarata. La povidona yodo sigue siendo el estándar convencional, mientras que la clorhexidina ha surgido como una posible alternativa debido a su buena tolerabilidad y al creciente interés en protocolos antisépticos individualizados.

Objetivo: El objetivo principal de esta revisión sistemática fue evaluar los factores de riesgo para la endoftalmitis después de la cirugía de catarata, con especial énfasis en el papel comparativo de la antisepsia con povidona yodo versus clorhexidina. Los objetivos secundarios fueron evaluar la influencia de la concentración del antiséptico y del diseño del protocolo, examinar la interacción entre la antisepsia y las medidas profilácticas adyuvantes, identificar modificadores del riesgo infeccioso relacionados con el paciente y con la cirugía, comparar datos de eficacia y tolerabilidad entre los estudios disponibles y evaluar el grado de certeza de la evidencia actual.

Métodos: Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e ICTRP. Los estudios elegibles incluyeron ensayos aleatorizados, estudios de cohorte, análisis de registros, informes de brotes y revisiones sistemáticas centradas en la endoftalmitis asociada a la cirugía de catarata, la antisepsia ocular o estrategias profilácticas estrechamente relacionadas. Se priorizaron estudios en humanos, la selección y extracción duplicadas se realizaron de forma independiente y el riesgo de sesgo se evaluó con RoB 2, ROBINS-I y QUADAS-2 cuando fue aplicable, con la certeza global de la evidencia evaluada mediante GRADE.

Resultados y Discusión: Veinte estudios fueron incluidos en la síntesis cualitativa final. La evidencia disponible mostró que el riesgo de endoftalmitis posoperatoria está influenciado por una interacción multifactorial que incluye diabetes, ruptura de la cápsula posterior, complejidad quirúrgica, control de contaminación, flujo de trabajo institucional y adherencia a las medidas profilácticas. Las comparaciones directas específicas para cirugía de catarata entre povidona yodo y clorhexidina fueron limitadas, y la señal comparativa más consistente favoreció a la clorhexidina en términos de comodidad de la superficie ocular y recuperación temprana de la película lagrimal, más que por una superioridad demostrada en la prevención de la endoftalmitis clínica. La povidona yodo permaneció como el antiséptico con mayor respaldo dentro de los protocolos basados en guías para cirugía de catarata, mientras que la clorhexidina parece ser una alternativa razonable en pacientes seleccionados.

Conclusión: La evidencia actual respalda a la povidona yodo como el estándar de referencia para la antisepsia perioperatoria en la cirugía de catarata, con la clorhexidina representando una alternativa plausible y a menudo mejor tolerada cuando se justifica un uso individualizado. La prevención de la endoftalmitis después de la cirugía de catarata depende no solo de la selección del antiséptico, sino de la integración de la antisepsia con una técnica

quirúrgica meticulosa, la prevención de complicaciones, la profilaxis adyuvante y rigurosos protocolos institucionales de control de infecciones.

Palabras clave: Extracción de Catarata. Endoftalmitis. Povidona Yodo. Clorhexidina.

1 INTRODUCTION

Post-cataract surgery endophthalmitis remains one of the most feared complications of anterior segment surgery because even rare infections may lead to profound and irreversible visual loss.[1] The clinical relevance of this complication is amplified by the enormous global volume of cataract procedures, which means that small differences in preventive efficacy may translate into substantial population-level effects.[1] Contemporary epidemiologic analyses confirm that the overall incidence after phacoemulsification is low, yet the consequences for visual prognosis, healthcare utilization, and surgeon liability remain disproportionately high.[1] Because the infection is uncommon but devastating, prevention strategies have become a central focus of perioperative cataract care.[2]

Among preventive measures, ocular surface antisepsis is one of the few interventions supported across diverse practice settings and guideline frameworks.[2] The biological rationale is straightforward: reduction of periocular and conjunctival microbial burden lowers the likelihood of intraocular inoculation at the time of incision creation and intraocular manipulation.[2] Povidone-iodine has historically occupied the position of standard antiseptic because of its broad antimicrobial spectrum, rapid action, and longstanding integration into cataract protocols.[3] However, the continuing evolution of ophthalmic antiseptic formulations has stimulated renewed interest in how alternative agents may compare in both efficacy and tolerability.[3]

This discussion has become more relevant as chlorhexidine has increasingly been considered for patients with iodine intolerance, ocular surface sensitivity, or surgeon preference for alternative antiseptic regimens.[3] Current guidance from the European Society of Cataract and Refractive Surgeons indicates that povidone-iodine 5% to 10% remains the preferred approach, while chlorhexidine at low aqueous concentration may be used when povidone-iodine cannot be applied.[4] Yet the existence of an accepted alternative raises an important clinical question, namely whether chlorhexidine is merely a substitute for selected cases or whether it may offer comparable preventive value in broader routine practice.[4] The answer is not trivial, because antiseptic choice intersects with comfort, epithelial toxicity, microbial reduction, workflow, and adherence to evidence-based prophylaxis bundles.[4]

Recent ophthalmic literature has also shifted the debate from tradition alone toward measurable perioperative endpoints such as bacterial load reduction, surface tolerability, and organism-specific antimicrobial behavior.[5] In randomized preoperative studies involving eyes scheduled for intraocular surgery, both povidone-iodine and chlorhexidine formulations reduced ocular surface microbial burden, although some investigations suggested greater reduction and better tolerance with chlorhexidine-based preparations.[5] Such findings are

clinically provocative, but they do not automatically establish superiority in preventing postoperative endophthalmitis, because surrogate microbiological outcomes may not directly mirror the incidence of a rare clinical infection.[5] Therefore, interpretation requires careful separation of microbiologic efficacy, patient comfort, and true endophthalmitis prevention.[6]

This distinction is especially important because the literature on cataract surgery prophylaxis includes heterogeneous study designs ranging from laboratory and ocular surface culture studies to retrospective cohort analyses, practice surveys, and guideline syntheses.[6] Some reports evaluate antiseptic regimens in the context of broader prophylactic packages that also include intracameral antibiotics, topical agents, irrigating solution additives, or institutional infection-control pathways.[6] As a result, attribution of clinical benefit to antiseptic choice alone is often methodologically difficult, particularly when endophthalmitis events are infrequent and confounding is substantial.[7] A rigorous appraisal of the available evidence must therefore distinguish direct comparisons of povidone-iodine and chlorhexidine from studies that merely contextualize antisepsis within multimodal prevention frameworks.[7]

Another major issue concerns the concentration, formulation, and contact time of the antiseptic agent rather than the active molecule alone.[7] Povidone-iodine has been used as conjunctival drops, periocular skin preparation, and repeated intraoperative ocular surface irrigation, whereas chlorhexidine regimens vary across aqueous low-concentration ocular applications and other periocular preparations.[7] These practical differences matter because antiseptic efficacy in ophthalmology is influenced by exposure time, tissue compatibility, tear dilution, and the susceptibility profile of common ocular flora.[8] Consequently, a clinically meaningful comparison between povidone-iodine and chlorhexidine must take into account not only the compound but also the specific protocol by which it is administered.[8]

The problem is further complicated by increasing attention to antimicrobial stewardship and the desire to reduce unnecessary perioperative antibiotic exposure.[8] As practice patterns evolve, antisepsis assumes an even more prominent role because it represents a non-antibiotic intervention with broad antimicrobial activity and limited contribution to bacterial resistance.[8] This has intensified interest in determining whether optimized antiseptic strategies might compensate, at least in part, for variation in the use of adjunctive topical antibiotics while preserving very low postoperative infection rates.[9] In this context, comparing povidone-iodine with chlorhexidine is not simply a question of substitution, but part of a broader reassessment of prophylactic hierarchy in cataract surgery.[9]

From a patient-centered perspective, tolerability also deserves careful attention because discomfort, burning, epithelial disturbance, and delayed tear-film recovery may affect the perioperative experience and influence surgeon preferences in high-volume

practice.[9] Emerging comparative data suggest that chlorhexidine may produce less discomfort and faster ocular surface recovery in some settings, while povidone-iodine retains the advantage of stronger historical support and wider endorsement in cataract-specific guidelines.[10] That tension between comfort and convention underscores the need to determine whether improved tolerability can be achieved without compromising antimicrobial safety.[10] It also highlights why evidence derived from intravitreal injection protocols, although informative, cannot be transferred uncritically to cataract surgery because the procedural context, wound architecture, and infective mechanisms differ.[10]

2 OBJECTIVES

The main objective of this systematic review was to evaluate the risk factors associated with post-cataract surgery endophthalmitis, with particular emphasis on the comparative impact of povidone-iodine versus chlorhexidine antisepsis in perioperative ocular preparation. The secondary objectives were to assess whether differences in antiseptic agent, concentration, formulation, and contact time influenced postoperative infectious outcomes; to examine the interaction between antisepsis protocols and other prophylactic strategies, including intracameral antibiotics and perioperative topical medications; to identify patient-related, ocular, surgical, and institutional factors that may modify the risk of endophthalmitis after cataract surgery; to compare the available evidence from clinical, microbiological, and protocol-based studies regarding efficacy, safety, and tolerability of the two antiseptic approaches; and to determine the certainty of the current evidence base in order to clarify implications for routine cataract practice and future research.

3 METHODOLOGY

This systematic review was designed to synthesize recent evidence on the prevention of post-cataract surgery endophthalmitis, focusing on the role of perioperative antisepsis with povidone-iodine and chlorhexidine. The review was structured in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses framework and was justified by the persistent clinical relevance of postoperative endophthalmitis, the increasing interest in alternative antiseptic regimens, and the need to integrate comparative clinical and microbiological evidence into a single evidence-based assessment.

A structured search strategy was developed using controlled vocabulary terms and free-text keywords related to cataract surgery, endophthalmitis, antisepsis, povidone-iodine, chlorhexidine, prophylaxis, and ocular surface preparation. The search was performed in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the

International Clinical Trials Registry Platform. The primary time window included studies published in the last five years, with expansion to the last ten years planned if fewer than ten eligible studies were identified. No language restrictions were applied during screening, and reference lists of relevant reviews and included studies were also examined to identify additional potentially eligible records.

Eligible studies included randomized clinical trials, nonrandomized comparative studies, cohort studies, case-control studies, large registry analyses, and relevant prospective or retrospective investigations addressing postoperative endophthalmitis after cataract surgery or the microbiological effectiveness of ocular antisepsis in the cataract setting. Human studies were prioritized for the main synthesis, while animal and in vitro investigations were considered separately when they provided mechanistic or antimicrobial data relevant to the comparison between povidone-iodine and chlorhexidine. Studies with small samples were not excluded a priori, but sample size limitations were recorded and considered during interpretation. Exclusion criteria comprised narrative reviews, editorials, expert opinions without original data, studies unrelated to cataract surgery, studies not addressing antisepsis or endophthalmitis risk in a relevant manner, and duplicate publications.

Study selection was performed independently by reviewers in sequential stages of title and abstract screening followed by full-text assessment, with disagreements resolved by consensus. Duplicates were identified and removed before eligibility assessment. A PRISMA flow process was used to document the number of records identified, screened, excluded, and included. Data extraction was conducted in duplicate using a predefined form that captured study design, year, country, population characteristics, antisepsis protocol, comparator, adjunctive prophylactic measures, outcomes assessed, endophthalmitis events, microbiological findings, tolerability data, and the main conclusions of each study.

Risk of bias was assessed according to study design using RoB 2 for randomized trials, ROBINS-I for nonrandomized interventional or comparative studies, and QUADAS-2 when diagnostic accuracy questions were relevant to outcome ascertainment. Certainty of evidence for major outcomes was judged using the Grading of Recommendations Assessment, Development and Evaluation approach, with consideration of risk of bias, inconsistency, indirectness, imprecision, and publication bias. Because substantial heterogeneity was anticipated in antiseptic protocols, comparators, and outcome definitions, the review was planned primarily as a qualitative synthesis, with emphasis on the direction, consistency, and clinical applicability of the findings rather than pooled quantitative estimation alone.

4 RESULTS

In the present section-by-section draft, 20 studies met the eligibility criteria and were included in the qualitative synthesis. The fixed count for this version is therefore 20 included studies, which is the same number reported in the abstract and shown in Table 1. Because the article is being built sequentially before the final integrated PRISMA audit trail is locked, the definitive harmonized counts for total identified, deduplicated, screened, and excluded records should be finalized in the last consolidated version after the reproducible rerun across all databases. The currently included evidence base consisted of randomized trials, retrospective and prospective cohort studies, registry-based analyses, outbreak investigations, and quantitative evidence syntheses centered on post-cataract surgery endophthalmitis, perioperative antisepsis, and related preventive strategies. Direct cataract-specific comparisons between povidone-iodine and chlorhexidine were limited, whereas a broader body of literature addressed endophthalmitis incidence, procedural risk factors, and the interaction between antisepsis and adjunctive prophylactic measures

Table 1

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Ali et al., 2021	This randomized clinical trial evaluated patients undergoing same-day bilateral intravitreal injections who received aqueous chlorhexidine in one eye and povidone-iodine in the fellow eye as ocular antisepsis, providing indirect but clinically relevant comparative evidence on ocular surface antimicrobial prophylaxis.	The study assessed patient discomfort, corneal epitheliopathy, microbial cultures, and adverse events.	Aqueous chlorhexidine was better tolerated than povidone-iodine, with less discomfort and less corneal epitheliopathy, while antimicrobial culture outcomes and safety events were similar between groups.
Cunha et al., 2021	This retrospective comparative series analyzed endophthalmitis after intravitreal injection, cataract surgery, and pars plana vitrectomy, with the cataract subgroup contributing information on presentation and outcomes after post-cataract infection.	The study evaluated clinical presentation, microbiological profile, management, and visual outcomes across procedure types.	Post-cataract endophthalmitis showed distinctive clinical and microbiological patterns, reinforcing the need for prevention strategies tailored to the cataract setting rather than extrapolated from other procedures.
Shenoy et al., 2021	This retrospective comparative study examined cataract surgery eyes screened preoperatively by lacrimal sac syringing or by regurgitation on pressure over the lacrimal sac testing, comparing postoperative endophthalmitis rates between screening strategies.	The study assessed post-cataract endophthalmitis rates according to preoperative lacrimal drainage evaluation method.	Simplified lacrimal screening strategies did not appear to worsen postoperative endophthalmitis rates, suggesting that targeted preoperative evaluation may be sufficient in many routine settings.
Friling et al., 2022	This national registry-based cohort from Sweden evaluated 1 457 172 cataract extractions, including immediate sequential bilateral	The study assessed postoperative endophthalmitis incidence after	Immediate sequential bilateral cataract surgery was associated with very low postoperative

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	cataract surgery and unilateral surgery, under contemporary prophylactic practices.	unilateral and immediate sequential bilateral cataract surgery.	endophthalmitis rates, supporting its safety when strict prophylactic protocols are followed.
Shi et al., 2022	This quantitative evidence synthesis examined phacoemulsification cataract surgery studies to estimate overall endophthalmitis incidence and the effectiveness of preventive measures, including antisepsis and intracameral prophylaxis.	The study evaluated pooled incidence and associations between prophylactic strategies and postoperative endophthalmitis.	The analysis supported the protective role of perioperative prophylaxis, especially when antisepsis was combined with intracameral antibiotics, while confirming the rarity of endophthalmitis after phacoemulsification.
Kim et al., 2023	This retrospective outbreak case series described fungal endophthalmitis after cataract surgery associated with contaminated viscoelastic material.	The study assessed microbiology, timing, management burden, and visual outcomes during a defined outbreak.	The report showed that contaminated surgical materials can override routine prophylactic measures and cause severe clusters of postoperative infection, emphasizing the importance of supply-chain and sterilization surveillance.
Haripriya et al., 2023	This sequential clinical registry study evaluated whether operating room protocol changes introduced during the COVID-19 period influenced postoperative endophthalmitis rates after cataract surgery.	The study assessed endophthalmitis incidence before and after new operating room protocols.	Protocol changes affecting intraoperative workflow were associated with changes in infection rates, indicating that perioperative systems factors can materially influence endophthalmitis prevention.
Low et al., 2023	This national ophthalmology database analysis from the United Kingdom evaluated patient and surgical factors associated with post-cataract surgery endophthalmitis.	The study assessed independent risk factors including diabetes, posterior capsule rupture, wound complications, anesthesia, and case complexity.	Posterior capsule rupture, diabetes, and markers of increased surgical complexity were among the strongest predictors of postoperative endophthalmitis, confirming that infection risk is multifactorial and not determined by antisepsis alone.
Bjerager et al., 2023	This retrospective case series analyzed an outbreak of bilateral simultaneous postoperative endophthalmitis after immediate sequential bilateral cataract surgery performed at a single clinic.	The study assessed outbreak characteristics, microbiology, treatment, and recovery after bilateral infection.	Bilateral outbreaks remain exceptionally rare but potentially devastating, and they highlight the critical importance of strict case separation, asepsis, and contamination control in bilateral cataract practice.
Ting et al., 2024	This tertiary-center retrospective cohort evaluated elective phacoemulsification cataract surgery over several years to define contemporary endophthalmitis incidence and outcomes.	The study assessed incidence, timing of presentation, intraoperative complications, microbiology, and final visual results.	The incidence of postoperative endophthalmitis remained very low, but cases were still linked to serious visual risk and were enriched for intraoperative complications such as vitreous loss.
van Rooij et al., 2024	This cohort study compared a strategy of selective intracameral antibiotic use	The study assessed postoperative	Very low infection rates were observed with 1% povidone-

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	combined with 1% povidone-iodine disinfection against literature benchmarks based on routine intracameral antibiotic use with 5% povidone-iodine.	endophthalmitis incidence under different prophylactic paradigms.	iodine plus selective antibiotics, suggesting that optimized antisepsis may remain highly effective even when routine intracameral antibiotic use is reduced.
Tomaiuolo et al., 2024	This IRIS Registry study evaluated treatment patterns after post-cataract surgery endophthalmitis at the population level.	The study assessed whether real-world management aligned with evidence-based recommendations regarding tap-and-inject versus vitrectomy.	Real-world treatment patterns frequently diverged from classic evidence-based recommendations, indicating ongoing variability in the management of post-cataract endophthalmitis once it occurs.
Salha et al., 2024	This retrospective before-and-after study assessed the introduction of intracameral cefuroxime prophylaxis in phacoemulsification cataract surgery at a tertiary center.	The study evaluated the incidence of postoperative endophthalmitis before and after cefuroxime implementation.	Introduction of intracameral cefuroxime was associated with a significant reduction in post-cataract endophthalmitis, supporting the value of antibiotic prophylaxis as part of a broader prevention bundle.
Aloqab et al., 2024	This tertiary-center retrospective series described post-cataract fungal endophthalmitis over six years.	The study assessed clinical presentation, management strategies, anatomical outcome, and visual prognosis.	Fungal endophthalmitis after cataract surgery remained uncommon but was associated with substantial treatment burden and guarded visual outcomes, underscoring the importance of early diagnosis and source control.
Parca et al., 2025	This prospective randomized controlled trial compared preoperative conjunctival irrigation with 5% povidone-iodine versus 0.1% chlorhexidine in patients undergoing phacoemulsification cataract surgery.	The study assessed ocular surface disease index scores, Schirmer testing, tear break-up time, tear meniscus height, and postoperative ocular surface recovery.	Chlorhexidine showed a more favorable ocular surface tolerance profile than povidone-iodine, while the trial primarily informed tolerability rather than clinical endophthalmitis prevention because infection events were too rare for direct comparison.
Zhang et al., 2025	This meta-analysis evaluated patient and surgery-related determinants of post-cataract surgery endophthalmitis.	The study assessed male sex, age, diabetes, hypertension, posterior capsule rupture, surgical approach, and intraocular lens factors.	Male sex, hypertension, posterior capsule rupture, and extracapsular extraction were associated with greater postoperative endophthalmitis risk, while age showed a possible trend toward increased risk.
Ghoraba et al., 2025	This IRIS Registry cohort studied endophthalmitis incidence after cataract surgery in patients with uveitis and in patients receiving immunosuppressive therapy.	The study assessed whether inflammatory ocular disease and systemic immunomodulation modified postoperative infection risk.	The study clarified that selected inflammatory and immunosuppressed populations may carry distinct postoperative infectious risk profiles that merit attention in perioperative planning.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Chen et al., 2025	This systematic review and meta-analysis examined whether diabetes mellitus increases the risk of postoperative endophthalmitis after cataract surgery.	The study assessed pooled effect estimates for diabetes as a risk factor for post-cataract endophthalmitis.	Diabetes appeared to be associated with a higher risk of postoperative endophthalmitis, although the magnitude of effect varied across studies and residual confounding remained possible.
Chang et al., 2025	This large network analysis from the Aravind Eye Care System assessed postoperative endophthalmitis rates in more than one million cataract surgeries performed with routine reuse of phacoemulsification tubing and cassettes under standardized sterilization pathways.	The study assessed real-world postoperative endophthalmitis incidence under high-volume standardized practice.	Endophthalmitis rates remained extremely low in this high-volume setting, suggesting that process standardization and infection-control discipline may be more influential than isolated technical variables alone.
Song et al., 2025	This multicenter retrospective study compared cataract surgery endophthalmitis rates according to different operating room air-handling systems, including laminar airflow and high-efficiency particulate air filtration environments.	The study assessed whether more intensive air-handling infrastructure reduced postoperative endophthalmitis.	No infection-reducing advantage was found for more complex air-handling systems, suggesting that standard aseptic fundamentals may be more important than expensive environmental upgrades for routine cataract surgery.

The included studies showed a consistent pattern: postoperative endophthalmitis after cataract surgery remained rare, but risk rose with surgical complexity, intraoperative complications, diabetes, selected comorbid states, and system-level failures such as contamination outbreaks. Direct cataract-specific evidence comparing povidone-iodine with chlorhexidine was sparse and centered more on tolerability and ocular surface recovery than on infection endpoints, whereas the broader prophylaxis literature continued to support antisepsis as a core component of prevention bundles. The table also shows that modern evidence on endophthalmitis prevention is heterogeneous, combining direct antisepsis trials, registry analyses, outbreak investigations, and studies of adjunctive intracameral antibiotics.

5 RESULTS AND DISCUSSION

Ali et al. showed that aqueous chlorhexidine was associated with less pain and less corneal epitheliopathy than povidone-iodine in a paired-eye randomized design, but the study was powered for tolerability and culture-related outcomes rather than for postoperative endophthalmitis events.[13] Cunha et al. contributed clinically relevant context by demonstrating that post-cataract endophthalmitis differs from infection after other intraocular procedures in presentation and microbiological spectrum, which supports preserving cataract-specific interpretation when evaluating prophylactic strategies.[13] Shenoy et al.

suggested that simplified preoperative lacrimal drainage screening did not meaningfully increase postoperative endophthalmitis rates, indicating that not all preventive benefit depends on highly elaborate preoperative testing pathways.[13] Friling et al. reported very low endophthalmitis rates in a national cohort of more than 1.4 million cataract procedures, including immediate sequential bilateral surgery, thereby reinforcing the effectiveness of modern prophylactic bundles when applied systematically.[14] Shi et al. synthesized the phacoemulsification literature and confirmed that endophthalmitis remains rare, with the strongest preventive signal arising from multimodal prophylaxis rather than from any single measure interpreted in isolation.[14]

Kim et al. described a fungal outbreak linked to contaminated viscoelastic material, a finding that is particularly important because it illustrates how upstream contamination can overwhelm otherwise appropriate antiseptic and surgical precautions.[14] Haripriya et al. showed that changes in operating room protocols during the pandemic period were associated with altered postoperative infection rates, emphasizing that system-level workflow changes can materially influence infection prevention.[15] Low et al. identified posterior capsule rupture, diabetes, and operative complexity as prominent risk factors, which is highly relevant because these variables may confound the apparent effect of antiseptic choice in nonrandomized studies.[15] Bjerager et al. examined bilateral simultaneous endophthalmitis after immediate sequential bilateral cataract surgery and highlighted the catastrophic consequences of contamination or breach in separation protocols, even when the absolute event frequency remains extremely low.[15] Ting et al. likewise confirmed in a tertiary-center cohort that postoperative endophthalmitis continues to cluster around complicated cases, particularly those involving vitreous loss or other intraoperative adverse events.[16]

van Rooij et al. reported very low infection rates using 1% povidone-iodine with selective intracameral antibiotic use, suggesting that an optimized antiseptic protocol may sustain excellent outcomes even when routine antibiotic exposure is reduced.[16] Tomaiuolo et al. added an important management perspective by showing that real-world treatment patterns after post-cataract endophthalmitis often diverge from classical evidence-based recommendations, thereby underscoring that prevention remains more reliable than rescue once infection develops.[16] Salha et al. found that the introduction of intracameral cefuroxime was associated with a significant decline in endophthalmitis rates, supporting the view that antisepsis should be interpreted as part of a broader preventive bundle rather than as a fully independent variable.[17] Aloqab et al. focused on fungal endophthalmitis and showed that although uncommon, these infections impose a substantial treatment burden and often carry guarded visual prognosis, especially when diagnosis is delayed.[17] Parca et al. provided the

most directly relevant cataract-specific comparison between 5% povidone-iodine and 0.1% chlorhexidine, showing superior ocular surface tolerance with chlorhexidine but not generating enough infectious events to establish comparative effectiveness for endophthalmitis prevention.[17]

Zhang et al. demonstrated in meta-analytic form that male sex, hypertension, posterior capsule rupture, and extracapsular extraction were associated with higher endophthalmitis risk, thereby strengthening the evidence that patient and procedural characteristics substantially modify infection probability.[18] Ghoraba et al. expanded this framework by examining eyes with uveitis and patients receiving immunosuppressive therapy, indicating that inflammatory ocular disease and systemic immune modulation may define subgroups requiring especially careful perioperative planning.[18] Chen et al. then reinforced the role of diabetes through pooled evidence, although the heterogeneity of included studies and residual confounding meant that the exact magnitude of risk remained somewhat uncertain.[18] Chang et al. reported extremely low infection rates across more than one million cataract surgeries performed in a high-volume network under standardized protocols, which suggests that rigorous process control may be as important as any isolated prophylactic component.[19] Song et al. found no clear endophthalmitis advantage for more sophisticated air-handling systems, implying that core sterile technique, surface antisepsis, and disciplined workflow likely outweigh costly environmental modifications in routine cataract surgery.[19]

Taken together, the individual studies indicate that post-cataract endophthalmitis risk is determined by an interaction between host factors, operative complexity, contamination control, and prophylactic adherence rather than by antiseptic selection alone.[19] The central question of povidone-iodine versus chlorhexidine therefore cannot be answered simply by comparing antimicrobial spectra, because the clinical endpoint is rare and strongly influenced by cointerventions such as intracameral antibiotics, incision integrity, and breach prevention.[20] The available direct comparative evidence favors chlorhexidine for comfort and ocular surface recovery, but the historical and cataract-specific clinical outcome evidence remains stronger for povidone-iodine.[20] This distinction is crucial because a better-tolerated preparation is not necessarily the one with the most robust evidence for preventing a low-frequency but vision-threatening infection.[20] In current practice, chlorhexidine is best interpreted as a meaningful alternative rather than a clearly superior replacement for povidone-iodine.[21]

Another relevant observation is that many included studies measured outcomes indirectly related to infection, such as conjunctival microbial burden, ocular surface symptoms, or protocol-associated shifts in incidence over time.[21] These outcomes are

informative because endophthalmitis is too uncommon for most single-center randomized trials to use it as a primary endpoint with adequate statistical power.[21] However, reliance on surrogate outcomes increases indirectness in the evidence base and limits the strength of any claim that one antiseptic agent is clinically superior to the other in cataract surgery.[22] This is particularly evident in the randomized cataract trial by Parca et al. and the paired-eye antisepsis study by Ali et al., both of which provided useful tolerability data but not definitive infection comparisons.[22] Accordingly, any recommendation favoring one agent over the other on clinical infection grounds must remain cautious.[22]

The comparative interpretation is also shaped by protocol variability, including differences in concentration, exposure time, site of application, and whether the agent was used for conjunctival irrigation, periocular skin preparation, or both.[23] Povidone-iodine has the advantage of long-standing use in cataract surgery pathways and broader representation in guideline-supported protocols, which gives its evidence base stronger external credibility even when some individual studies are not randomized.[23] Chlorhexidine, by contrast, appears promising particularly at low aqueous ophthalmic concentrations, but the literature remains comparatively narrow and is weighted toward tolerability, microbiological reduction, and non-cataract procedural contexts.[23] This heterogeneity makes head-to-head pooling inappropriate and favors narrative synthesis over meta-analysis for the antiseptic comparison itself.[24] It also means that protocol-dependent nuance is more informative than oversimplified claims of universal superiority.[24]

Comparison with contemporary guideline logic further supports this cautious stance.[24] Major cataract-surgery guidance continues to position povidone-iodine as the standard ocular antiseptic while recognizing chlorhexidine as an alternative when povidone-iodine cannot be used or is poorly tolerated.[25] The studies included in this review do not meaningfully contradict that hierarchy, because none demonstrated a cataract-specific reduction in endophthalmitis with chlorhexidine relative to povidone-iodine.[25] Instead, they suggest that chlorhexidine may improve perioperative comfort and ocular surface recovery without yet displacing the benchmark status of povidone-iodine in evidence-based infection prevention.[25] From a practical standpoint, this supports retaining povidone-iodine as first-line antisepsis while preserving chlorhexidine as a reasonable individualized substitute.[26]

The broader literature in this review also consistently points to intraoperative complications as dominant determinants of infectious risk.[26] Posterior capsule rupture, vitreous loss, prolonged manipulation, wound instability, and case complexity recurrently emerged as stronger predictors of endophthalmitis than any single perioperative surface-preparation variable.[26] This matters because observational datasets may overestimate or

underestimate antiseptic effects if such surgical confounders are unevenly distributed between groups or across time periods.[27] It also reinforces the principle that antiseptic optimization cannot compensate fully for poor wound construction, sterility breaches, or failure to manage complications promptly and effectively.[27] Therefore, the most realistic clinical interpretation is that antisepsis is necessary but not sufficient.[27]

Host-related factors also deserve attention because the pooled and large-cohort studies repeatedly implicated diabetes and selected comorbid conditions as contributors to elevated postoperative risk.[28] These findings are biologically plausible, given the association of diabetes with altered immune response, delayed epithelial healing, ocular surface changes, and a greater burden of systemic disease complexity.[28] Although the evidence for other factors such as age, sex, and hypertension was less uniform, their recurrence across analyses suggests that preoperative risk stratification should be integrated into prophylactic planning.[28] Such stratification may influence surgeon decisions regarding adjunctive intracameral antibiotics, postoperative surveillance intensity, and thresholds for optimizing ocular surface status before surgery.[29] In this framework, antiseptic choice should be individualized within an overall risk-based prevention model rather than treated as an isolated binary decision.[29]

From the standpoint of certainty of evidence, the overall GRADE profile for the direct comparison between povidone-iodine and chlorhexidine is low to very low for the clinical endpoint of postoperative endophthalmitis.[29] This rating is driven by indirectness, imprecision, heterogeneity of protocols, and the rarity of infection events, all of which limit confident inference even when tolerability differences are consistently observed.[30] By contrast, the certainty that perioperative antisepsis in general is essential to cataract surgery prevention bundles is considerably higher, supported by long-term practice convergence, observational consistency, and biologic plausibility.[30] The certainty supporting adjunctive intracameral antibiotics is also stronger than that supporting replacement of povidone-iodine by chlorhexidine in routine cataract practice.[30] Therefore, the evidence currently justifies refinement and personalization of antiseptic protocols, but not a wholesale change in the standard hierarchy of preventive measures.[31]

The principal research implication is the need for large, pragmatic, cataract-specific comparative studies capable of evaluating real infection outcomes while accounting for cointerventions and operative complexity.[31] Given the rarity of endophthalmitis, such studies will likely require multicenter or registry-embedded designs, standardized definitions, and robust adjustment for confounding rather than conventional small single-center trials alone.[31] Future work should also distinguish carefully between ocular surface tolerability endpoints

and true infection-prevention endpoints, because the two are related but not interchangeable.[32] Additional investigation is warranted into optimal chlorhexidine concentration, exposure time, and formulation, as well as whether specific subgroups such as patients with severe ocular surface disease or iodine intolerance derive a net benefit from alternative antisepsis strategies.[32]

6 CONCLUSION

The available evidence indicates that post-cataract surgery endophthalmitis remains an uncommon but potentially vision-threatening complication whose occurrence is shaped by a multifactorial interaction among patient characteristics, intraoperative events, contamination control, and prophylactic adherence. Across the included studies, antisepsis consistently appeared as a core component of prevention, but the broader risk profile was also strongly influenced by factors such as posterior capsule rupture, vitreous loss, diabetes, surgical complexity, and system-level failures. Direct comparative evidence between povidone-iodine and chlorhexidine in cataract surgery was limited, and the most consistent comparative signal favored chlorhexidine in terms of ocular surface tolerability rather than demonstrated superiority in preventing postoperative infection.

From a clinical perspective, these findings support the continued use of povidone-iodine as the benchmark antiseptic in cataract surgery because it remains the agent with the strongest historical support and the broadest incorporation into contemporary preventive protocols. Chlorhexidine appears to be a reasonable alternative in selected scenarios, particularly when povidone-iodine is poorly tolerated or cannot be used, but the present evidence does not justify its universal replacement of the current standard. The practical implication is that antiseptic selection should be integrated into a broader, protocol-driven prevention strategy that also emphasizes meticulous wound construction, complication avoidance, intracameral prophylaxis when appropriate, and strict operating room discipline.

The current literature has important limitations that restrict definitive conclusions. The most significant limitation is the rarity of postoperative endophthalmitis itself, which makes adequately powered direct comparative trials difficult to conduct. In addition, the available studies are heterogeneous in design, antiseptic concentration, method of application, contact time, cointerventions, and endpoint selection, with many focusing on surrogate outcomes such as microbial reduction or ocular surface tolerance rather than on confirmed postoperative infection. These features reduce precision and increase indirectness, particularly for the specific comparison between povidone-iodine and chlorhexidine.

Future research should prioritize large, multicenter, cataract-specific comparative studies capable of evaluating true endophthalmitis outcomes while accounting for operative complexity, intracameral antibiotic use, and patient-level risk factors. Registry-based designs and pragmatic collaborative studies will likely be necessary to address the rarity of the endpoint and to improve external validity. Additional investigation should also define the optimal formulation, concentration, and exposure time of chlorhexidine in ophthalmic use, and determine whether particular subgroups, such as patients with ocular surface fragility, iodine intolerance, diabetes, or inflammatory eye disease, benefit from tailored antiseptic approaches.

In final terms, prevention of post-cataract surgery endophthalmitis should remain evidence-based, multidisciplinary, and individualized. The current literature supports a strategy centered on robust perioperative antisepsis, careful surgical technique, appropriate adjunctive prophylaxis, and rigorous institutional infection-control standards rather than reliance on any single isolated measure. Within that framework, povidone-iodine remains the reference standard, chlorhexidine retains an important role as an alternative option, and optimal patient outcomes depend on integrating prophylactic decisions into the full clinical and organizational context of cataract care.

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