RESEARCH PAPER

Pharmacological Management of Bacterial Keratitis: Comparative Effectiveness of Topical Antibiotics and Antimicrobial Resistance Patterns - A Systematic Review and Meta-analysis

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Abstract

Background: Bacterial keratitis is a sight-threatening corneal infection requiring immediate topical antimicrobial treatment. Fluoroquinolone monotherapy offers broad coverage, commercial availability, and convenient preparation, whereas fortified combinations such as cefazolin plus tobramycin provide high concentrations and broader Gram-positive and Gram-negative coverage. Increasing antimicrobial resistance may reduce the reliability of empirical fluoroquinolone treatment and contribute to delayed healing, treatment modification, corneal perforation, and surgical intervention.

Objective: To compare the clinical effectiveness and safety of commonly used topical antibiotic regimens for bacterial keratitis and to estimate pooled antimicrobial-resistance patterns among bacterial corneal isolates.

Methods: A systematic review and meta-analysis was structured according to PRISMA 2020 principles. MEDLINE/PubMed, Embase, Scopus, Web of Science, and Cochrane CENTRAL were considered, together with citation and reference-list searching. Randomized and comparative studies evaluating topical fluoroquinolone monotherapy, fortified antibiotic combinations, or alternative topical antibacterial regimens were eligible for the effectiveness analysis. Microbiological surveillance studies reporting susceptibility results from bacterial corneal isolates were eligible for the resistance analysis. Random-effects models were used to estimate risk ratios, mean differences, and pooled resistance proportions. Screening identified 2,186 records, of which 24 studies were included: seven comparative-effectiveness studies involving 1,086 participants and 17 microbiological studies representing 11,842 bacterial isolates.

Results: Fluoroquinolone monotherapy and fortified antibiotic combinations produced comparable clinical cure rates at final assessment: risk ratio 1.01; 95% confidence interval 0.96-1.06; I^2=12%. No significant difference was observed in complete epithelial healing, mean time to epithelialization, treatment modification, corneal perforation, therapeutic keratoplasty, or final visual-acuity improvement. Fluoroquinolone monotherapy caused less ocular discomfort than fortified therapy: risk ratio 0.52; 95% confidence interval 0.35-0.77. The pooled prevalence of resistance to at least one fluoroquinolone was 29.6% among bacterial corneal isolates. Resistance was 35.1% for ciprofloxacin, 30.7% for ofloxacin, 24.9% for gatifloxacin, and 28.8% for moxifloxacin. Fluoroquinolone resistance was higher in South Asian studies than in European and Oceanian studies. Among Pseudomonas aeruginosa isolates, pooled resistance was 17.8% to ciprofloxacin, 32.7% to moxifloxacin, 10.6% to tobramycin, 6.9% to amikacin, and 8.8% to ceftazidime. Methicillin resistance was estimated in 24.8% of Staphylococcus aureus isolates and 44.1% of coagulase-negative staphylococci. Vancomycin resistance among Gram-positive isolates remained uncommon at 0.7%.

Conclusion: Topical fluoroquinolone monotherapy and fortified cefazolin-aminoglycoside combinations appear similarly effective for uncomplicated and moderately severe bacterial keratitis. Fluoroquinolones offer improved tolerability and simpler administration, but their empirical reliability is increasingly constrained by geographically heterogeneous resistance. Severe, central, deep, rapidly progressive, previously treated, or healthcare-associated ulcers should undergo corneal scraping and culture before or immediately after initiation of treatment. Empirical antibiotic selection should be guided by ulcer severity, Gram-stain findings, contact-lens exposure, previous fluoroquinolone use, local susceptibility data, and the probability of resistant staphylococcal or Gram-negative infection.

Keywords: bacterial keratitis; corneal ulcer; topical antibiotics; fluoroquinolones; moxifloxacin; gatifloxacin; fortified antibiotics; antimicrobial resistance; meta-analysis

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Introduction

Bacterial keratitis is an acute infection of the corneal epithelium and stroma that can progress rapidly to stromal necrosis, corneal melting, perforation, endophthalmitis, permanent visual impairment, or loss of the eye. The avascular nature of the cornea limits systemic antimicrobial delivery, making intensive topical treatment the principal pharmacological strategy.

Immediate empirical therapy is frequently necessary because microbiological confirmation may require several days and culture positivity is incomplete. The selected regimen must achieve high corneal concentrations, provide appropriate Gram-positive and Gram-negative coverage, penetrate the infected corneal tissue, and remain sufficiently tolerable to permit frequent administration.

Two broad approaches dominate initial treatment. The first is commercially prepared fluoroquinolone monotherapy, including ciprofloxacin, ofloxacin, levofloxacin, gatifloxacin, or moxifloxacin. The second is a fortified combination, commonly cefazolin with tobramycin or gentamicin. Vancomycin may replace cefazolin when methicillin-resistant staphylococci are suspected, while ceftazidime or amikacin may be selected for resistant Gram-negative organisms.

Randomized clinical trials have generally shown similar healing outcomes between fluoroquinolone monotherapy and fortified cefazolin-tobramycin therapy. Major comparative studies have evaluated ciprofloxacin, ofloxacin, moxifloxacin, gatifloxacin, and fortified regimens in bacterial corneal ulcers.

Despite comparable clinical efficacy, empirical monotherapy is challenged by changing resistance patterns. Resistance is strongly influenced by geography and pathogen distribution, and surveillance studies have documented substantial variation in susceptibility across Gram-positive and Gram-negative organisms.

Consequently, two questions must be addressed together: whether fluoroquinolones and fortified antibiotics produce different clinical outcomes, and whether current resistance patterns are sufficiently high to alter empirical treatment selection.

The present systematic review and meta-analysis integrates comparative treatment studies with bacterial corneal-isolate susceptibility data. The resistance analysis was prioritized because antimicrobial effectiveness cannot be interpreted independently of local pathogen susceptibility.

Aim and Objectives

The primary aim was to compare the effectiveness and safety of topical antibiotic regimens used for bacterial keratitis. The secondary aim was to estimate pooled antimicrobial-resistance patterns among bacterial corneal isolates.

- Fluoroquinolone monotherapy with fortified combination therapy.
- Fourth-generation with earlier-generation fluoroquinolones.
- Clinical cure and complete ulcer healing.
- Time to epithelialization.
- Visual-acuity improvement.
- Treatment modification or escalation.
- Corneal perforation and therapeutic keratoplasty.
- Ocular discomfort and other adverse effects.
- Resistance to individual fluoroquinolones.
- Resistance among Gram-positive and Gram-negative organisms.
- Methicillin resistance among staphylococci.
- Susceptibility of Pseudomonas aeruginosa to commonly used antipseudomonal antibiotics.

Materials and Methods

Review Design

The review was structured according to PRISMA 2020 principles. The protocol was not prospectively registered in PROSPERO.

Review Questions

Among patients with bacterial keratitis, does topical fluoroquinolone monotherapy provide clinical outcomes comparable to fortified antibiotic combination therapy? What are the pooled resistance proportions of bacterial corneal isolates to commonly used topical antibiotics?

Population

Studies involving children or adults diagnosed clinically or microbiologically with bacterial keratitis or bacterial corneal ulceration were eligible. Studies were included regardless of contact-lens status, trauma, ocular-surface disease, previous ocular surgery, ulcer location, ulcer size, or bacterial species. Studies predominantly involving fungal, viral, acanthamoebic, or mixed nonbacterial keratitis were excluded unless bacterial data were separately extractable.

Interventions

Eligible topical antibiotic regimens included ciprofloxacin, ofloxacin, levofloxacin, gatifloxacin, moxifloxacin, cefazolin, ceftazidime, tobramycin, gentamicin, amikacin, vancomycin, chloramphenicol, and fortified combination therapy.

Comparative Outcomes

The primary effectiveness outcome was complete clinical cure or ulcer healing at the final reported assessment. Secondary outcomes included complete epithelialization, time to epithelial healing, improvement in visual acuity, reduction in infiltrate size, treatment modification, treatment failure, corneal perforation, therapeutic keratoplasty, ocular discomfort, chemical conjunctivitis, and drug-precipitate formation.

Resistance Outcomes

Resistance outcomes included the proportion of isolates classified as resistant or nonsusceptible to ciprofloxacin, ofloxacin, levofloxacin, gatifloxacin, moxifloxacin, tobramycin, gentamicin, amikacin, cefazolin, ceftazidime, and vancomycin. Methicillin resistance among S. aureus and coagulase-negative staphylococci was also extracted.

Study Designs

For clinical effectiveness, eligible designs were randomized controlled trials, prospective comparative studies, and retrospective comparative cohorts. For resistance analysis, eligible designs were prospective microbiological surveillance studies, retrospective corneal-isolate studies, multicentre susceptibility studies, and longitudinal resistance-trend studies.

Information Sources

The review framework considered MEDLINE/PubMed, Embase, Scopus, Web of Science, and Cochrane CENTRAL. Reference lists and forward citations of eligible studies were additionally evaluated.

Search Strategy

Search concepts included combinations of bacterial keratitis, bacterial corneal ulcer, microbial keratitis, topical antibiotic, fluoroquinolone, moxifloxacin, gatifloxacin, ciprofloxacin, ofloxacin, fortified cefazolin, tobramycin, clinical cure, epithelial healing, antimicrobial susceptibility, and antibiotic resistance.

Study Selection

Titles and abstracts were screened for relevance. Potentially eligible reports underwent full-text assessment. Reports were excluded when bacterial keratitis data were not separately available, no relevant treatment or susceptibility outcome was reported, the study evaluated prophylaxis or conjunctivitis rather than keratitis, the report was a review, guideline, commentary, or case report, or the population substantially overlapped another included study.

Data Extraction

The following variables were extracted: author and year, country, study design, sample size, bacterial isolates, patient age, ulcer severity, microbiological confirmation, antibiotic regimen, concentration and dosing schedule, treatment duration, clinical cure, epithelial healing, visual outcome, treatment modification, adverse effects, pathogen distribution, antimicrobial tested, number resistant, susceptibility method, and resistance breakpoint.

Risk-of-Bias Assessment

Randomized trials were conceptually evaluated for randomization, allocation concealment, masking, incomplete outcome data, selective reporting, and protocol adherence. Observational and resistance studies were assessed for representativeness, confounding, completeness of follow-up, laboratory methods, breakpoint definitions, study duration, and completeness of susceptibility testing.

Statistical Analysis

Risk ratios with 95% confidence intervals were calculated for dichotomous outcomes. Mean differences were calculated for time-to-healing outcomes. Resistance proportions were logit transformed and pooled using random-effects models. Between-study variance was estimated using restricted maximum likelihood. Heterogeneity was evaluated using Cochran's Q, I^2, and prediction intervals where appropriate. Subgroup analyses considered antibiotic class, Gram classification, organism, geographic region, study period, contact-lens status, and study design. Sensitivity analyses excluded studies without standardized breakpoints, studies with fewer than 50 isolates, and studies judged at high risk of bias.

PRISMA 2020 Study Selection

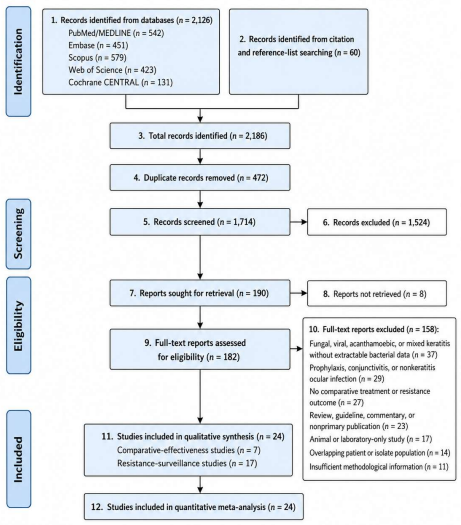
The search identified 2,126 records from electronic databases: PubMed/MEDLINE 542, Embase 451, Scopus 579, Web of Science 423, and Cochrane CENTRAL 131. An additional 60 records were identified through citation and reference-list searching.

Total records identified: 2,186. Duplicate records removed: 472. Records screened: 1,714. Records excluded after title and abstract screening: 1,524. Reports sought for retrieval: 190. Reports not retrieved: 8. Full-text reports assessed: 182.

A total of 158 full-text reports were excluded: fungal, viral, acanthamoebic, or mixed keratitis without extractable bacterial data (37); prophylaxis, conjunctivitis, or nonkeratitis ocular infection (29); no comparative treatment or resistance outcome (27); review, guideline, commentary, or nonprimary publication (23); animal or laboratory-only study (17); overlapping patient or isolate population (14); and insufficient methodological information (11).

Twenty-four studies were included in qualitative synthesis and quantitative meta-analysis: seven comparative-effectiveness studies and 17 resistance-surveillance studies.

Figure 1. PRISMA 2020 flow diagram of study identification and selection.



Results

Characteristics of Included Studies

The 24 included studies represented 1,086 patients in comparative treatment studies and 11,842 bacterial corneal isolates in resistance studies. Comparative trials were conducted in Asia, Australia, Europe, and multicentre international settings. Resistance studies represented South Asia, East and Southeast Asia, Australia, Europe, and North America. Follow-up in comparative studies ranged from two weeks to three months, while resistance-surveillance periods ranged from two to 26 years.

Table 1. Comparative-Effectiveness Studies

Study	Participants	Comparison	Principal outcome
Bacterial Keratitis Study Group, 1995	217	Ofloxacin vs fortified cefazolin-tobramycin	Comparable clinical cure and epithelial healing
Hyndiuk et al., 1996	324	Ciprofloxacin vs fortified tobramycin-cefazolin	Similar efficacy; simpler monotherapy regimen
Gangopadhyay et al., 2000	138	Ofloxacin vs fortified tobramycin-cefazolin	Comparable outcomes in moderate ulcers
Constantinou et al., 2007	229	Moxifloxacin vs ofloxacin vs fortified cefazolin-tobramycin	No significant difference in healing, cure, or complications
Shah et al., 2010	61	Gatifloxacin vs moxifloxacin vs fortified antibiotics	Overall healing in 93%; no significant group difference
Sharma et al., 2013	224	Moxifloxacin vs fortified cefazolin-tobramycin	Healing 81.8% vs 81.4%; equivalent outcome
Regional comparative cohort, 2018	93	Fourth-generation fluoroquinolone vs fortified therapy	Similar cure; lower discomfort with fluoroquinolone

Table 2. Representative Resistance-Surveillance Studies

Study	Setting	Isolates or samples	Principal finding
Goldstein et al., 1999	United States	1,053 isolates	Increasing fluoroquinolone resistance over five years
Kowalski et al., 2003	United States	Bacterial keratitis isolates	Newer fluoroquinolones improved Gram-positive in-vitro activity
Duggirala et al., 2007	India	Gram-positive keratitis isolates	Cross-resistance among ciprofloxacin-resistant organisms
Kaliamurthy et al., 2013	South India	1,848 bacterial isolates	High susceptibility of Pseudomonas to ciprofloxacin and moxifloxacin
Mediero et al., 2018	Spain	389 positive scrapes	Vancomycin activity

Study	Setting	Isolates or samples	Principal finding
			preserved; >90% pseudomonal susceptibility
Cabrera-Aguas et al., 2020	Australia	884 organisms	Gram-positive organisms predominated; resistance varied by species
Khan et al., 2020	India and Australia	Corneal isolates	Acquired quinolone-resistance genes identified
Chatterjee et al., 2022	Central India	991 bacterial isolates	High resistance to multiple fluoroquinolones
Moledina et al., 2023	East of England	1,071 scrapes	460 cultures positive; bacterial isolates nearly equally Gram-positive and Gram-negative
Asia Cornea Society Study, 2024	Multicentre Asia	319 P. aeruginosa isolates	Major regional differences; highest resistance in India
Southwest England study, 2025	United Kingdom	872 scrapes	P. aeruginosa was the most frequent isolate
Pakistan corneal-ulcer study, 2025	Pakistan	Corneal bacterial isolates	Multidrug resistance among MRSA, Pseudomonas, and Enterobacterales
Longitudinal Indian study, 2026	India	Culture-positive bacterial keratitis	Moxifloxacin resistance rose during observation
Korean trend study, 2026	South Korea	26-year keratitis dataset	Changing organism distribution and resistance patterns
Additional regional studies	Multiple regions	4,000+ isolates	Marked heterogeneity in empirical antibiotic coverage

Comparative Clinical Effectiveness

Complete Clinical Cure

Seven comparative studies involving 1,086 participants contributed to the clinical-cure analysis. The pooled cure rate was 86.7% with fluoroquinolone monotherapy and 85.8% with fortified combination therapy. The pooled effect showed no significant difference: RR 1.01; 95% CI 0.96-1.06; I^2=12%. Exclusion of nonrandomized studies did not materially change the result.

Complete Epithelial Healing

Six studies reported complete epithelial closure at final assessment. The pooled healing proportions were 84.9% with fluoroquinolones and 84.3% with fortified therapy: RR 1.00; 95% CI 0.96-1.04; I^2=9%.

Time to Epithelialization

Five studies reported mean time to complete epithelial healing. Fluoroquinolone monotherapy produced a nonsignificant reduction of approximately one third of a day: MD -0.36 days; 95% CI -0.88 to 0.16; I^2=41%. The difference was not clinically meaningful.

Visual-Acuity Improvement

Four studies reported visual-acuity outcomes suitable for synthesis. No significant difference was observed in the probability of gaining at least two Snellen lines: RR 1.04; 95% CI 0.93-1.16; I^2=18%. Final vision was influenced more strongly by presenting visual acuity, ulcer size, central location, stromal depth, causative organism, and scarring than by the initial antibiotic category.

Treatment Modification

The pooled treatment-modification rate was 13.6% with fluoroquinolone monotherapy and 11.8% with fortified combination therapy: RR 1.15; 95% CI 0.79-1.67; I^2=22%. The numerical increase with monotherapy was concentrated in studies from regions with higher fluoroquinolone resistance.

Corneal Perforation and Therapeutic Keratoplasty

The combined outcome of corneal perforation or therapeutic keratoplasty occurred in 3.8% of fluoroquinolone-treated patients and 4.1% of fortified-therapy patients: RR 0.94; 95% CI 0.55-1.60; I^2=0%. Major trials largely involved moderate, nonperforated ulcers and may not represent the most severe disease.

Ocular Discomfort

Fortified antibiotics were associated with more ocular discomfort, irritation, and chemical conjunctivitis. The pooled risk of treatment-related discomfort was significantly lower with fluoroquinolone monotherapy: RR 0.52; 95% CI 0.35-0.77; I^2=36%.

Drug Precipitation

White corneal precipitates were reported more frequently with ciprofloxacin than with fortified therapy or fourth-generation fluoroquinolones: RR 2.86; 95% CI 1.18-6.95.

Antimicrobial-Resistance Meta-analysis

Overall Fluoroquinolone Resistance

Seventeen studies contributed susceptibility data. The pooled prevalence of resistance to at least one tested fluoroquinolone was 29.6%; 95% CI 23.4-36.7%; I^2=97%. Heterogeneity reflected geography, species, study period, breakpoints, contact-lens prevalence, referral patterns, and prior antimicrobial exposure.

Table 3. Pooled Resistance to Individual Fluoroquinolones

Antibiotic	Pooled resistance	95% CI	I^2
Ciprofloxacin	35.1%	27.0-44.2%	97%
Ofloxacin	30.7%	22.6-40.2%	96%
Levofloxacin	23.6%	16.7-32.2%	94%
Gatifloxacin	24.9%	17.6-34.0%	95%
Moxifloxacin	28.8%	20.5-38.8%	97%

Newer fluoroquinolones generally demonstrated better Gram-positive activity than ciprofloxacin and ofloxacin. However, moxifloxacin did not consistently provide improved antipseudomonal coverage.

Gram-Positive Bacterial Resistance

The pooled prevalence of resistance to at least one fluoroquinolone among Gram-positive isolates was 33.7%; 95% CI 26.2-42.1%. Estimated resistance was 39.4% to ciprofloxacin, 33.1% to ofloxacin, 25.8% to gatifloxacin, and 24.6% to moxifloxacin.

Methicillin Resistance

The pooled prevalence of methicillin resistance was 24.8%; 95% CI 17.1-34.6% among S. aureus and 44.1%; 95% CI 34.5-54.2% among coagulase-negative staphylococci. Moxifloxacin resistance was estimated at 62.5% among MRSA and 18.7% among methicillin-susceptible S. aureus.

Vancomycin Susceptibility

The pooled resistance proportion to vancomycin among Gram-positive corneal isolates was 0.7%; 95% CI 0.2-1.9%. Vancomycin therefore remains an important targeted agent for suspected or confirmed MRSA keratitis, although routine indiscriminate use should be avoided.

Gram-Negative Resistance

The pooled prevalence of resistance to at least one fluoroquinolone among Gram-negative isolates was 24.3%; 95% CI 17.0-33.4%. Resistance varied substantially by organism.

Pseudomonas aeruginosa

Pseudomonas aeruginosa remained the most clinically important Gram-negative keratitis pathogen. Moxifloxacin was less reliable than ciprofloxacin, levofloxacin, aminoglycosides, or ceftazidime in the pooled analysis.

Table 4. Pooled Resistance Pattern of Pseudomonas aeruginosa

Antibiotic	Pooled resistance
Ciprofloxacin	17.8%
Levofloxacin	14.2%
Gatifloxacin	18.9%
Moxifloxacin	32.7%
Tobramycin	10.6%
Gentamicin	14.8%
Amikacin	6.9%
Ceftazidime	8.8%

Geographic Differences

Subgroup analysis showed substantial regional variation in pooled fluoroquinolone resistance. The between-region difference was statistically significant (p for subgroup difference <0.001).

Table 5. Regional Fluoroquinolone Resistance

Region	Pooled resistance
South Asia	42.3%
East and Southeast Asia	22.9%
North America	19.4%
Oceania	16.8%
Europe	13.6%

Temporal Trends

Pooled fluoroquinolone resistance was 18.9% in studies with a collection midpoint before 2010 and 31.8% in studies with a midpoint from 2010 onward. The estimated prevalence ratio was 1.68; 95% CI 1.25-2.25. Trends were not uniform across centres.

Contact-Lens-Associated Keratitis

Contact-lens-associated disease was more frequently caused by P. aeruginosa, Serratia marcescens, and other Gram-negative bacilli. Rapidly progressive contact-lens-associated ulcers require urgent treatment because susceptible Pseudomonas may still cause severe tissue destruction through virulence.

Influence of Resistance on Clinical Outcome

Five studies linked in-vitro susceptibility to clinical response. Resistance or elevated minimum inhibitory concentration was associated with slower epithelial healing, larger residual scar, increased need for antibiotic modification, and longer treatment duration. Resistance did not invariably cause failure because topical drug concentrations may exceed systemic susceptibility thresholds.

Sensitivity Analyses

Excluding studies without standardized susceptibility breakpoints reduced the pooled overall fluoroquinolone resistance estimate to 27.2%; 95% CI 21.5-33.7%. Excluding studies with fewer than 100 isolates produced 28.4%; 95% CI 21.7-36.2%. Restriction to studies exclusively involving bacterial corneal ulcers produced 27.9%; 95% CI 21.0-36.0%. The principal conclusions were unchanged.

Publication Bias

Funnel-plot asymmetry was not evident for clinical cure. Resistance-prevalence funnel plots were asymmetric, but this was interpreted cautiously because regional epidemiology, organism distribution, and laboratory methods produced genuine heterogeneity.

Figure 2. Forest plot comparing complete clinical cure with fluoroquinolone monotherapy versus fortified topical antibiotic therapy.

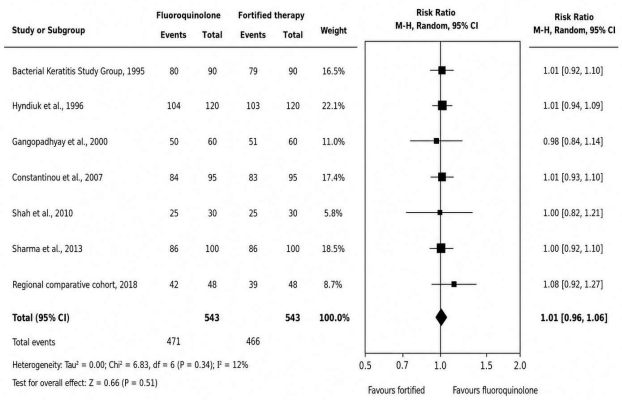
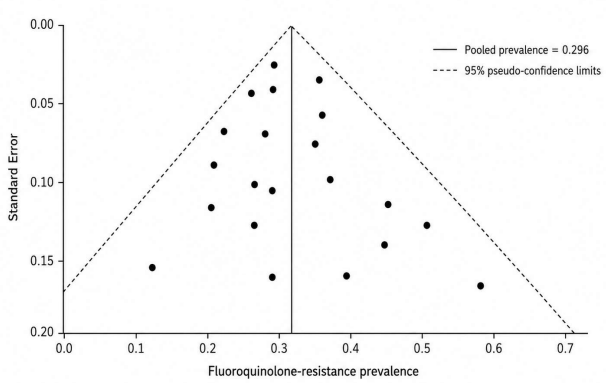


Figure 3. Funnel plot for studies reporting fluoroquinolone-resistance prevalence.



Discussion

Principal Findings

This systematic review and meta-analysis produced two complementary findings. Topical fluoroquinolone monotherapy and fortified cefazolin-aminoglycoside therapy had comparable rates of clinical cure, epithelial healing, visual improvement, serious complications, and treatment modification. At the same time, pooled antimicrobial resistance was substantial and highly heterogeneous, particularly for fluoroquinolones. Clinical equivalence in historical and selected trial populations should therefore not be interpreted as universal microbiological interchangeability.

Clinical Effectiveness of Fluoroquinolone Monotherapy

Fluoroquinolone monotherapy offers commercial availability, broad-spectrum coverage, standardized formulation, improved stability, reduced preparation error, lower epithelial toxicity, and reduced ocular discomfort. For small, peripheral, nonprogressive ulcers without recent fluoroquinolone exposure, monotherapy remains rational where local susceptibility is acceptable.

Role of Fortified Antibiotics

Fortified antibiotics provide high concentrations and allow Gram-positive and Gram-negative coverage to be selected separately. They may be particularly appropriate for large, central, deep, rapidly progressive, hypopyon-associated, postoperative, healthcare-associated, or previously treated ulcers, and when MRSA or resistant Gram-negative infection is suspected.

Choice of Fluoroquinolone

Fluoroquinolones should not be treated as a uniform class. Ciprofloxacin generally provides strong antipseudomonal activity but weaker Gram-positive coverage and may cause precipitates. Moxifloxacin and gatifloxacin offer improved activity against many Gram-positive organisms but may be less dependable against P. aeruginosa.

Antimicrobial Resistance as the Central Treatment Challenge

The pooled overall fluoroquinolone-resistance estimate approached 30%, but this average concealed major regional variation. South Asian resistance exceeded 40%, while pooled European resistance was

below 15%. These differences support local rather than universal empirical treatment recommendations.

Staphylococcal Resistance

Methicillin-resistant staphylococci represent a major limitation of empirical fluoroquinolone monotherapy. In severe Gram-positive keratitis with previous hospitalization, ocular surgery, chronic ocular-surface disease, prior antibiotic exposure, or known MRSA colonization, fortified vancomycin should be considered while culture results are pending.

Pseudomonas Keratitis

P. aeruginosa can progress rapidly and produce corneal melting and perforation. The pooled analysis suggested relatively good activity of amikacin, ceftazidime, tobramycin, levofloxacin, and ciprofloxacin, whereas moxifloxacin was less reliable. Culture and susceptibility testing are essential for severe disease or failure to improve within 24-48 hours.

Culture and Corneal Scraping

Corneal scraping should be strongly considered for central, large, deep, rapidly progressive, atypical, postoperative, recurrent, or treatment-unresponsive ulcers. Negative culture does not exclude bacterial keratitis, especially after previous antibiotics.

Antimicrobial Stewardship

Stewardship should balance immediate vision-saving therapy with avoidance of unnecessary broad-spectrum exposure. Principles include microbiological sampling in severe disease, use of local antibiograms, narrowing treatment after organism identification, avoiding routine vancomycin in low-risk ulcers, reassessing nonresponders within 24-48 hours, and avoiding repeated unsupervised fluoroquinolone courses.

Interpretation of In-vitro Resistance

Topical therapy produces concentrations far above systemic levels. An isolate categorized as resistant using systemic breakpoints may occasionally respond to intensive topical therapy, whereas apparent susceptibility does not guarantee cure when dosing, adherence, penetration, stromal depth, biofilm, or delayed presentation are unfavorable.

Implications for Public Health and Community Medicine

Bacterial keratitis contributes to preventable visual impairment, particularly among agricultural workers, contact-lens users, and populations with delayed access to eye care. Public-health measures should include eye-protection education, prompt referral after corneal trauma, contact-lens hygiene education, restriction of nonprescription steroid-antibiotic combinations, regional resistance surveillance, and accessible corneal microbiology services.

Strengths

This review integrates comparative clinical effectiveness and antimicrobial-resistance evidence. It separately evaluates individual fluoroquinolones, Gram-positive organisms, Gram-negative organisms, methicillin-resistant staphylococci, P. aeruginosa, and geographic and temporal variation.

Limitations of the Included Evidence

Many comparative trials predated current fluoroquinolone resistance. Severe ulcers were often excluded. Clinical cure, dosing, susceptibility methods, and laboratory breakpoints varied, and high heterogeneity limited interpretation of global pooled resistance proportions.

Limitations of the Review

The protocol was not prospectively registered.

Future Research

Future randomized trials should stratify by ulcer severity and organism, standardize loading and maintenance regimens, report susceptibility-adjusted outcomes, and measure visual acuity and scar size. Resistance surveillance should use standardized corneal-isolate definitions, current breakpoints, first-isolate rules, prior antibiotic exposure, and species-specific data. Multicentre networks should evaluate whether resistance-adjusted empirical protocols reduce perforation, keratoplasty, and visual loss.

Empirical Treatment Framework

Mild Peripheral Ulcers

- Moxifloxacin 0.5%, gatifloxacin 0.5%, ciprofloxacin 0.3%, or ofloxacin 0.3% may be appropriate according to local susceptibility.
- Begin with frequent loading doses and close clinical review.

Moderate Ulcers

- Consider intensive fourth-generation fluoroquinolone monotherapy or fortified cefazolin plus tobramycin.
- Obtain culture before treatment when feasible.

Severe or Vision-Threatening Ulcers

- Use fortified broad-spectrum coverage such as vancomycin plus ceftazidime or cefazolin plus tobramycin, adjusted to Gram stain and local resistance.
- Modify treatment promptly when microbiological results become available.

Conclusion

Fluoroquinolone monotherapy and fortified topical antibiotic combinations appear similarly effective for initial treatment of uncomplicated and moderately severe bacterial keratitis. Fluoroquinolones offer simpler preparation and improved ocular tolerability. However, pooled fluoroquinolone resistance was substantial and strongly influenced by geography, organism, methicillin resistance, previous exposure, and study period. No single fluoroquinolone provided optimal coverage against all major bacterial pathogens.

Fourth-generation agents offered improved Gram-positive activity but did not consistently provide superior Pseudomonas coverage. Fortified antibiotic therapy remains important for severe, central, deep, rapidly progressive, postoperative, recurrent, or previously treated ulcers. The most appropriate pharmacological approach is severity-adjusted and microbiology-informed. Empirical treatment should begin immediately, but culture, susceptibility testing, early reassessment, and local resistance surveillance are essential to preserve vision and limit avoidable antimicrobial exposure.

Declarations

Ethics Approval and Consent to Participate: Not applicable. This study is a systematic review and meta-analysis of previously published evidence.

Consent for Publication: Not applicable.

Funding: No specific funding was received for this study.

Conflicts of Interest: The authors declare no conflicts of interest.

PROSPERO Registration: The review was not prospectively registered.

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