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Statins as a possible factor affecting fluoroquinolone resistance of coagulase-negative *Staphylococcus* in the conjunctiva: a case-control study

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Background: Conjunctival bacterial flora is a common cause of endophthalmitis after ophthalmic procedures. This study investigated the conjunctival bacterial flora, especially coagulase-negative *Staphylococcus* (CoNS), and their antibiotic sensitivity in patients who underwent ophthalmic procedures. Factors related to fluoroquinolone resistance were also investigated.

Methods: In total, 167 samples were analyzed from 135 patients who underwent cataract surgery or intravitreal injection at Kosin University Gospel Hospital between April 14, 2014, and September 29, 2016. Bacterial identification was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry or VITEK 2 equipment. Antibiotic sensitivity tests were performed using an AST-P600 card with VITEK 2 equipment. Clinical information was extracted from patients' medical records. Sixty-eight individuals with conjunctival flora containing CoNS were classified into the fluoroquinolone-sensitive and fluoroquinolone-resistant CoNS groups, and their characteristics were compared.

Results: A total of 192 isolates of Gram-positive bacteria were identified, including *Staphylococcus epidermidis* (33.3%), *Corynebacterium* spp. (18.8%), and CoNS other than *S. epidermidis* (9.2%). Of the 106 CoNS isolates, 68.9%, 69.8%, and 58.5% were sensitive to ciprofloxacin, levofloxacin, and norfloxacin, respectively. In patients with CoNS, statin use within 3 months before sample collection was significantly associated with fluoroquinolone resistance (p=0.016). Statin use was a significant risk factor for fluoroquinolone resistance in multivariate logistic regression analysis (odds ratio, 4.86; 95% confidence interval, 1.25–18.91; p=0.022).

Conclusions: CoNS, including *S. epidermidis*, was the most common conjunctival bacterial flora, with a fluoroquinolone sensitivity rate ranging from 58.5% to 69.8% in patients undergoing ophthalmic procedures. Statin use was a significant risk factor for fluoroquinolone resistance.

Keywords: Cataract extraction; Fluoroquinolones; Hydroxymethylglutaryl-CoA reductase inhibitors; Intravitreal injections; Staphylococcus

Introduction

Although endophthalmitis is a rare complication of cataract surgery and intravitreal injection, it is important to understand antimicrobial resistance with regard to the causative bacteria of endophthalmitis, as this serious ophthalmic dis-

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ease can cause vision loss [1,2]. Since many cataract surgeries and intravitreal injections are performed worldwide, the occurrence of endophthalmitis is increasing. Conjunctival bacterial flora comprises 82% of the causative bacteria of endophthalmitis after cataract surgery [3]. Therefore, regular monitoring for changes in conjunctival flora and antimicrobial susceptibility are required to appropriately select antibiotic eye drops that will prevent endophthalmitis and empirical antibacterial agents for its treatment [1,4,5]. However, because this information varies by region and time, a regular regional monitoring system is necessary [4]. Fluoroquinolones were introduced as antibacterial agents in eye drops in 1990. Between 1990 and the early 2000s, fluoroquinolones were the primary antibiotic eye drops used because conjunctival bacteria had low associated resistance. However, resistance to fluoroquinolones is steadily increasing, especially in coagulase-negative *Staphylococcus* (CoNS) species [2,6,7]. The risk factors for fluoroquinolone-resistant (FR) *Staphylococcus* present in the conjunctiva include the use of topical antibiotics (including fluoroquinolones) within 3 months, previous hospitalization and ophthalmic procedures [8]. After intravitreal injection, antimicrobial prophylaxis with fluoroquinolone eye drops may increase resistance due to multi-step mutations that can arise during short-term and repeated exposure [2].

Statins are commonly used medications to treat hyperlipidemia. In addition to their cholesterol-lowering effect, statins also have antibacterial effects against *Streptococcus pneumoniae* and *Staphylococcus aureus*; therefore, their potential as new antibacterial agents has also been assessed [9]. However, their widespread use for cardiovascular protection has instead created selective pressure for resistance. Ironically, it also has the potential to promote antibiotic resistance [10,11].

The present study investigated the conjunctival microbiota and antimicrobial susceptibility of patients who underwent cataract surgery and intravitreal injection. Our aim was to establish a basis for the selection of prophylactic antibiotics for ophthalmic procedure and empirical antibiotics for the treatment of endophthalmitis. We also sought to identify factors related to antimicrobial resistance, including a history of statin use, which has antibacterial effects.

Methods

Ethical statements: This study was approved by the Institutional Review Board of the Kosin University Gospel Hospital (KUGH 2017-11-045-003). This retrospective study utilized data collected as a part of routine clinical care. The Institutional Review Board of the Kosin University Gospel Hospital determined that the study met IRB exemption criteria based on the retrospective nature of the study and participant consent was therefore not required.

1. Subjects

This retrospective study included patients who underwent cataract extraction, posterior intraocular lens implantation, or intravitreal injection at the Department of Ophthalmology at Kosin University Gospel Hospital between April 14, 2014, and September 29, 2016. Among 135 such patients who also underwent conjunctival colonization culture, 167 specimens were collected. We also included samples of one case in which a patient underwent another ophthalmic procedure during the study period. So if the procedure was repeated, samples were collected from a minimum of 1 to a maximum of 3 times. Among them, samples were collected only once in 105 patients (105 specimens), twice in 28 patients (56 specimens), and three times in two patients (6 specimens). Based on the medical records, the following clinical parameters were collected: age at the time of sample collection, sex, type of ophthalmic disease for which the procedure was performed (cataract, diabetic retinopathy, macular dystrophy or macular degeneration, retinal vascular occlusion, glaucoma), procedure type (phacoemulsification with posterior chamber lens implantation, intravitreal injection, pars plana vitrectomy, laser photocoagulation), diabetes, hypertension, chronic viral hepatitis (including hepatitis B and C), alcohol consumption, and smoking history. The patients' histories of ophthalmologic procedures and hospitalization within 3 months before sample collection were also evaluated. The following measurements were performed: fasting blood glucose, glycosylated hemoglobin, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride levels.

2. Methods

1) Sample collection and storage

Specimens were collected from the lower conjunctival

sac by scraping the lower eyelid laterally with a polyester-tipped swab (23-400-122, Fisherbrand) after inversion of the lower eyelid before applying the eye drop anesthetic. No prophylactic antibacterial eye drops were administered before surgery. Immediately after inoculation on 5% blood agar, the specimens were cultured at 37 °C in an incubator (Water-Jacketed CO2 Incubator, Forma Scientific, Inc.) for up to 7 days. The bacterial colonies were plated on fresh 5% blood agar or MacConkey medium to obtain pure colonies, and the strains were classified according to the colony shape. Subsequently, 1 mL of a mixture of 60% glycerol and *Brucella* broth in a 3:7 ratio was dissolved for 1–2 weeks and stored in a –70 °C ultra-low temperature freezer.

2) Bacteria identification and antimicrobial susceptibility testing

A total of 167 frozen samples collected from 135 patients were thawed and re-inoculated on 5% blood agar or MacConkey medium using a 10-μL loop (SPL Life Sciences). A total of 261 strains were identified by subculturing. The bacteria were identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS, Bruker Daltonics GmbH) or VITEK 2 system (bioMerieux, Marcy l'Etoile). Bacterial identification and susceptibility tests were performed using ID (GP or GN) cards and AST-P600) cards on VITEK-2 equipment, respectively. The minimum inhibitory concentration (MIC, μg/mL) was reported according to Clinical and Laboratory Standards Institute (CLSI) standards [12].

3) Factors related to fluoroquinolone resistance of CoNS in conjunctival flora

The CoNS strains isolated from the conjunctival flora of 68 patients were classified according to fluoroquinolone resistance. Strains that were moderately resistant or resistant to ciprofloxacin, levofloxacin, and/or norfloxacin were categorized as FR CoNS. In contrast, strains that were sensitive to all three fluoroquinolones were categorized as non-FR CoNS. If more than one FR CoNS were identified from one patient, the groups were classified based on CoNS with a high degree of resistance. In addition to the clinical information surveyed on all 68 subjects, the history of statin use within 3 months before sample collection was also investigated.

4) Statistical analysis

For comparisons between two groups, the chi-square or Fisher exact tests were used for categorical variables, while Mann-Whitney *U*-tests were performed for numerical variables. Statistical significance was set at $p<0.05$. Variables that were significant in univariate analysis were reanalyzed in multivariate analysis using the "enter" method to check the influence between variables. The KoreaPlus statistical program (Embedded in SPSS 26.0 Statistics) for Windows (Datasolution Inc.) was used to perform these analyses.

Results

1. Clinical characteristics of the study participants

Among the study participants, 15 (11.1%) had a history of chronic viral hepatitis including hepatitis B and C. Fifteen patients (11.1%) had undergone ophthalmic procedures within 3 months before sample collection (0–7 procedures) and 35 (25.9%) had been hospitalized for any reason (duration, 1–23 days) (Table 1).

Table 1. Demographic characteristics of the patients (n=135)

Characteristic	No. (%)
Age (yr), median (range)	62 (20–88)
Male sex	79 (58.5)
Conjunctival swab culture	
Bacterial growth	107 (82.9)
Ophthalmic procedure	
Phacoemulsification with posterior chamber lens implantation	33 (24.4)
Intravitreal injection	100 (74.1)
Others	2 (1.4)
Ophthalmic disease	
Cataract	33 (24.4)
Diabetic retinopathy	45 (33.3)
Macular dystrophy, macular degeneration	34 (25.2)
Retinal vascular occlusion	16 (11.9)
Glaucoma	21 (15.6)
Others	7 (5.2)
Other diseases and conditions	
Diabetes mellitus	67 (49.6)
Hypertension	38 (28.1)
Viral hepatitis	15 (11.1)
Alcohol drinking	50 (37.0)
Smoking	38 (28.1)
Ophthalmic procedure within 3 mo before sample collection	15 (11.1)
Hospital admission within 3 mo before sample collection	35 (25.9)

2. Types of cultured strains and their antimicrobial susceptibility

Among a total of 167 samples collected from 135 patients, 261 bacterial strains were isolated. There were 192 (73.6%) Gram-positive bacteria and 69 (26.4%) Gram-negative bacteria (Table 2). Antimicrobial susceptibility was tested for 123 of the 192 Gram-positive strains (84 strains of *Staphylococcus epidermidis*, 22 strains of CoNS excluding *S. epidermidis*, 11 strains of *S. aureus*, and 6 strains of *Enterococcus* spp.). Among them, 12.2% (15/123) were sensitive to penicillin, while 70.7% (87/123), 71.5% (88/123), and 61.0% (75/123) of strains were susceptible to ciprofloxacin, levofloxacin, and norfloxacin, respectively. CoNS strains (106 strains) were 68.9% (73/106), 69.8% (74/106), and 58.5% (62/106) susceptible to ciprofloxacin, levofloxacin, and norfloxacin, respectively (Table 3). In 22 patients, two or more strains of the same CoNS species were identified in samples from the same round of sample collection. Among them, 21 had *S. epidermidis*; the other had *Staphylococcus haemolyticus*. Twelve cases showed different antimicrobial susceptibilities among these bacteria, with 54.5% (12/22) of the same type of CoNS showing different susceptibilities.

3. Factors associated with fluoroquinolone resistance in CoNS

Of the 68 patients from which CoNS were isolated, 31 and 37 were in the non-FR CoNS and FR CoNS groups, respectively. The bacteria identified in the 31 non-FR CoNS patients were *S. epidermidis* (27 patients), *Staphylococcus lentus* (2 patients), *S. haemolyticus* (1 patient), and *Staphylococcus capitis* (1 patient), while the 37 FR CoNS patients included *S. epidermidis* (29 patients), *S. haemolyticus* (4 patients), *Staphylococcus hominis* (3 patients), and *S. capitis* (1 patient). Hospitalization before sample collection was slightly higher in the FR CoNS group, but the difference was not statistically significant (p=0.077).

The FR CoNS group was significantly associated with history of statin use within 3 months before sample collection (p=0.016), total cholesterol over than 200 mg/dL (p=0.006), and LDL cholesterol over than 130 mg/dL (p=0.002). The FR CoNS group was significantly associated with a history of viral hepatitis (p=0.006) (Table 4).

Table 2. Microbial isolates from the conjunctiva (n=261)

Microbial	No. (%)
Gram-positive bacteria	192 (73.6)
Staphylococcus epidermidis	87 (33.3)
Corynebacterium spp.	49 (18.8)
CoNS other than *S. epidermidis*	24 (9.2)
Staphylococcus aureus	11 (4.2)
Enterococcus spp.	6 (2.3)
Micrococcus spp.	5 (1.9)
Other Gram-positive bacteria[a]	10 (3.8)
Gram-negative bacteria	69 (26.4)
Ochrobactrum spp.	21 (8.0)
Achromobacter spp.	15 (5.7)
Pseudomonas spp.	12 (4.6)
Brevundimonas spp.	5 (1.9)
Enterobacter spp.	4 (1.5)
Other Gram-negative bacteria[b]	12 (4.6)

CoNS, coagulase-negative *Staphylococcus*.
[a]Other Gram-positive bacteria: *Trueperella* spp. (n=1), *Propionibacterium* spp. (n=1), *Paenibacillus* spp. (n=1), *Microbacterium* spp. (n=2), *Kocuria* spp. (n=3), *Dermabacter* spp. (n=1), *Clostridium* spp. (n=1).
[b]Other Gram-negative bacteria: *Acinetobacter* spp. (n=2), *Proteus* spp. (n=2), *Delftia* spp. (n=2), *Sphingomonas* spp. (n=2), *Stenotrophomonas* spp. (n=2), *Cupriavidus* spp. (n=1), *Morganella* spp. (n=1).

Table 3. Antibiotic susceptibilities of 123 Gram-positive bacteria isolated from conjunctiva

Antibiotic susceptibility	Gram-positive bacteria, No. (%)			
	Staphylococcus epidermidis (n=84)	CoNS other than *S. epidermidis* (n=22)	*Staphylococcus aureus* (n=11)	*Enterococcus* (n=6)
Benzylpenicillin	5 (6.0)	2 (9.1)	2 (18.2)	6 (100)
Ciprofloxacin	59 (70.2)	14 (63.6)	9 (81.8)	5 (83.3)
Levofloxacin	60 (71.4)	14 (63.6)	9 (81.8)	5 (83.3)
Norfloxacin	48 (57.1)	14 (63.6)	9 (81.8)	4 (66.7)
Linezolid	84 (100)	22 (100)	11 (100)	6 (100)
Vancomycin	84 (100)	22 (100)	11 (100)	6 (100)
Tigecycline (n=121)	84 (100)	20 (100)	11 (100)	6 (100)

CoNS, coagulase-negative *Staphylococcus*.

When only statin intake history and total cholesterol >200 mg/dL were included for the multivariate analysis two variables were related to fluoroquinolone resistance; a history of statin intake significantly increased the risk of fluoroquinolone resistance (odds ratio [OR], 4.86; 95% confidence interval [CI], 1.25–18.91; p=0.022) (Table 5).

Discussion

Although prophylactic antibiotic use before and after cataract surgery and intravitreal injection can prevent endophthalmitis, prophylactic ocular antimicrobial administration has increased fluoroquinolone resistance [8]. Some experts argue that these prophylactic eye drops are necessary and that information on the type of conjunctival flora and their antimicrobial susceptibility reported in the community can help to select the appropriate antibacterial agents [4,13]. The present study was designed to provide this information.

In this study, 107 (82.9%) conjunctival swab culture samples from 135 patients were culture positive. The previously reported positivity rates for conjunctival bacteria through traditional culture techniques range from 75%–82% or 14%–86% [1,14,15].

Worldwide, the most common bacterium in the conjunctiva is CoNS, primarily *S. epidermidis*, while *S. aureus*, *Corynebacterium* spp., *Pseudomonas aeruginosa*, and *Haemophilus influenzae* are also common [7,16-22]. Among the conjunctival flora, the reported proportions of CoNS,

Table 5. Multivariate model for predictors of fluoroquinolone-resistant CoNS

Variable	β	SE	p-value	OR (95% CI)
Statin use	1.581	0.693	0.022	4.86 (1.25–18.91)
Cholesterol >200 mg/dL	−1.582	0.758	0.037	0.21 (0.05–0.91)

CoNS, coagulase-negative *Staphylococcus*; SE, standard error; OR, odds ratio; CI, confidence interval.

Table 4. Comparison of clinical characteristics in patients with CoNS as conjunctival flora according to FR

Characteristic	Non-FR CoNS (n=31)	FR CoNS (n=37)	$\chi 2$ or U tests	p-value
Male sex (n=68)	20 (64.5)	23 (62.2)	0.04	0.841
Age (yr)	60.9±14.4	63.9±13.6	500	0.365
Ophthalmic disease				
Cataract	9 (29.0)	15 (40.5)	0.98	0.323
Glaucoma	4 (12.9)	10 (27.0)	2.06	0.151
Other diseases and conditions				
Diabetes mellitus	16 (51.6)	20 (54.1)	0.04	0.841
Hypertension	7 (22.6)	10 (27.0)	0.18	0.673
Viral hepatitis	0	8 (21.6)	7.60	0.006[b]
Alcohol drinking	14 (45.2)	14 (37.8)	0.37	0.541
Smoking	11 (35.5)	15 (40.5)	0.18	0.669
Ophthalmic procedure within 3 mo before sample collection	5 (16.1)	7 (18.9)	0.09	0.764
Hospital admission within 3 mo before sample collection	5 (16.1)	13 (35.1)	3.13	0.077
Statin use	5 (16.1)	16 (43.2)	5.81	0.016
Blood test results[c]				
Cholesterol over 200 mg/dL (n=27, n=27)	12 (44.4)	3 (11.1)	7.48	0.006
HDL less 40 mg/dL (n=24, n=26)	6 (25.0)	11 (42.3)	1.67	0.197
LDL over 130 mg/dL (n=27, n=27)	9 (33.3)	0	10.80	0.002[b]
TG over 150 mg/dL (n=27, n=26)	11 (40.7)	14 (53.8)	0.91	0.339
FBS over 125 mg/dL (n=23, n=21)	12 (52.2)	7 (33.3)	1.59	0.208
HbA1C over 6% (n=15, n=11)	13 (86.7)	10 (90.9)	0.11	0.738

Values are presented as number (%) or mean±standard deviation.
CoNS, coagulase-negative *Staphylococcus*; FR, fluoroquinolone-resistant; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride; FBS, fasting blood glucose; HbA1C, glycosylated hemoglobin.
[a]Pearson $\chi 2$ test (categorical variable) or Mann-Whitney U test (numerical variable).
[b]Fisher exact test.
[c]The n values in parentheses are the number of patients in Non-FR CoNS and FR CoNS, respectively.

S. epidermidis, *S. aureus*, *Corynebacterium* spp., and other Gram-positive and Gram-negative bacteria were 33%–77%, 35%–76%, 4%–23%, 0%–45%, 3%–16%, and 6%–20%, respectively; these findings are comparable to the results of the present study, with proportions of 43%, 33%, 4%, 19%, 8%, and 26%, respectively [16,18,23,24].

In a study conducted in Korea in 2000, only 82.5% of the CoNS showed sensitivity to ciprofloxacin before cataract surgery. A 2006 study reported that only 69.2% of CoNS showed ciprofloxacin sensitivity, while 78.7% showed levofloxacin sensitivity among conjunctival flora before cataract surgery [7,25]. The Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) study reported CoNS sensitivities to levofloxacin of 86.1% and 43.2% in methicillin-sensitive (MS) and methicillin-resistant (MR) strains, respectively [26,27]. The present study did not separately confirm methicillin sensitivity. The sensitivities of CoNS to ciprofloxacin and levofloxacin were 68.9% and 69.8%, respectively. These sensitivities were higher than that of MR CoNS and lower than that of MS CoNS reported previously. Among staphylococcal isolates, the sensitivity of fluoroquinolone in the ocular flora before cataract surgery in Taiwan was 75%–82.5%, which is slightly lower than that reported previously [4]. In this study, 54.5% (12/22) of 22 patients with two or more identical species of CoNS among the samples from the same round were colonized with the same species of CoNS, but with different antimicrobial susceptibilities. More than 40% of cases of the same species of CoNS showed different susceptibilities to antibacterial agents in a previous study of conjunctival flora before cataract surgery [28].

Fluoroquinolones are broad-spectrum bactericidal antibacterial agents used to treat Gram-positive, Gram-negative, and anaerobic bacteria. They are mainly used as prophylactic antibacterial agents before and after ophthalmic surgery. However, among the bacteria that cause eye infections, resistance to fluoroquinolones is on the rise [28].

The results of this study showed that significantly more patients in the FR CoNS group had a history of statin use within 3 months before sample collection (p=0.016), as well as normal total cholesterol and LDL cholesterol levels (p=0.006, p=0.002).

Statins are 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors and are antihyperlipidemic agents widely prescribed worldwide to lower cholesterol. Statins are also known to have antibacterial effects against pneumococci and *S. aureus*, and simvastatin and atorvastatin are the drugs with the most potential as antibiotics. Statins have been thought to block antibiotic resistance by exerting a synergistic effect with existing antibiotics, attenuating virulence factors, strengthening human immunity, or assisting wound healing. However, their widespread use for cardiovascular protection has instead created selective pressure for resistance. Ironically, it also has the potential to promote antibiotic resistance. Current evidence better supports blocking potential antimicrobial resistance, but a role in promoting antibiotic resistance cannot be ruled out. At low antibiotic concentrations (up to several hundred times the MIC), the growth rate of susceptible bacteria is slightly reduced, allowing the growth of multiple new resistant mutant strains and the proliferation of antibiotic-resistant bacteria. Because the maximum plasma concentration that can be achieved at the dose of statins used to treat hyperlipidemia is hundreds to thousands of times lower than the MIC, statins are unlikely to exert significant systemic antibacterial effects. However, a greater concern is that patients with bacteremia may be exposed to low systemic antimicrobial concentrations, which may result in selective pressure for resistance. When bacteria are exposed to antibacterial drugs for a long period of time, the death of susceptible bacteria can be accelerated and resistant bacteria can become dominant. Elucidating the mechanism of antibacterial activity of statins may perhaps clarify their role in antibiotic resistance [10,11]. In addition, statin use may explain the higher proportions of patients with normal total and LDL cholesterol levels in the FR CoNS group than in the non-FR CoNS group. However, due to the small number of participants, the present study could not confirm the relationship between the growth of CoNS resistance to fluoroquinolones and statin use.

Factors known to contribute to the acquisition of fluoroquinolone resistance in *S. aureus* and CoNS include recent ophthalmic surgery before cataract surgery, recent hospitalization, use of fluoroquinolone eye drops within 3 months, treatment history of intravitreal injection, use of systemic antibacterial agents, use of eye drops containing preservatives, use of fluoroquinolone eye drops for 3 months to 1 year, and use of other antibacterial eye drops within 1 year [8]. However, the present study did not identify these factors as related to the acquisition of fluoroquinolone resistance, which was likely due not only to the small number of study

subjects but also to the limitations of a retrospective study based only on medical records from a single institution.

This study has several limitations. Compared to previous studies, statistical significance could not be confirmed for some factors owing to the small number of study subjects. Because this study used a traditional culture method without polymerase chain reaction and genome sequencing, the sensitivity to accurately identify the actual flora was low [29,30]. However, using polymerase chain reaction and genome sequencing, it is difficult to determine whether a bacterium is related to a clinical ophthalmic disease, despite the superior sensitivity of these methods compared to traditional culture methods [22]. In addition, the antimicrobial susceptibility information based on the CLSI criteria used in this study may differ from drug concentrations that can be reached after the administration of ocular antimicrobial agents in local ocular structures, as these are determined based on expected drug concentrations achieved in the serum, plasma, and cerebrospinal fluid [2]. Therefore, it may be difficult to directly apply this sensitivity information to the conjunctival flora of the eye tissue [4,28,31]. Antimicrobial resistance to fluoroquinolones has gradually increased since the 1990s. Although resistance to old-generation fluoroquinolones (ciprofloxacin, ofloxacin, and levofloxacin) exceeds that of new-generation fluoroquinolones (gatifloxacin and moxifloxacin), the resistance to newer fluoroquinolones is also increasing [2]. However, among the antibacterial eye drops mainly used in clinical practice, this study did not test sensitivity to 4th-generation fluoroquinolones (gatifloxacin and moxifloxacin).

In conclusion, CoNS, including *S. epidermidis*, accounted for 42.5% of the conjunctival flora of patients undergoing cataract surgery and intravitreal injection, with sensitivity to quinolone antibacterial agents ranging from 58.5% to 69.8%. A history of statin use was a significant risk factor for the development of resistance to fluoroquinolones. Additional large-scale studies are necessary to confirm the relationship between statins and fluoroquinolone resistance.

Article information

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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Author contributions

Conceptualization: YRH, SJL. Data curation: YRH, SJL. Formal analysis: CEO. Investigation: YRH, SJL, CEO. Methodology: YRH, SJL. Supervision: SJL. Validation: YRH, SJL. Writing – original draft: YRH. Writing – review & editing: YRH, SJL.

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