Conjunctival sac bacterial flora isolated prior to cataract surgery

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Objective: To determine the trends of conjunctival sac bacterial flora isolated from patients prior to cataract surgery.

Subjects and methods: The study comprised 579 patients (579 eyes) who underwent cataract surgery. Specimens were collected by lightly rubbing the inferior palpebral conjunctival sac with a sterile cotton swab 2 weeks before surgery, and then cultured for isolation of bacteria and antimicrobial sensitivity testing. The bacterial isolates and percentage of drug-resistant isolates were compared among age groups and according to whether or not patients had diabetes mellitus, hyperlipidemia, dialysis therapy, oral steroid use, dry eye syndrome, or allergic conjunctivitis.

Results: The bacterial isolation rate was 39.2%. There were 191 strains of Gram-positive cocci, accounting for the majority of all isolates (67.0%), among which methicillin-sensitive coagulase-negative staphylococci was the most frequent (127 strains, 44.5%), followed by methicillin-resistant coagulase-negative staphylococci (37 strains, 12.7%). All 76 Gram-positive bacillary isolates (26.7%) were from the genus Corynebacterium. Among the 16 Gram-negative bacillary isolates (5.9%), the most frequent was Escherichia coli (1.0%). The bacterial isolation rate was higher in patients 60 years old, and was lower in patients with dry eye syndrome, patients under topical treatment for other ocular disorders, and patients with hyperlipidemia. There was no significant difference in bacterial isolation rate with respect to the presence/absence of diabetes mellitus, steroid therapy, dialysis, or a history of allergic conjunctivitis.

Methicillin-resistant coagulase-negative staphylococci showed a significantly higher detection rate in diabetic patients than nondiabetic patients (20.3% versus 7.0%, P < 0.05). The percentage of all isolates resistant to levofloxacin, cefmenoxime, and tobramycin was 14.0%, 15.2%, and 17.9%, respectively, with no significant differences among these drugs.

Conclusion: The high bacterial isolation rate in patients 60 years old and the high methicillin-resistant coagulase-negative staphylococci isolation rate in patients with diabetes are important to consider for prevention of perioperative infections.

Keywords: endophthalmitis, cataract surgery, conjunctival sac, bacterial flora, diabetes mellitus

Introduction

Age-related cataract is responsible for 48% of world blindness, which represents about 18 million people. Cataract surgery has become widespread in developed countries thanks to advances in procedures and instruments, and almost all patients achieve recovery of visual acuity as a matter of course after treatment. Further, incidence of endophthalmitis after cataract surgery is decreasing. However, if postoperative endophthalmitis occurs, there is a high risk of loss of vision with
consequent adverse effects on the patient’s quality of life. At the same time, the responsibility for endophthalmitis is a mental burden for the surgeon.

It has been reported that indigenous bacteria in the conjunctival sac influence the bacterial pathogens causing endophthalmitis after cataract surgery. It is likely that conjunctival sac bacterial flora would be altered by factors that affect a patient’s general condition such as diabetes mellitus, corticosteroid use, and aging. Accordingly, this study was conducted to compare isolates from the conjunctival sac bacterial flora prior to cataract surgery in order to identify differences of isolates and resistance to antimicrobial agents related to patient factors such as the presence/absence of diabetes mellitus, hyperlipidemia, oral steroid therapy, dry eye syndrome requiring topical medication, other ocular conditions except requiring topical antimicrobial agents, and allergic conjunctivitis.

**Subjects and methods**

The study population comprised 579 patients (579 eyes) who underwent cataract surgery in the Department of Ophthalmology of Saiseikai Kurihashi Hospital during a 3.5-year period from January 2004 to June 2007. The patients were enrolled in a consecutive manner. All patients provided informed consent, this study was conducted in accordance with the Declaration of Helsinki, and only one eye was investigated even in patients with cataracts affecting both eyes. There were 234 men (40.4%) and 345 women (59.6%) who ranged in age from 51 to 100 years (mean ± standard deviation: 71.7 ± 9.5 years).

Two weeks before cataract surgery, specimens for bacteriologic examination were collected from the conjunctival sac, without anesthesia, by lightly rubbing the inferior palpebral conjunctiva with a sterile cotton swab, and were transferred within 1 hour to the clinical laboratory of the hospital for plating on blood agar medium and chocolate agar medium. Cultures were incubated at 35°C for 24–48 hours. Neither anaerobic nor enrichment cultures were performed. Antimicrobial sensitivity testing of the bacterial isolates was carried out by the microbroth dilution technique in accordance with the Clinical and Laboratory Standards Institute (document M100-S17) using the disc diffusion method and a fully automated microbiology system (RAISUS; Nissui Pharmaceutical Co, Ltd, Tokyo, Japan).

The variables investigated were the conjunctival sac bacterial isolation rate, details of the bacterial isolates, and percentage of drug-resistant isolates, which were compared among age groups and according to the presence/absence of diabetes mellitus, hyperlipidemia, dialysis therapy, oral steroid use, usage of eye drops excluding antibacterial medicine, dry eye syndrome, or allergic conjunctivitis. Patients with dry eye syndrome were only enrolled in this study if they were receiving treatment with artificial tears or hyaluronic acid eye drops. Patients excluding dry eye syndrome were compared by the existence of usage of eye drops containing preservatives. Among patients with diabetes, the result was compared by the level of hemoglobin A1c.

Preoperative administration with levofloxacin (LVFX) eye drops for 3 days, which was evaluated in a multicenter study sponsored by the Japanese Association for Ocular Infection, was employed in this study routinely, and no oral antibacterial medicine was applied before cataract surgery. The patients were also treated routinely with faropenem sodium hydrate (Farom; Murom, Tokyo, Japan) at a dose of 600 mg daily for 4 days after cataract surgery.

Statistical analyses were performed using IBM SPSS for Windows (v 14.0; SPSS, Inc, Chicago, IL). The 2 × 2 Chi square test was employed for categorical comparison.

**Results**

None of the patients in this study contracted endophthalmitis after cataract surgery.

Bacteria were isolated from 227 (39.2%) of the 579 eyes studied. Of these 227 eyes, a single isolate was detected in 179 eyes (78.9%), while there were two isolates in 39 eyes (17.2%), three isolates in eight eyes (3.5%), and four isolates in one eye (0.4%).

In more detail, there were 191 strains of Gram-positive cocci, accounting for 67.0% of all isolates, as well as 127 strains (44.5%) of methicillin-sensitive coagulase-negative staphylococci, 37 strains (12.7%) of methicillin-resistant coagulase-negative staphylococci, eight strains (2.9%) of methicillin-sensitive *Staphylococcus aureus*, and three strains (1.0%) of methicillin-resistant *S. aureus* (Table 1). Among 76 Gram-positive bacilli isolates (26.7%), all were of the genus *Corynebacterium*. There was only one Gram-negative coccus isolated (0.4%), which was identified as *Moraxella catarrhalis*. There were 16 Gram-negative bacillary isolates (5.9%), including three *Escherichia coli* isolates (1.0%); two isolates (0.7%) each of *Pseudomonas aeruginosa*, *Acinetobacter* spp, and nonglucose-fermenting bacteria; and one isolate (0.4%) each of *Proteus vulgaris*, *Proteus mirabilis*, *Enterobacter aerogenes*, *Serratia marcescens*, *Klebsiella oxytoca*, and *Alcaligenes* spp.

The bacterial isolation rate was significantly lower for patients aged ≤60 years compared with patients 61–70 years,
The presence/absence of diabetic retinopathy and hemoglobin A1c significantly difference in bacterial isolation rate in relation to diabetics and nondiabetics (Table 3). There was also no bacterial isolation rate did not differ significantly between (142/304 eyes, 46.7%). The bacterial isolation rate was

71–80 years, and ≥81 years old (P < 0.001; Table 2). The bacterial isolation rate did not differ significantly between diabetics and nondiabetics (Table 3). There was also no significant difference in bacterial isolation rate in relation to presence/absence of diabetic retinopathy and hemoglobin A1c level (Tables 3 and 4). No statistically significant differences were noted in relation to the presence/absence of dialysis therapy, oral steroid use, or allergic conjunctivitis (Table 3).

In relation to whether the patients were using eye drops or not, the bacterial isolation rate was significantly lower (P < 0.001) for the group using eye drops (85/275 eyes, 30.9%) than for those without it (208/483, 43.1%). A significantly lower (P < 0.05) bacterial isolation rate was also noted for patients with hyperlipidemia (55/169, 32.5%) than for those without it (171/410, 42.0%).

For methicillin-resistant coagulase-negative staphylococci, the percentage of resistant organisms was significantly greater (P < 0.05) in diabetic patients (13 strains, 20.3%) than in nondiabetic patients (eight strains, 7.0%).

Of the 285 strains isolated, 40 strains (14.0%) were resistant to LVFX. For cefmenoxime, 39 (15.2%) out of 257 strains were resistant, while 42 (17.9%) out of 245 strains were resistant to tobramycin. The percentage of resistant organisms did not differ significantly among these antimicrobial agents. Resistance to all three of these drugs was demonstrated by six methicillin-resistant coagulase-negative staphylococci strains, two enterococcal strains, and one methicillin-resistant S. aureus (Figure 1).

**Discussion**

Endophthalmitis after cataract surgery is a severe complication that can occur no matter how strictly the sterility of the operative field is maintained and despite aseptic surgical manipulations/instruments. Risk factors in the surgical procedures and background of the patients are as previously

### Table 1 Bacterial isolates and rates

<table>
<thead>
<tr>
<th>Gram-positive cocci</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus epidermidis (MSCNS)</td>
<td>127</td>
<td>44.5%</td>
</tr>
<tr>
<td>Staphylococcus epidermidis (MRCNS)</td>
<td>37</td>
<td>12.7%</td>
</tr>
<tr>
<td>Staphylococcus aureus (MSSA)</td>
<td>8</td>
<td>2.9%</td>
</tr>
<tr>
<td>Staphylococcus aureus (MRSA)</td>
<td>3</td>
<td>1.0%</td>
</tr>
<tr>
<td>Enterococcus spp</td>
<td>6</td>
<td>2.0%</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>2</td>
<td>0.7%</td>
</tr>
<tr>
<td>α-Streptococcus</td>
<td>6</td>
<td>2.0%</td>
</tr>
<tr>
<td>Streptococcus equinus</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Streptococcus equinus</td>
<td>1</td>
<td>0.4%</td>
</tr>
<tr>
<td>Streptococcus pneumonia (PSSP)</td>
<td>1</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

**Gram-positive bacilli** | 76 | 26.7%

| Corynebacterium spp | 76 | 26.7%

**Gram-negative cocci** | 1 | 0.4%

| Moraxella catarrhalis | 1 | 0.4%

**Gram-negative bacilli** | 16 | 5.9%

| Escherichia coli | 3 | 1.0%
| Pseudomonas aeruginosa | 2 | 0.7%
| Acinetobacter spp | 2 | 0.7%
| Nonglucose-fermenting bacteria | 2 | 0.7%
| Proteus vulgaris | 1 | 0.4%
| Proteus mirabilis | 1 | 0.4%
| Enterobacter aerogenes | 1 | 0.4%
| Serratia marcescens | 1 | 0.4%
| Klebsiella oxytoca | 1 | 0.4%
| Alcaligenes spp | 1 | 0.4%
| Haemophilus influenzae | 1 | 0.4%

### Table 2 Bacterial detection rate dependent on age

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Culture positive/total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤60</td>
<td>12/73 (16.4%)</td>
</tr>
<tr>
<td>61–70</td>
<td>72/177 (40.7%)</td>
</tr>
<tr>
<td>71–80</td>
<td>91/228 (39.9%)</td>
</tr>
<tr>
<td>≥81</td>
<td>52/101 (51.5%)</td>
</tr>
</tbody>
</table>

Note: 2×2 Chi square test.

### Table 3 Bacterial detection rate dependent on background

<table>
<thead>
<tr>
<th>Culture positive/total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
</tr>
<tr>
<td>Dialysis</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Steroid therapy</td>
</tr>
<tr>
<td>Dry eye syndrome</td>
</tr>
<tr>
<td>Usage of any eye drops</td>
</tr>
<tr>
<td>Allergic conjunctivitis</td>
</tr>
</tbody>
</table>

**Notes:** *P < 0.05; **P < 0.001, 2 × 2 Chi square test.

### Table 4 Bacterial detection rate dependent on hemoglobin A1c level

<table>
<thead>
<tr>
<th>Hemoglobin A1c level</th>
<th>Culture positive/total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8</td>
<td>38/100 (38.0%)</td>
</tr>
<tr>
<td>≥7</td>
<td>33/97 (34.0%)</td>
</tr>
<tr>
<td>≥6</td>
<td>50/139 (36.0%)</td>
</tr>
<tr>
<td>&lt;6</td>
<td>21/58 (36.2%)</td>
</tr>
<tr>
<td>&lt;5</td>
<td>62/170 (36.5%)</td>
</tr>
<tr>
<td>&lt;4</td>
<td>9/27 (33.3%)</td>
</tr>
<tr>
<td>&lt;3</td>
<td>67/181 (37.0%)</td>
</tr>
<tr>
<td>&lt;2</td>
<td>4/16 (25.0%)</td>
</tr>
</tbody>
</table>
Infection.12 The pathogens causing endophthalmitis are
study sponsored by the Japanese Association for Ocular
L VFX eye drops, which was evaluated in a multicenter
Ciulla et al15 and 3-day preoperative sterilization with
postcataract surgery endophthalmitis include preoperative
importance is attached to preventive measures for this
strains, and one methicillin-resistant
retinopathy, and cataract surgery combined with another
capsular rupture, a prior diagnosis of proliferative diabetic
reported, for example, in men, aged patients, and those with
old age was the only factor
in bacterial detection rate among diabetic patients in relation
to hemoglobin A1c, diabetic retinopathy, or glycosuria. The
reason for this is unclear, but it is possible that these factors
have little influence on the microbial flora in the conjunctival
sac. Microorganisms isolated from the eye, especially from
parts of the ocular surface such as the conjunctiva and cornea,
are in direct contact with the external environment and are
thought to originate from the palpebral skin influenced by
the general condition as well as the meibomian glands and
oral indigenous flora. Therefore, these multiple origins could
be a reason.

It was found that hyperlipidemia, dry eye syndrome,
and use of other topical ocular medication were associated
with significantly lower bacterial detection rates. It has been
reported that hypercholesterolemia leads to changes in the
composition of nasolacrimal duct fluid, so it is possible that
such changes may affect the conjunctival sac and its bacterial
flora, which are located upstream of the nasolacrimal duct,16
although the precise mechanism is yet to be clarified.
Regarding dry eye syndrome, only patients who were using
artificial tears or hyaluronic acid eye drops were enrolled,
and they showed a lower bacterial detection rate as did the
patients using other types of eye drops. Honda et al compared
bacterial isolation rates from the conjunctival sac between
patients receiving topical medication for glaucoma and
those not receiving such medication.10 Bacterial detection
rate was 40.3% in the topical medication group, which
was significantly lower than the rate of 67.8% in the group
without topical medication (P < 0.05, Fisher’s test). These
results were similar to the present findings and a washout
effect of eye drops may be involved. On the other hand, Hori
et al reported that the percentage of LVFX-resistant isolates
obtained from the conjunctival sac was higher in patients
who had dry eye syndrome compared with healthy subjects.17
They stated that it remains unclear whether fragility of the
ocular surface in patients with this syndrome or bacterial
contamination of the eyelids and fingers due to application
of topical medication is responsible for this finding. Although
no such difference in the percentage of LVFX-resistant
microorganisms was obtained in the present study (data not
shown), this possibility should be kept in mind.

It has been documented that bacteria isolated from
the conjunctival sac in healthy persons are usually
nonpathogenic, with S. epidermidis being found frequently,
which is part of the indigenous skin flora.18 Coagulase-
negative staphylococci was the most frequent isolate in the

**Figure 1** Resistance to levofloxacin, cefmenoxime, and tobramycin was shown in six methicillin-resistant coagulase-negative staphyloccoci strains, two enterococcal strains, and one methicillin-resistant Staphylococcus aureus strain.

**Abbreviations:** CNS, coagulase-negative staphyloccoci; MRCNS, methicillin-resistant coagulase-negative staphyloccoci; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive Staphylococcus aureus; NFB, nonglucose-fermenting bacteria.

reported, for example, in men, aged patients, and those with
capsular rupture, a prior diagnosis of proliferative diabetic
retinopathy, and cataract surgery combined with another
intraocular surgical procedure on the same day.13,14 Great
importance is attached to preventive measures for this
complication. Evidence-based prophylactic measures for
postcataract surgery endophthalmitis include preoperative
instillation of povidone-iodine eye drops as described by
Ciulla et al15 and 3-day preoperative sterilization with
LVFX eye drops, which was evaluated in a multicenter
study sponsored by the Japanese Association for Ocular
Infection.13 The pathogens causing endophthalmitis are
mainly indigenous bacteria from sites on the ocular surface
such as the conjunctival sac, eyelids, and meibomian glands.
These microorganisms can be diminished by disinfection,
but it is impossible to completely eradicate them even by
the strongest disinfection protocol. Microorganisms that
are resistant to disinfectants or antimicrobial agents may
also be encountered. Although the evidence-based measures
that have been demonstrated to be effective for prevention
of endophthalmitis after cataract surgery are favorably
regarded, it would seem likely that uniform employment of
such measures could entail some risk. Therefore, the present
study was undertaken to identify significant risk factors.

It is generally agreed that administration of corticosteroids,
diabetes mellitus, and old age, which reduce immunity,
are associated with a higher bacterial detection rate.6–8 In
the present series, however, old age was the only factor
associated with a statistically higher bacterial detection
rate and no significant difference in bacterial detection was
noted in relation to the presence/absence of steroid therapy
or diabetes. Furthermore, there was no significant difference
in bacterial detection rate among diabetic patients in relation
to hemoglobin A1c, diabetic retinopathy, or glycosuria. The
reason for this is unclear, but it is possible that these factors
have little influence on the microbial flora in the conjunctival
sac.
present investigation as well. The isolation rate of methicillin-resistant coagulase-negative staphylococci among coagulase-negative staphylococci was significantly higher in patients with diabetes mellitus than in nondiabetic patients. Possible reasons for this include a compromised immune status due to diabetes, diabetic infections, use of antimicrobial drugs, and opportunistic infections. This also points to the importance of maintaining caution about bacterial drug resistance even if microorganisms are not virulent. Increased drug resistance rates have been pointed out for *Corynebacterium* spp. 19

There is some apprehension regarding an increase of microbial drug resistance due to widespread use of LVFX eye drops. The drug resistance rate increases progressively along with increased use of such eye drops. It is recommended in Japan to administer LVFX eye drops from 3 days before cataract surgery for prevention of postoperative endophthalmitis. 18 In the present study, this protocol was followed in all patients, and no oral antibacterial medicine was administered before cataract surgery.

However, indiscriminate use of LVFX could not only lead to masking of resistant microorganisms but could also result in the potential risk of causing an increase in drug resistance. Therefore, attention should be paid to the possible presence of resistant microorganisms especially in elderly patients and patients with dry eye syndrome like those with higher bacterial isolation rates in this study. The same caution should be exercised for diabetic patients since multidrug-resistant isolates with resistance to LVFX, cefmenoxime, and tobramycin were more frequent among diabetics in the present study.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**


