

Methicillin-Resistant *Staphylococcus aureus* and Methicillin-Resistant Coagulase-Negative Staphylococci From Conjunctivas of Preoperative Patients

Tsuyoshi Kato*[†] and Seiji Hayasaka[†]

*Division of Ophthalmology, Asahi General Hospital, Toyama, Japan; and [†]Department of Ophthalmology, Toyama Medical and Pharmaceutical University, Toyama, Japan

Abstract: To evaluate the incidence and characteristics of carriers of conjunctival methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase-negative Staphylococci (MRCNS) among preoperative patients at an eye clinic, bacterial growth was studied in 978 conjunctival specimens of 628 preoperative patients without signs of ocular infection. Specimens were evaluated for growth of bacteria on nutrient agar plate, blood agar plate, or chocolate agar plate for 2 days at 37°C. Methicillin resistance was confirmed by disk diffusion and agar screening methods. Susceptibilities of the bacterial strain to ampicillin (ABPC), cefazolin (CEZ), minocycline (MINO), gentamicin (GM), erythromycin (EM), vancomycin (VCM), and ofloxacin (OFLX) were determined by the disk diffusion method. Of the 628 patients (978 eyes), 352 patients (580 eyes) had positive bacterial growth. Among them, 8 (13 eyes) had MRSA growth and 2 (4 eyes) had MRCNS growth. The rate of nasolacrimal duct obstruction was significantly higher in eyes with positive bacterial growth than in eyes with negative growth. Of the 10 patients (17 eyes) with MRSA or MRCNS growth, 8 were older than 80 years, 5 had the same bacterial strains in the anterior nares and throat, 6 had nasolacrimal duct obstruction, 3 had dry eye, and 9 had been recently hospitalized. All 10 bacterial strains were resistant to ABPC, CEZ, and EM, but were sensitive to MINO and OFLX. Five strains were resistant and 5 were sensitive to GM. Two strains examined were sensitive to VCM. After topical antibiotic use for 0.5 to 6 months, the bacterial strains were eliminated. Two of the 17 eyes with MRSA or MRCNS growth did not undergo surgery. No postoperative endophthalmitis developed in 976 of the 978 eyes. Ophthalmologists should be aware that about 50% of preoperative patients without signs of ocular infection may have bacterial growth on the conjunctiva, and that elderly patients with nasolacrimal duct obstruction, dry eye, and recent hospital stays may be carriers of MRSA or MRCNS. **Jpn J Ophthalmol 1998;42:461-465** © 1998 Japanese Ophthalmological Society

Key Words: Carriers, conjunctiva, methicillin-resistant coagulase-negative Staphylococci, methicillin-resistant *Staphylococcus aureus*, preoperative patients, postoperative endophthalmitis.

Introduction

Postoperative endophthalmitis may be caused by *Staphylococcus aureus* and *Staphylococcus epidermidis*.¹⁻⁸ In particular, methicillin-resistant strains that are resistant to multiple antibiotics have increased

worldwide and are recognized as corneal and intraocular pathogens.^{2,9-11} *S. epidermidis* is the predominant subgroup of coagulase-negative staphylococci. To avoid an outbreak of infection in a hospital ward and to prevent postoperative endophthalmitis caused by methicillin-resistant strains, we examined the incidence and characteristics of carriers of methicillin-resistant *S. aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCNS) grown from the conjunctival specimens of preoperative patients without signs of ocular infection.

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Address correspondence and reprint requests to: Tsuyoshi KATO, MD, Department of Ophthalmology, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-0194, Japan

Table 1. Preoperative Patients Examined for Bacteria

	Patients (n = 628)	Eyes (n = 978)
Age (years)		
Mean	70.2	
Range	4-94	
Sex		
Men	257	
Women	371	
Planned surgery		
Cataract	502	816
Glaucoma	44	70
Retina-vitreous	15	17
Strabismus	18	18
Pterygium	30	32
Eyelid	11	16
Others	8	9

Subjects and Methods

We examined 978 eyes of 628 preoperative patients (257 men and 371 women) who were seen in the outpatient eye clinic at Asahi General Hospital, a 200-bed community hospital between April 1994 and March 1997. The mean age was 70.2 years (range: 4-94 years). Most of the patients were scheduled for cataract surgery (Table 1). Included were patients with nasolacrimal duct obstruction who had no pus, and those with dry eye who had decreased lacrimation by the Schirmer test, but had no staining by rose bengal and fluorescein tests. Excluded were those with signs of ocular infection, such as blepharitis, conjunctivitis, keratitis, and dacryocystitis. Individuals with malignancy, severe diabetes mellitus, or infectious disease in other organs were also excluded.

For bacteriologic study, a sterile dry swab (Culturette ez, Becton Dickinson, Cockeysville, MD, USA) was applied to the inferior conjunctival fornix

of one eye. No topical anesthetics were instilled. Each swab was transported to the bacteriology laboratory within 30 minutes and inoculated into growth media. Specimens were evaluated for growth of bacteria on nutrient agar plate, blood agar plate, or chocolate agar plate for 2 days at 37°C. If staphylococci grew, *S. aureus* was differentiated from coagulase-negative staphylococci strains by coagulase production. The disk diffusion and agar screening methods were used to detect methicillin resistance.¹² In the disk diffusion method, resistance was confirmed by distribution of bacterial growth inhibitory zone diameters against ceftizoxime (CZX) and methicillin (DMPPC) by Showa disk¹³⁻¹⁵ (Showa Pharmaceutical, Tokyo) for 18 hours at 35°C. In the agar screening method, methicillin resistance of isolates was defined as growth on modified Mueller-Hinton agar (Kyokuto Pharmaceutical, Tokyo) supplemented with 4% sodium chloride, 4 µg/mL oxacillin, and 12.5 µg/mL CZX after incubation for 40 hours at 35°C. Susceptibilities of the strain to ampicillin (ABPC), cefazolin (CEZ), minocycline (MINO), gentamicin (GM), erythromycin (EM), vancomycin (VCM), and ofloxacin (OFLX) were determined by the disk diffusion method using the Showa disk.^{16,17}

Nasolacrimal duct patency was tested by lacrimal sac irrigation with 0.9% NaCl aqueous solution.

The results were analyzed by the chi-square test. A probability of less than 0.01 was considered statistically significant.

Results

Of the 628 preoperative patients (978 eyes) whose conjunctival specimens were examined, 352 patients (580 eyes) had positive bacterial growth (Table 2). Of the 28 patients (47 eyes) with *S. aureus* growth in conjunctival specimens, 8 patients (13 eyes) had

Table 2. Bacterial Culture Grown From Conjunctival Sacs of Preoperative Patients

Bacterial Culture	Number of Patients (n = 628)	Number of Eyes (n = 978)
Positive	352 (56.1%)	580 (59.3%)
<i>Staphylococcus aureus</i>	28	47
MRSA	8	13
Other than MRSA	20	34
Coagulase-negative staphylococci	149	251
MRCNS	2	4
Other than MRCNS	147	247
Negative	276 (43.9%)	398 (40.7%)

MRSA: Methicillin-resistant *S. aureus*, MRCNS: methicillin-resistant coagulase-negative staphylococci.

Table 3. Bacterial Culture Grown From Conjunctival Sac and Nasolacrimal Duct Patency

Bacterial Culture	Nasolacrimal Duct	
	Patent	Obstructed
Positive (<i>n</i> = 580)		
MRSA or MRCNS (<i>n</i> = 17)	8	9 (52.9%)
Other than MRSA or MRCNS (<i>n</i> = 563)	504	59 (10.5%)*
Negative (<i>n</i> = 398)	379	19 (4.8%)*

MRCNS: Methicillin-resistant coagulase-negative staphylococci, MRSA: methicillin-resistant *Staphylococcus aureus*.
* *P* < 0.01.

MRSA growth. Of the 149 patients (251 eyes) with coagulase-negative staphylococci growth in conjunctival specimens, 2 patients (4 eyes) had MRCNS growth.

The results of bacterial culture from the conjunctival sac and nasolacrimal duct patency are shown in Table 3. Of the 17 eyes with MRSA or MRCNS growth, 9 (52.9%) had obstructed nasolacrimal duct. Of the 563 eyes with growth other than MRSA or MRCNS, 59 (10.5%) had an obstructed duct. Of the 398 eyes with negative bacterial growth, 19 (4.8%) had an obstructed nasolacrimal duct. The rate of nasolacrimal duct obstruction was significantly higher in eyes with positive bacterial growth than in eyes with negative growth.

Of the 8 patients with MRSA growth in the conjunctiva, 4 had the same bacteria growing in the anterior nares and throat (Table 4). Of the 2 patients with MRCNS growth in the conjunctiva, 1 had the same bacteria growing in the anterior nares and

throat. Of the 10 patients with methicillin-resistant strain growth, 8 were older than 80 years, 6 had nasolacrimal duct obstruction, and 3 had dry eye. Of these 10 patients, 9 had been recently hospitalized, and 1 had diabetes mellitus.

Antibiotic susceptibilities were studied in 10 methicillin-resistant strains (Table 5). All 10 strains were resistant to ABPC, CEZ, and EM, but were sensitive to MINO and OFLX. Five strains were resistant and 5 were sensitive to GM. Two strains examined were sensitive to VCM.

Topical antibiotics including 1.0% MINO, 0.3% OFLX, 0.3% GM, and 0.5% VCM were used to treat these patients (Table 6). Topical instillation and lacrimal sac irrigation with sensitive antibiotics were performed to eliminate the methicillin-resistant strains. Patients with nasolacrimal duct obstruction needed a 1- to 6-month course of antibiotics. The methicillin-resistant strains were eliminated within 1 month in patients without nasolacrimal duct obstruction.

Patients with methicillin-resistant strains in the anterior nares and throat gargled daily with 0.5% Povidone-iodine, and 10% Povidone-iodine ointment was applied to their noses. No regrowth of the strain in the anterior nares and throat was noted after 3 months of treatment.

A total of 398 eyes with negative bacterial growth underwent the planned surgery. A total of 563 eyes with positive bacterial growth other than MRSA and MRCNS were treated with topical instillation of broad-spectrum antibiotics. Of the 17 eyes with MRSA or MRCNS growth, 15 eyes underwent the planned surgery after two or more subsequent tests

Table 4. Patients With Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Methicillin-Resistant Coagulase-Negative Staphylococci (MRCNS) Growth

Patient No.	Age (years)	Sex	Planned Surgery	Conjunctival Culture	Anterior Nares and Throat Culture	Other Eye Disease	Systemic Disease	Recent Hospitalization	Recent Use of Antibiotic
1	70	F	Cataract	MRSA	—	NLDO, DE	Bone Fracture	+	—
2	81	F	Cataract	MRSA	—	NLDO	HT	+	—
3	93	F	Cataract	MRSA	MRSA	NLDO	HT	+	+
4	82	F	Cataract	MRSA	MRSA	—	HT	+	—
5	84	F	Cataract	MRSA	—	NLDO	Hepatitis	—	—
6	83	F	Cataract	MRSA	MRSA	DE	HT	+	—
7	82	M	Cataract	MRSA	—	—	Ileus	+	—
8	86	M	Cataract	MRSA	MRSA	DE	Tbc	+	+
9	73	M	Cataract	MRCNS	—	NLDO	DM	—	—
10	81	M	Cataract	MRCNS	MRCNS	NLDO	HT	+	—

DE: Dry eye, DM: diabetes mellitus, HT: systemic hypertension, NLDO: nasolacrimal duct obstruction, Tbc: lung tuberculosis, —: negative or absent, +: present.

Table 5. Antibiotic Susceptibility

Patient No.	Conjunctival Culture	Antibiotic						
		ABPC	CEZ	MINO	GM	EM	VCM	OFLX
1	MRSA	—	—	3+	3+	—		2+
2	MRSA	—	—	2+	—	—		2+
3	MRSA	—	—	3+	3+	—		1+
4	MRSA	—	—	2+	—	—	3+	1+
5	MRSA	—	—	2+	—	—		3+
6	MRSA	—	—	3+	1+	—		2+
7	MRSA	—	—	2+	—	—		1+
8	MRSA	—	—	2+	2+	—	3+	1+
9	MRCNS	—	—	3+	3+	—		3+
10	MRCNS	—	—	2+	—	—		2+

Susceptibility was determined by disk diffusion methods using Showa disk.

ABPC: ampicillin, CEZ: cefazolin, EM: erythromycin, GM: gentamicin, MINO: minocycline, OFLX: ofloxacin, VCM: vancomycin.

showing negative growth. Two patients (2 eyes) did not undergo surgery because their systemic condition deteriorated. No postoperative endophthalmitis developed in 976 of the 978 eyes.

Discussion

Bacterial endophthalmitis can devastate the eye unless treated promptly with sensitive antibiotics. To reduce the incidence of postoperative endophthalmitis, the use of preoperative or intraoperative antibiotics is generally accepted.¹⁸ Yasumoto et al¹⁹ reported that of 200 elderly subjects without ocular infection, 116 (58%) had positive bacterial growth on the conjunctiva. They further noted that of 39 eyes with growth of *S. aureus*, 11 (28.2%) had MRSA; and of 78 eyes with growth of *S. epidermidis*, 7 (8.9%) had methicillin-resistant *S. epidermidis*

(MRSE). Ugomori et al²⁰ showed that of 52 subjects with clinically normal conjunctiva, 16 (30.8%) had positive bacterial growth. Asano et al²¹ reported that the percentage of MRSA to the total number of *S. aureus* strains each year was 15.2% in 1989, 17.4% in 1990, and 25.0% in 1991; and the percentage of MRSE to the total number of *S. epidermidis* strains was 0.5% in 1989, 2.3% in 1990, and 2.4% in 1991. Ooishi²² showed that about 20% of *S. aureus* isolated from ocular infections was MRSA. In the present study, 352 (56%) of the 628 preoperative patients had bacterial growth on the conjunctiva; of 28 patients with growth of *S. aureus*, 8 (28.6%) had MRSA growth; and of 149 patients with growth of coagulase-negative staphylococci, 2 (1.3%) had MRCNS. Ophthalmologists should be aware that about one half of preoperative patients without signs of ocular infection have bacterial growth as normal bacterial flora in the conjunctiva.

Methicillin-resistant *S. aureus* and MRCNS are intraocular pathogens.² Methicillin-resistant *S. aureus* colonization precedes infection, and the anterior nares is a major reservoir.^{23,24} Muder et al²³ reported that 73% of all MRSA infections occurred among MRSA carriers. If MRSA carriers are admitted for ocular surgery, an outbreak of MRSA in a ward and endophthalmitis may ensue. To avoid these problems, preoperative patients should be examined bacteriologically before admission. We report here the incidence and characteristics of carriers with MRSA and MRCNS among preoperative patients. Increased rates of staphylococcal carriage have been reported in hemodialysis patients, intravenous drug abusers, patients with dermatologic disease, and individuals with insulin-dependent diabetes mellitus.²⁴ In the present study, elderly patients with nasolacrimal

Table 6. Topical Antibiotic

Patient No.	Conjunctival Culture	Antibiotic Used Topically	Duration (month)
1	MRSA	MINO, GM	1.0
2	MRSA	MINO, OFLX	4.0
3	MRSA	MINO, GM	3.0
4	MRSA	VCM	0.7
5	MRSA	MINO, OFLX	6.0
6	MRSA	MINO	0.5
7	MRSA	MINO	0.7
8	MRSA	VCM	0.7
9	MRCNS	MINO, GM	1.0
10	MRCNS	MINO, OFLX	2.0

GM: Gentamicin, MINO: minocycline, MRCNS: methicillin-resistant coagulase-negative staphylococci, MRSA: methicillin-resistant *Staphylococcus aureus*, OFLX: ofloxacin, VCM: vancomycin.

MINO, 1.0%; OFLX, 0.3%; GM, 0.3%; CM, 0.5%.

duct obstruction, dry eye, and recent hospitalization had MRSA or MRCNS growth on the conjunctiva. In particular, the eyes with nasolacrimal duct obstruction had a higher incidence of MRSA or MRCNS growth than the eyes without obstruction. Physicians should be aware that patients with such conditions may be at risk of MRSA and MRCNS infection.

Methicillin-resistant *S. aureus* is reportedly resistant to multiple antibiotics.¹⁹ Methicillin-resistant *S. aureus* and MRCNS grown from conjunctival specimens in the present study were resistant to ABPC, CEZ, and EM, but sensitive to MINO, OFLX, and VCM. To eliminate a bacterial strain, antibiotics should be used when in vitro susceptibility is demonstrated, and the anterior nares and throat should be treated. In the present study, MINO, OFLX, GM, and VCM were administered in 8, 3, 3, and 2 patients with MRSA or MRCNS growth, respectively. Single or combined topical instillation of these antibiotics were used. Patients with nasolacrimal duct obstruction needed 1 to 6 months of treatment. In those patients, lacrimal sac irrigation with the bacteria-sensitive antibiotic should be added, as in the present study.

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