• Clinical Research •

Ocular bacterial infections at a tertiary eye center in China: a 5-year review of pathogen distribution and antibiotic sensitivity

Wen Gao[1,3], *Tian Xia*[2], *Hua–Bo Chen*[2], *Xiao–Jing Pan*[2], *Yu–Sen Huang*[2], *Xin Wang*[2], *Yan–Ling Dong*[2], *Li–Xin Xie*[2]

[1]School of Medicine, Shandong University, Jinan 250012, Shandong Province, China

[2]State Key Laboratory Cultivation Base, Shandong Provincial Key Laboratory of Ophthalmology, Shandong Eye Institute, Shandong First Medical University & Shandong Academy of Medical Sciences, Qingdao 266071, Shandong Province, China

[3]Anhui No.2 Provincial People's Hospital, Hefei 230041, Anhui Province, China

Correspondence to: Li-Xin Xie. Shandong Eye Institute, 5 Yanerdao Road, Qingdao 266071, Shandong Province, China. lixin_xie@hotmail.com

Received: 2019-04-22 Accepted: 2019-11-20

Abstract

● **AIM:** To provide statistical evidence for the use of antibiotics in ophthalmology by assessing the distribution and antibiotic sensitivity of bacterial isolates from ocular specimens with suspected microbial infections.

● **METHODS:** This study applied a retrospective analysis of 3690 bacterial isolates from ocular specimens, which were obtained from the conjunctiva, cornea, aqueous humor, vitreous body, and other ocular sites of the patients at Shandong Eye Institute in northern China from January 2013 to December 2017. The parameters assessed mainly included the distribution of isolated bacteria and the results of susceptibility tests for antibiotics. In the analysis of antibiotic sensitivities, the bacteria were divided into four groups according to gram staining, and statistical methods were used to compare their antibiotic sensitivities.

● **RESULTS:** Among the 3690 isolated bacterial strains, *Staphylococcus epidermidis* (2007, 54.39%) accounted for the highest proportion. As for the total isolates, their sensitivity rate to gatifloxacin was up to 90.01%, with four types of gram-stained bacteria being all highly sensitive to it, but their sensitivity rate to levofloxacin was only 51.91%. The sensitivity rate of gram-negative bacilli (G-B) to levofloxacin was 83.66%, significantly higher than the other three types of gram-stained bacteria ($P<0.05$). Gram-positive cocci (G+C, 97.95%) and gram-positive bacilli (G+B, 97.54%) were more sensitive to vancomycin than gram-negative cocci (G-C, 70.59%) and G-B (68.57%; $P<0.05$). For fusidic acid, the sensitivity rates of G+C (89.83%) and G+B (73.37%) were significantly higher than that of G-B (29.83%; $P<0.05$). The gram-negative bacteria's sensitivity rate to cefuroxime was as low as 59.25%, but only G-B was less sensitive to cefuroxime (57.28%), while G-C was still highly sensitive (89.29%). The sensitivity rate of gram-positive bacteria to moxifloxacin was as high as 80.28%, but only G+C was highly sensitive to moxifloxacin (81.21%), while G+B was still less sensitive (32.00%).

● **CONCLUSION:** *Staphylococcus epidermidis* is the predominant isolate in all ocular specimens with bacteria. Gatifloxacin is more suitable for topical prophylactic use than levofloxacin in ophthalmology when necessary. Vancomycin and fusidic acid both have better effects on gram-positive bacteria than gram-negative bacteria. More accurate antibiotic sensitivity analysis results can be obtained when a more detailed bacterial classification and more appropriate statistical methods are performed.

● **KEYWORDS:** bacteria; ocular infections; pathogen; antibiotic sensitivity

DOI:10.18240/ijo.2020.01.08

Citation: Gao W, Xia T, Chen HB, Pan XJ, Huang YS, Wang X, Dong YL, Xie LX. Ocular bacterial infections at a tertiary eye center in China: a 5-year review of pathogen distribution and antibiotic sensitivity. *Int J Ophthalmol* 2020;13(1):54-60

INTRODUCTION

Ocular bacterial infections, which are associated with many risk factors including contact lenses, trauma, surgery, age, dry eye state, chronic nasolacrimal duct obstruction and previous ocular infections[1-2], are common in ophthalmology and vary from self-limiting to sight-threatening[3]. In the treatment of bacterial infections, pathogenic bacteria must be identified to ensure appropriate antimicrobial treatment. Broad-spectrum antibiotics have been commonly used to treat ocular infections, but pathogenic bacteria have shown a decreased sensitivity to widely used broad-spectrum antibiotics[4]. Therefore, we retrospectively assessed the bacterial isolates from ocular specimens with suspected microbial infections in northern China, hoping to find more sensitive antibiotics for different kinds of pathogens and help ophthalmologists make effective decisions in treating ocular bacterial infections.

Pathogen distribution and antibiotic sensitivity are constantly changing over time, so it is necessary to summarize regularly. There have been many studies on antibiotic sensitivity, which were conducted according to the classification of gram-positive and gram-negative bacteria or direct enumeration of the sensitivity rates. The question whether further classifying gram-stained bacteria and comparing the sensitivity rate by a statistical analysis can lead to more accurate results in antibiotic sensitivity studies has not attracted enough attention. We did get some notable results when a detailed classification of the tested bacterial isolates and a statistical analysis of the sensitivity rate were conducted in the current study.

SUBJECTS AND METHODS

Ethical Approval This retrospective study was approved by the Institutional Review Board of Shandong Eye Institute. Because of its retrospective nature, the requirement of informed consent was waived. All study conduct adhered to the tenets of the Declaration of Helsinki.

A retrospective review of the records of ocular isolates was conducted from January 2013 to December 2017 at Shandong Eye Institute, a major tertiary eye center in northern China. Clinical specimens were obtained from the conjunctiva, cornea, aqueous humor, vitreous body, eyelid margin, lacrimal passage, orbital contents, and other ocular sites of the patients in the Inpatient Wards and Outpatient Clinics. Cultures were performed using liquid (nutrient broth) and solid (chocolate agar, blood agar, and MacConkey agar) media. Bacterial isolates were identified, and dilution antimicrobial susceptibility testing was made and interpreted using automated microbiology systems, *i.e.*, VITEK II compact 30 before 2016 and Microscan Walkaway 96 after 2016, at the clinical microbiology laboratory of our institution according to the Clinical and Laboratory Standards Institute's Guidelines. The parameters assessed mainly included the distribution of isolated bacteria and the results of susceptibility tests for antibiotics. Only nonrepetitive isolates that underwent susceptibility testing were included in this study, and not all antimicrobials were tested against each isolate.

Most data were collected from the Laboratory Information System used by our clinical microbiology laboratory. Positive results were inputted into a Microsoft Excel spreadsheet file, which included patient name, patient ID number, patient age, collection date, ward type, collection site, organism isolated and minimum inhibitory concentration values against various antibiotics. For a small amount of uncertain data, such as "intraoperative specimen", the patients' medical records were checked to ensure the accurate collection site. We also obtained a five-year statistical report on the antibiotic sensitivity from the Laboratory Information System. In the analysis of antibiotic sensitivities, the bacteria were divided into four groups according to gram staining, and statistical methods were used to compare their antibiotic sensitivities.

Statistical Analysis Data were analyzed using the SPSS (version 19.0; SPSS, Inc., Chicago, IL, USA). The spearman correlation analysis was used to study the correlation between two variables. Comparisons of categorical variables were conducted using the Chi-square test. A P-value <0.05 at 95% CI was considered statistically significant.

RESULTS

A total of 11 530 ocular specimens with suspected microbial infections were submitted for microbiological evaluation. Among these specimens, 3625 (31.44%) showed bacterial growth, and 3690 bacterial strains were isolated. The positivity rates of the bacterial cultures from years 2013 to 2017 were 30.82%, 35.26%, 25.76%, 25.88%, and 36.56%, respectively. The change in the annual culture positivity rate was not statistically significant (P=0.747). Among the patients corresponding to positive bacterial culture specimens, 1513 were male and 2112 were female, with a male-female ratio of 1:1.40. The average age of the patients was 49.65±22.21 (range 4d-102y). Among the 3625 bacterial specimens, 2849 (78.59%) were obtained from the conjunctiva, 569 (15.70%) from the cornea, and 111 (3.06%) from the aqueous humor or vitreous body. The remaining 96 (2.65%) specimens were gathered from the lacrimal passage, eyelid margin, orbital contents and other ocular sites.

The distribution of bacterial genera isolated from ocular specimens with suspected microbial infections between 2013 and 2017 is presented in Table 1. A total of 3690 strains (32 genera and 140 species) were isolated. Among these strains, 3037 were gram-positive cocci (G+C; 82.30%), 407 were gram-negative bacilli (G-B; 11.03%), 221 were gram-positive bacilli (G+B; 5.99%), and 25 were gram-negative cocci (G-C; 0.68%). The most common bacterial genera were *Staphylococcus* (2706, 73.33%), *Corynebacterium* (161, 4.36%), *Neisseria* (19, 0.51%), and *Pseudomonas* (91, 2.47%) in G+C, G+B, G-C, and G-B, with *Staphylococcus epidermidis* (*S. epidermidis*; 2007, 54.39%), *Corynebacterium xerosis* (160, 4.34%), *Neisseria mucosa* (7, 0.19%), and *Pseudomonas aeruginosa* (77, 2.09%) being the main isolates, respectively. The predominant bacterial isolate was *S. epidermidis* (2007, 54.39%), followed by *Staphylococcus aureus* (260, 7.05%), *C. xerosis* (160, 4.34%), *Staphylococcus hominis* (125, 3.39%),

Table 1 Distribution of bacterial genera isolated from ocular specimens with suspected microbial infections between 2013 and 2017

Type of bacterial isolates	Number of isolates (*n*=3690)	%
G+C	3037	82.30
Staphylococcus	2706	73.33
Streptococcus	141	3.82
Enterococcus	88	2.38
Micrococcus	49	1.33
Kocuria	33	0.89
Granulicatella	11	0.30
Others	9	0.24
G-B	407	11.03
Pseudomonas	91	2.47
Serratia	37	1.00
Sphingomonas	33	0.89
Proteus	29	0.79
Escherichia	28	0.76
Klebsiella	27	0.73
Acinetobacter	25	0.68
Enterobacter	20	0.54
Morganella	19	0.51
Haemophilus	12	0.33
Others	86	2.33
G+B	221	5.99
Corynebacterium	161	4.36
Bacillus	33	0.89
Actinomyces	12	0.33
Rothia	7	0.19
Arcanobacterium	5	0.14
Others	3	0.08
G-C	25	0.68
Neisseria	19	0.51
Moraxella	6	0.16
Total	3690	100

Staphylococcus haemolyticus (115, 3.12%), and *P. aeruginosa* (77, 2.09%). Neither the annual changes in the proportions of the above major strains nor those in the proportions of G+C, G+B, G-C, and G-B were statistically significant ($P>0.05$). The distribution of bacteria isolated from different ocular sites between 2013 and 2017 is presented in Table 2. *S. epidermidis* was the predominant bacterial isolate in the conjunctiva, cornea, aqueous humor or vitreous body, and other ocular sites, respectively. In addition, *S. aureus* was one of the most common bacteria in the conjunctiva, cornea, as well as aqueous humor or vitreous body.

The sensitivities of the bacterial isolates to the antibiotics available in our institution are shown in Table 3. The sensitivity rate of the total isolates to gatifloxacin was up to 90.01%, with G+C, G+B, G-C, and G-B being all highly sensitive. For levofloxacin, the sensitivity rate of the total isolates was only 51.91%, whereas that of G-B was 83.66%, significantly higher than that of G+C, G+B, and G-C ($P<0.05$). For vancomycin, the sensitivity rate of gram-positive bacteria was as high as 97.92% (3112/3178), while that of gram-negative bacteria was only 68.97% (60/87). Moreover, the sensitivity rates of G+C and G+B to vancomycin were significantly higher than those of G-C and G-B ($P<0.05$). For fusidic acid, the sensitivity rate of gram-positive bacteria was as high as 88.91% (2702/3039),

Table 2 Distribution of bacteria isolated from different ocular sites between 2013 and 2017

Bacterial isolates from different ocular sites	Number of isolates (*n*=3690)	%
Conjunctiva	2892	78.37
Staphylococcus epidermidis	1661	45.01
Staphylococcus aureus	213	5.77
Corynebacterium xerose	130	3.52
Staphylococcus hominis	97	2.63
Staphylococcus haemolyticus	97	2.63
Staphylococcus lentus	57	1.54
Enterococcus faecalis	44	1.19
Streptococcus mitis	27	0.73
Pseudomonas aeruginosa	27	0.73
Others	539	14.61
Cornea	579	15.69
Staphylococcus epidermidis	256	6.94
Pseudomonas aeruginosa	39	1.06
Staphylococcus aureus	34	0.92
Corynebacterium xerose	24	0.65
Staphylococcus hominis	19	0.51
Staphylococcus haemolyticus	16	0.43
Micrococcus luteus	13	0.35
Streptococcus mitis	11	0.30
Others	167	4.53
Aqueous humor or vitreous body	118	3.20
Staphylococcus epidermidis	42	1.14
Staphylococcus aureus	9	0.24
Staphylococcus hominis	6	0.16
Bacillus subtilis	6	0.16
Pseudomonas aeruginosa	5	0.14
Bacillus cereus	5	0.14
Others	45	1.22
Other ocular sites	101	2.74
Staphylococcus epidermidis	47	1.27
Pseudomonas aeruginosa	6	0.16
Escherichia coli	4	0.11
Staphylococcus aureus	4	0.11
Others	40	1.08
Total	3690	100

"Other ocular sites" included lacrimal passage, eyelid margin, orbital contents and so on.

Table 3 Sensitivities of the antibiotics available in our institution %

Antibiotics	Total	G+C	G+B	G-C	G-B
Tigecycline	99.59 (1700/1707)	99.59 (1681/1688)	100.00 (11/11)	-	100.00 (8/8)
Vancomycin	97.15 (3172/3265)	97.95 (2914/2975)	97.54 (198/203)	70.59 (12/17)	68.57 (48/70)
Rifampicin	94.48 (2876/3044)	94.90 (2718/2864)	90.84 (119/131)	90.00 (9/10)	76.92 (30/39)
Gatifloxacin	90.01 (3044/3382)	92.69 (2548/2749)	91.12 (195/214)	81.48 (22/27)	71.17 (279/392)
Cefuroxime	89.28 (3058/3425)	94.35 (2603/2759)	87.74 (186/212)	89.29 (25/28)	57.28 (244/426)
Fusidic acid	85.40 (2766/3239)	89.83 (2578/2870)	73.37 (124/169)	52.63 (10/19)	29.83 (54/181)
Ceftazidime	81.99 (1498/1827)	84.41 (1056/1251)	69.62 (110/158)	90.91 (20/22)	78.79 (312/396)
Amikacin	81.61 (324/397)	5.00 (2/40)	100.00 (6/6)	100.00 (1/1)	90.00 (315/350)
Moxifloxacin	80.30 (2123/2644)	81.21 (2105/2592)	32.00 (16/50)	100.00 (1/1)	100.00 (1/1)
Ofloxacin	67.40 (2402/3564)	66.63 (1911/2868)	64.22 (149/232)	78.57 (22/28)	73.39 (320/436)
Gentamicin	66.59 (2455/3687)	65.96 (2004/3038)	64.95 (139/214)	56.52 (13/23)	72.57 (299/412)
Tobramycin	64.13 (2271/3541)	63.50 (1823/2871)	62.87 (149/237)	75.00 (21/28)	68.64 (278/405)
Levofloxacin	51.91 (1941/3739)	46.28 (1430/3090)	71.30 (154/216)	60.87 (14/23)	83.66 (343/410)
Ciprofloxacin	44.61 (1793/4019)	43.36 (1329/3065)	26.86 (137/510)	60.00 (15/25)	74.46 (312/419)

"-" means no antibiotic susceptibility testing was conducted.

Table 4 Sensitivity ranking results of the antibiotics

Stains	Sensitivity ranking ($P<0.05$)
Total	TGC>VAN>RIF>GAT, CXM>FDA>CAZ, AMK, MFX>OFX, GEN>TOB>LVX>CIP
G+C	TGC>VAN>RIF, CXM>GAT>FDA>CAZ>MFX>OFX, GEN>TOB>LVX>CIP
G+B	VAN>GAT, RIF, CXM>FDA, LVX, CAZ, GEN, OFX, TOB>MFX, CIP (FDA>TOB)
G-C	CAZ>LVX, CIP, GEN, FDA
G-B	AMK>LVX, CAZ, RIF, CIP, OFX, GEN, GAT, TOB, VAN, CXM>FDA (LVX>CIP>CXM)

Any sensitivity rate with a denominator number less than 15 was not included in this statistical analysis. TGC: Tigecycline; VAN: Vancomycin; RIF: Rifampicin; GAT: Gatifloxacin; CXM: Cefuroxime; FDA: Fusidic acid; CAZ: Ceftazidime; AMK: Amikacin; MFX: Moxifloxacin; OFX: Ofloxacin; GEN: Gentamicin; TOB: Tobramycin; LVX: Levofloxacin; CIP: Ciprofloxacin. "A>B, C" means the sensitivity of A was significantly higher than that of B and C ($P<0.05$), and no statistically significant difference was noted in the sensitivity of B and C ($P>0.05$).

whereas that of gram-negative bacteria was only 32.00% (64/200). In addition, the sensitivity rate of G+C to fusidic acid was significantly higher than that of G-C and G-B, and the sensitivity rate of G+B was significantly higher than that of G-B ($P<0.05$). For cefuroxime, the sensitivity rate of gram-negative bacteria was as low as 59.25% (269/454), but it was only G-B whose sensitivity rate was 57.28%, while the sensitivity rate of G-C was 89.29%, significantly higher than that of G-B ($P=0.001$). For moxifloxacin, the sensitivity rate of gram-positive bacteria was as high as 80.28% (2121/2642), but it was only G+C whose sensitivity rate was 81.21%, while the sensitivity rate of G+B was just 32.00%, significantly lower than that of G+C ($P=0.000$). The sensitivity ranking results of these antibiotics are shown in Table 4, and any sensitivity rate with a denominator number less than 15 was not included in this statistical analysis. Antibiotic sensitivities of fusidic acid and ciprofloxacin increased year by year ($Rs=0.900$, $P=0.037$), whereas the changes in other antibiotics were not statistically significant ($P>0.05$).

DISCUSSION

Ocular infections are potentially blinding diseases[5], and bacteria are the most frequently encountered pathogens affecting ocular structures. Bacteria can cause many types of ocular infections such as conjunctivitis, keratitis, blepharitis, orbital cellulitis, dacryocystitis and endophthalmitis[6]. In this retrospective study, 3690 bacterial strains from a tertiary eye center over a period of 5y were analyzed. From January 2013 to December 2017, the positivity rate of bacterial culture in ocular specimens with suspected microbial infections was 31.44%, similar to the result reported by Beijing Tongren Hospital, one of the major eye centers in northern China (29.0%)[7]. Such similarity of findings may be partially explained by the reason that the two hospitals are both in northern China.

In the present study, G+C (82.30%) were prominent in the total bacterial isolates, and *Staphylococcus* accounted for the highest proportion (73.33%). *S. epidermidis* (54.39%) was the predominant bacterial isolate in the conjunctiva,

Table 5 Antibiotic sensitivities form two different studies at our institute %

Parameters	IES	OBIS
Study time	2003-2010	2013-2017
Gentamicin susceptible	71.15 (74/104)	66.59 (2455/3687)
Tobramycin susceptible	77.22 (61/79)	64.13 (2271/3541)
Levofloxacin susceptible	81.82 (45/55)	51.91 (1941/3739)
Ciprofloxacin susceptible	69.52 (73/105)	44.61 (1793/4019)

IES: Infectious Endophthalmitis Study; OBIS: Ocular Bacterial Infections Study.

cornea, aqueous humor or vitreous body, and other ocular sites, respectively. This finding is similar to those obtained in Britain[8], America[9], Australia[10], and Chinese minorities[11]. *S. epidermidis* was considered to be the most common bacterial isolate in the normal conjunctival sac[12-13] and one of the main pathogens of bacterial conjunctivitis[14-15]; it was also reported to be the main cause of bacterial keratitis[16-17] and postoperative endophthalmitis[18-19]. In this study, the predominant bacterial isolates were *S. epidermidis* (2007, 54.39%), *S. aureus* (260, 7.05%), *C. xerosis* (160, 4.34%), *S. hominis* (125, 3.39%), *S. haemolyticus* (115, 3.12%), and *P. aeruginosa* (77, 2.09%), which was different from a report in northern Ethiopia[20], where *S. aureus* (40, 21.5%), *coagulase-negative staphylococci* (31, 16.7%), *P. aeruginosa* (21, 11.3%), and *E.coli* (15, 8%) were the most common isolates. Differences in the regions and environment may be the reason of the discrepancy[21].

The use of effective broad-spectrum antibiotics for treatment of ocular bacterial infections before the availability of results of pathogen identification and antibiotic susceptibility tests is advocated in many studies[5,22]. Empirical therapy relies on the susceptibility patterns of common bacteria isolated from eye specimens[23]. In the current study, the sensitivity rate of the total isolates to gatifloxacin was up to 90.01%, with G+C, G+B, G-C, and G-B being all highly sensitive to it, indicating that gatifloxacin is a broad-spectrum antibiotic with high sensitivity and is suitable for topical prophylactic use in ophthalmology. Levofloxacin has been the most frequently prescribed preoperative ophthalmic antibiotic for years, but our study showed that the sensitivity rate of the total isolates to it was low (51.91%), whereas that of G-B was high (83.66%). In an earlier study of 319 inpatients (319 eyes) diagnosed with infectious endophthalmitis at our institute[24], the sensitivity rates of bacteria to levofloxacin, tobramycin, gentamicin and ciprofloxacin were listed. Antibiotic sensitivities from two different studies at our institute are shown in Table 5. There was an obvious decline in the sensitivity of levofloxacin in the past few years. Meanwhile, Alabiad *et al*[25] argued that the resistance of fluoroquinolone including levofloxacin was common among all patient groups. According to the report by Huang *et al*[26] from our institution in 2009, G+C and G-B retained a high sensitivity to levofloxacin, but this current study showed that G+C were not as sensitive to levofloxacin (46.28%) as in the past (94.8%). Thus, levofloxacin may be no longer suitable for prophylactic use before eye surgery, but can be used to treat ocular infections caused by G-B.

In previous reports, no resistance to vancomycin was identified among bacteria isolated from all types of ocular infections, and the sensitivity to this drug was confirmed[27-28]. In our study, however, the sensitivity rates of G+C and G+B to vancomycin were significantly higher than those of G-C and G-B ($P<0.05$), which is consistent with the results reported by Schimel *et al*[9] For fusidic acid, the sensitivity rate of gram-positive bacteria was high (88.91%), contrary to that of gram-negative bacteria (32.00%), with the rate of G+C being significantly higher than that of G-C and G-B, and the rate of G+B being significantly higher than that of G-B. Thus, fusidic acid is recommended to treat gram-positive bacterial infections.

The sensitivity rate of gram-negative bacteria to cefuroxime was as low as 59.25%, but it was only G-B whose sensitivity rate was 57.28%, while the sensitivity rate of G-C was 89.29%, significantly higher than that of G-B. For moxifloxacin, the sensitivity rate of gram-positive bacteria was as high as 80.28%, but it was only G+C whose sensitivity rate was 81.21%, while the sensitivity rate of G+B was just 32.00%, significantly lower than that of G+C. These findings remind us that further classifying bacteria and comparing the sensitivity rate by a statistical analysis would lead to more accurate results when analyzing antibiotic sensitivity. Tigecycline is a new type of active intravenous broad-spectrum antibiotic, which was reported to be used for treating bacterial keratitis resistant to current antimicrobials[29] and corneal neovascularization[30]. Tigecycline (99.59%), vancomycin (97.15%), and rifampicin (94.48%) exhibited a high efficacy on the total isolates, and the sensitivity of tigecycline was significantly higher than that of vancomycin in our study. By ranking the sensitivities of the different gram-stained isolates to the antibiotics (Table 4), we can select antibiotics with higher sensitivity rates to obtain better therapeutic effects when needed.

The findings of this study may help ophthalmologists make more appropriate decisions for the treatment of ocular bacterial infections. However, the retrospective nature of this study and limitation of research time, which determined our sample size, ultimately restricted our analyses on the variation trend of the pathogen distribution and antibiotic sensitivity. Further investigations on ocular bacterial infections with larger sample sizes, longer time, and more advanced techniques will be conducted in the future.

In conclusion, our 5-year study found that *S. epidermidis* was the main isolate of all ocular specimens with bacteria. As a broad-spectrum antibiotic with high sensitivity, gatifloxacin is more suitable than levofloxacin for topical prophylactic use in ophthalmology, and levofloxacin is an effective drug for treating G-B. Vancomycin and fusidic acid both have better effects on gram-positive bacteria than gram-negative bacteria. More accurate antibiotic sensitivity analysis results can be obtained by further classifying gram-stained bacteria and comparing their sensitivities through statistical analysis.

ACKNOWLEDGEMENTS

Foundations: Supported by the National Natural Science Foundation of China (No.81670839); the Shandong Medical and Health Science and Technology Development Program (No.2016WS0265); the Qingdao People's Livelihood Science and Technology Project (No.16-6-2-14-nsh).

Conflicts of Interest: Gao W, None; **Xia T,** None; **Chen HB,** None; **Pan XJ,** None; **Huang YS,** None; **Wang X,** None; **Dong YL,** None; **Xie LX,** None.

REFERENCES

1 Galvis V, Tello A, Guerra A, Acuña MF, Villarreal D. Antibiotic susceptibility patterns of bacteria isolated from keratitis and intraocular infections at Fundación Oftalmológica de Santander (FOSCAL), Floridablanca, Colombia. *Biomedica* 2014;34(Suppl 1):23-33.

2 Choudhury R, Panda S, Sharma S, Singh DV. Staphylococcal infection, antibiotic resistance and therapeutics. Antibiotic Resistant Bacteria - A Continuous Challenge in the New Millennium. InTech, 2012.

3 Hemavathi, Sarmah P, Shenoy P. Profile of microbial isolates in ophthalmic infections and antibiotic susceptibility of the bacterial isolates: a study in an eye care hospital, Bangalore. *J Clin Diagn Res* 2014;8(1):23-25.

4 Oydanich M, Dingle TC, Hamula CL, Ghisa C, Asbell P. Retrospective report of antimicrobial susceptibility observed in bacterial pathogens isolated from ocular samples at Mount Sinai Hospital, 2010 to 2015. *Antimicrob Resist Infect Control* 2017;6:29.

5 Attisano C, Cibinel M, Strani G, Panepinto G, Pollino C, Furfaro G, Giardini F, Machetta F, Grignolo FM, Grandi G. Severe ocular bacterial infections: a retrospective study over 13y. *Ocul Immunol Inflamm* 2017;25(6):825-829.

6 Teweldemedhin M, Gebreyesus H, Atsbaha AH, Asgedom SW, Saravanan M. Bacterial profile of ocular infections: a systematic review. *BMC Ophthalmol* 2017;17(1):212.

7 Wang ZQ, Zhang Y, Sun XG. Resistance surveillance of ocular isolated bacteria in Beijing Tongren Hospital in 2007-2013. *Ophthalmol CHN* 2015;24:262-267.

8 Orlans HO, Hornby SJ, Bowler IC. *In vitro* antibiotic susceptibility patterns of bacterial keratitis isolates in Oxford, UK: a 10-year review. *Eye (Lond)* 2011;25(4):489-493.

9 Leung EH, Kuriyan AE, Flynn HW Jr, Miller D, Huang LC. Persistently vitreous culture-positive exogenous bacterial endophthalmitis. *Am J Ophthalmol* 2016;165:16-22.

10 Moloney TP, Park J. Microbiological isolates and antibiotic sensitivities in culture-proven endophthalmitis: a 15-year review. *Br J Ophthalmol* 2014;98(11):1492-1497.

11 Zhang Y, Liu ZR, Chen H, Fan YC, Duo J, Zheng H, Wang GJ, Li YC, Jiachu DB, Zewang GM. Comparison on conjunctival sac bacterial flora of the seniors with dry eye in Ganzi autonomous prefecture. *Int J Ophthalmol* 2013;6(4):452-457.

12 Tao H, Wang J, Li L, Zhang HZ, Chen MP, Li L. Incidence and antimicrobial sensitivity profiles of normal conjunctiva bacterial flora in the central area of China: a hospital-based study. *Front Physiol* 2017;8:363.

13 Zhang SD, He JN, Niu TT, Liu SS, Chan CY, Ren CY, Liu C, Pang CP, Qu Y, Li RX, Wang HL. Effectiveness of meibomian gland massage combined with topical levofloxacin against ocular surface flora in patients before penetrating ocular surgery. *Ocul Surf* 2018;16(1):70-76.

14 Pak KY, Kim SI, Lee JS. Neonatal bacterial conjunctivitis in Korea in the 21st Century. *Cornea* 2017;36(4):415-418.

15 Essa Abdullah F, Irfan Khan M, Waheed S. Current pattern of antibiotic resistance of clinical isolates among conjunctival swabs. *Pak J Med Sci* 2013;29(1):81-84.

16 Zhang Y, Wang ZQ, Sun XG. Etiological analysis and *in vitro* drug sensitivity of bacterial keratitis in northern China in the period of 2006-2015. *Zhonghua Yan Ke Za Zhi* 2017;53(9):662-667.

17 Sharifinejad M, Shokatpour N, Farnaghi F, Abedinyfar Z, Amoli FA, Doustdar F. Different genotypes of adhesion operon genes in *Staphylococcus epidermidis* isolates from various ocular infections. *Eye Contact Lens* 2018;44(Suppl 2):S277-S280.

18 Chang VS, Schwartz SG, Davis JL, Flynn HW Jr. Endophthalmitis following cataract surgery and intracameral antibiotic: Moxifloxacin resistant *Staphylococcus epidermidis*. *Am J Ophthalmol Case Rep* 2019;13:127-130.

19 Tanaka T, Ferreira BFA, Oliveira LMS, Kato JM, Gioia TSRD, Rossi F, Nakashima Y, Pimentel SLG, Yamamoto JH, Almeida Junior JN. Diagnostic value of pediatric blood culture bottles for acute postoperative endophthalmitis. *Clinics (Sao Paulo)* 2019;74:e837.

20 Teweldemedhin M, Saravanan M, Gebreyesus A, Gebreegziabiher D. Ocular bacterial infections at Quiha Ophthalmic Hospital, Northern Ethiopia: an evaluation according to the risk factors and the antimicrobial susceptibility of bacterial isolates. *BMC Infect Dis* 2017;17(1):207.

21 Sharma S. Diagnosis of infectious diseases of the eye. *Eye* 2012;26(2):177-184.

22 Sanfilippo CM, Morrissey I, Janes R, Morris TW. Surveillance of the activity of aminoglycosides and fluoroquinolones against ophthalmic pathogens from Europe in 2010-2011. *Curr Eye Res* 2016;41(5):581-589.

23 Rahman ZA, Harun A, Hasan H, Mohamed Z, Noor SS, Deris ZZ, Ismail N, Hassan AS, Ahmad F, Yaakub A. Ocular surface infections in northeastern state of Malaysia: a 10-year review of bacterial isolates and antimicrobial susceptibility. *Eye Contact Lens* 2013; 39(5):355-360.

24 Sun SY, Sun XY, Chen H, Zhao G. Etiological profiles and pathogen detection of infectious endophthalmitis. *Zhonghua Yi Xue Za Zhi* 2012;92(1):32-35.

25 Alabiad CR, Miller D, Schiffman JC, Davis JL. Antimicrobial resistance profiles of ocular and nasal flora in patients undergoing intravitreal injections. *Am J Ophthalmol* 2011;152(6):999-1004.e2.

26 Huang YS, Dai YH, Sun SY, Lan J, Xie LX. Study of different methods in reducing conjunctival bacteria before cataract surgery. *Zhonghua Yi Xue Za Zhi* 2009;89(35):2458-2461.

27 Shimizu Y, Toshida H, Honda R, Matsui A, Ohta T, Asada Y, Murakami A. Prevalence of drug resistance and culture-positive rate among microorganisms isolated from patients with ocular infections over a 4-year period. *Clin Ophthalmol* 2013;7:695-702.

28 Joseph J, Nirmalkar K, Mathai A, Sharma S. Clinical features, microbiological profile and treatment outcome of patients with *Corynebacterium* endophthalmitis: review of a decade from a tertiary eye care centre in southern India. *Br J Ophthalmol* 2016;100(2): 189-194.

29 Sueke H, Kaye S, Neal T, Murphy C, Hall A, Whittaker D, Tuft S, Parry C. Minimum inhibitory concentrations of standard and novel antimicrobials for isolates from bacterial keratitis. *Invest Ophthalmol Vis Sci* 2010;51(5):2519-2524.

30 Goktas S, Erdogan E, Sakarya R, Sakarya Y, Yılmaz M, Ozcimen M, Unlukal N, Alpfidan I, Tas F, Erdogan E, Bukus A, Ivacık IS. Inhibition of corneal neovascularization by topical and subconjunctival tigecycline. *J Ophthalmol* 2014;2014:452685.