Graefes Arch Clin Exp Ophthalmol (2011) 249:111–119
DOI 10.1007/s00417-010-1426-6

MISCELLANEOUS

Shifting trends in in vitro antibiotic susceptibilities for common bacterial conjunctival isolates in the last decade at the New York Eye and Ear Infirmary

Adebukola Adebayo · Jignesh G. Parikh · Steven A. McCormick · Mahendra K. Shah · Remedios S. Huerto · Guopei Yu · Tatyana Milman

Received: 2 December 2009 / Revised: 30 April 2010 / Accepted: 20 May 2010 / Published online: 8 June 2010

Abstract
Background Bacterial conjunctivitis is one of the most common forms of ocular diseases worldwide. The purpose of this study is to determine the most common pathogens causing bacterial conjunctivitis, their in vitro susceptibility to existing antibiotics, and the changing trends in bacterial resistance to antibiotics over the last decade.
Methods Records of all conjunctival bacterial cultures performed at the NYEEI Microbiology Laboratory from 1 January 1997 through 30 June 2008 were reviewed. Data on species of bacterial isolates and their in vitro susceptibility to the antibiotics tetracycline, trimethaprim/sulfamethoxazole (TMP/SMZ), imipenem, fluoroquinolones (ciprofloxacin, moxifloxacin, gatifloxacin), aminoglycosides (gentamicin, tobramycin), erythromycin, cefazolin, oxacillin, and vancomycin were collected.
Results Review of records yielded 20,180 conjunctival bacterial cultures, 60.1% of which were culture-positive. Of the culture-positive isolates, 76.6% were gram-positive and 23.4% were gram-negative pathogens. *Staphylococcus aureus* was the most common gram-positive pathogen isolated, and also the most commonly isolated pathogen overall. *Haemophilus influenzae* was the most common gram-negative pathogen. A significant increase in the percentage of methicillin-resistant *Staphylococcus aureus* (MRSA) was observed in the course of 11.5 years. The highest levels of antibiotic resistance were observed to tetracycline, erythromycin, and TMP/SMZ. Gram-positive isolates were least resistant to vancomycin, and gram-negative isolates were least resistant to imipenem. The lowest broad-spectrum antibiotic resistance was observed in the case of moxifloxacin, gatifloxacin, and aminoglycosides.
Conclusion *Staphylococcus aureus* is the most common pathogen in bacterial conjunctivitis. Conjunctival bacterial isolates demonstrated high levels of resistance to tetracycline, erythromycin and TMP/SMZ. Moxifloxacin and gatifloxacin appear to be currently the best choice for empirical broad-spectrum coverage. Vancomycin is the best antibiotic for MRSA coverage.

Keywords Shifting trends · Antibiotic susceptibilities · Bacterial conjunctival isolates

Conflict of interest There is no conflict of interest for any author.

Financial Support None.

A. Adebayo · J. G. Parikh (✉) · S. A. McCormick · M. K. Shah · R. S. Huerto · G. Yu · T. Milman
The New York Eye and Ear Infirmary,
310 East 14th street,
New York, NY 10003, USA
e-mail: JParikh@nyee.edu

A. Adebayo · J. G. Parikh · S. A. McCormick · M. K. Shah · R. S. Huerto · G. Yu · T. Milman
New York Medical College,
Valhalla, NY, USA

A. Adebayo
Albert Einstein College of Medicine,
Bronx, NY, USA

R. S. Huerto
St. Luke's Medical Center,
Quezon City, Philippines

Introduction

Conjunctivitis is the most common ocular disease worldwide [1, 2]. Bacterial conjunctivitis, the predominant kind of conjunctivitis, has the potential for significant ocular morbidity. Rapid destruction of the eye is enhanced by the presence of purulence, which characteristically accompanies bacterial infection [2–4].

Although most cases of conjunctivitis are self-limited, treatment with antibiotics has been shown to decrease discomfort and duration of symptoms, as well as diminish the potential for morbidity [5–8]. Frequently, antibiotics are started empirically before culture results are available, in order to increase the efficacy of treatment.

The ideal topical antibiotic for empirical treatment of bacterial conjunctivitis is the one that exhibits broad-spectrum coverage for ocular pathogens, including gram-positive and gram-negative bacteria [9]. Periodic studies to monitor the emerging antibiotic resistance trends are, therefore, crucial in guiding antibiotic selection.

This study was designed to determine the most common pathogens responsible for bacterial conjunctivitis and their in vitro susceptibility to existing antibiotics, as well as the changing trends in the resistance of these bacteria to antibiotics over the last decade. To the best of our knowledge, this is the largest study of its kind to date, and also the first of its kind in the northeastern United States.

Materials and methods

After obtaining New York Eye and Ear Infirmary (NYEEI) IRB ethics committee approval, microbiology records for all conjunctival cultures performed from 1 January 1997 through 30 June 2008 for presumed bacterial infections were reviewed. Culture samples were obtained following standard NYEEI protocol aseptic technique, according to which the specimen was collected with a cotton or Dacron (DuPont, Wilmington, DE, USA) swab under sterile conditions. Culture and sensitivity testing immediately followed specimen collection. The collections were inoculated onto chocolate agar, trypticase soy agar with 5% sheep blood, and thioglycollate broth (Becton Dickinson, Franklin Lakes, NJ, USA) and then placed in a 5% to 7% CO2 incubator at 37 degrees Celsius for 24 to 48 hours. Cultures were considered positive if they demonstrated heavy growth on media or thioglycollate, and/or moderate growth on chocolate agar, followed by identification of bacterial pathogen. The cultures were excluded from review if the identified organisms were constituents of normal conjunctival flora. The exception was made for cultures which grew *Streptococcus viridans* (*S. viridans*), which despite its being a conjunctival commensal has been shown to be pathogenic in ophthalmic infections [9, 10]. Cultures that grew fungus only, or fungus in conjunction with bacteria, were excluded.

The National Committee for Laboratory Standards guidelines were followed for routine disc diffusion (Kirby–Bauer method) and/or microdilution (Vitek 2, Automatic Microbial System, Raleigh, NC, USA) for minimum inhibitory concentration (MIC) susceptibility testing for the antibiotics tetracycline, trimethaprim/sulfa, imipenem, fluoroquinolones (ciprofloxacin, moxifloxacin, gatifloxacin), aminoglycosides (gentamicin, tobramycin), erythromycin, cefazolin, oxacillin, and vancomycin. MIC for some organisms (i.e., S. viridans, H. influenzae, S. pneumoniae, Moraxella sp., and Nisseria sp.) cannot be done using Vitek 2; thus, disc diffusion was utilized.

Statistical analysis was performed using a linear regression model to estimate the average biennial or annual change in the percentage of bacterial isolates, antibiotic resistances and their 95% confidence intervals (CI), as well as to test the statistical significances of time trends.

Results

The NYEEI microbiology laboratory performed 20,180 cultures for presumed bacterial conjunctivitis between 1 January 1997 and 30 June 2008. Of these, 12,134 (60.1%) were considered to be culture-positive, and 39.9% were considered culture-negative (21.5% grew conjunctival commensals other than *S. viridans*, and 18.4% had no growth). Fungi were identified in 0.8% of all cultures.

Of the culture-positive isolates, 9,920 (76.6%) were gram-positive and 2,844 (23.4%) gram-negative pathogens (Table 1). The percentage of gram-positive isolates increased with an average annual change (AAC) of +2.10% on an estimated linear regression model (p=0.0041) over 11.5 years. Gram-negative isolates decreased with an AAC of −2.10% (p=0.0042) over the same period.

Table 2 and Fig. 1 are representations of the prevalence of the six most commonly encountered isolates. *Staphylococcus*

Table 1 Positive cultures from 1997 to 2008

Year	Positive cultures	Gram positives	Gram negatives
1997	889	599 (67.4%)	290 (32.6%)
1998	839	604 (72%)	235 (28%)
1999	890	595 (66.8%)	295 (33.1%)
2000	915	629 (68.7%)	286 (31.3%)
2001	921	610 (66.2%)	311 (33.8%)
2002	879	550 (62.6%)	329 (37.4%)
2003	898	612 (68.2%)	286 (31.8%)
2004	1,127	988 (87.7%)	139 (12.3%)
2005	1,179	1,038 (88%)	141 (12%)
2006	1,229	1,064 (86.6%)	165 (13.4%)
2007	1,324	1,131 (85.4%)	193 (14.6%)
1/2008–6/2008	1,044	870 (83.3%)	174 (16.7%)
Total	12,134	9,290 (76.6%)	2,844 (23.4%)

Table 2 Prevalence of the top six isolates

	Gram positives	Staphylococcus aureus MRSA	MSSA	Total	Streptococcus pneumoniae	Streptococcus viridans
1997–1998	1,203	39 (7.2%)	501 (92.8%)	540 (44.9%)	82 (6.8%)	85 (7.1%)
1999–2000	1,224	67 (12.4%)	475 (87.6%)	542 (44.3%)	105 (8.6%)	84 (6.9%)
2001–2002	1,160	125 (22.7%)	425 (77.3%)	550 (47.4%)	114 (9.8%)	85 (7.3%)
2003–2004	1,600	255 (31.9%)	545 (68.1%)	800 (50.0%)	173 (10.8%)	190 (11.9%)
2005–2006	2,102	430 (40.1%)	642 (59.9%)	1,072 (51.0%)	219 (10.4%)	261 (12.4%)
2007–Jun 2008	2,001	498 (41.6%)	699 (58.4%)	1,197 (59.8%)	232 (11.6%)	274 (13.7%)
Total	9,290	1,414 (30.1% of 50.6%)	3,287 (69.9%of 50.6%)	4,701 (50.6%)	925 (10%)	979 (10.5%)
% of all isolates		(38.7%)			(7.6%)	(8.1%)
	Gram negatives	Hemophilus influenzae			Pseudomonas aeruginosa	Serratia marcescens
1997–1998	525	161 (30.7%)			76 (14.5%)	69 (13.1%)
1999–2000	581	213 (36.6%)			114 (19.6%)	74 (12.7%)
2001–2002	640	174 (27.2%)			134 (20.9%)	55 (8.6%)
2003–2004	425	108 (25.4%)			94 (22.1%)	30 (7.1%)
2005–2006	306	73 (23.9%)			66 (21.6%)	21 (6.9%)
2007–Jun 2008	367	103 (28.1%)			99 (27.0%)	41 (11.2%)
Total	2,844	832 (29.3%)			583 (20.5%)	290 (10.2%)
% of all isolates		(6.9%)			(4.8%)	(2.4%)

aureus (*S. aureus*) was the most commonly identified isolate (38.7%), and *Serratia marcescens* (*S. marcescens*) was the least prevalent isolate (2.4%) of the group. *S. aureus* constituted 50.6% of all gram-positive isolates [methicillin-resistant S. aureus (MRSA)=15.2%, methicillin-sensitive S. aureus (MSSA)=35.4%] , followed by *S. viridans* (10.5%) and *Streptococcus pneumoniae* (*S. pneumoniae*) (10.05%). *Haemophilus influenzae* (*H. influenza*) was the most common gram-negative isolate (29.3%), followed by *Pseudomonas aeruginosa* (*P. aeruginosa*) (20.5%), and *Serratia marcescens* (*S. marcescens*) (10.2%).

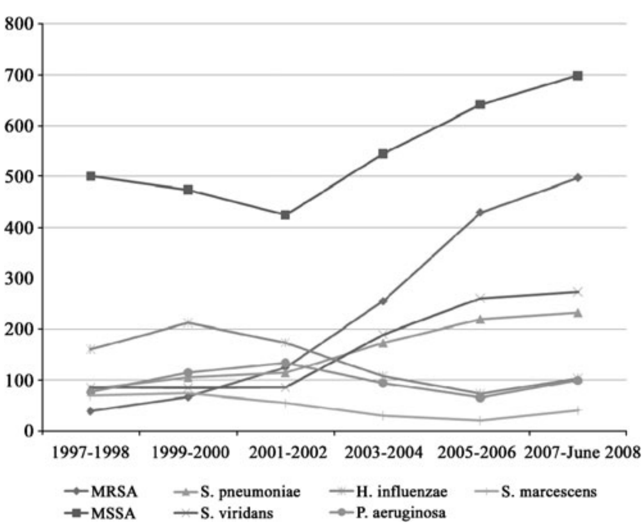

Fig. 1 Prevalence of top six bacterial isolates

Table 3 summarizes the average biennial change (ABC) for the top six isolates in the course of 11.5 years. *S. aureus* demonstrated an average biennial increase of 2.78% (p=0.011), as compared to other gram-positive isolates. Steady ABC in percentages of isolates were also noted for *S. pneumoniae* (+0.87%; p=0.005), *S. viridans* (+1.55%; p=0.007%), and *P. aeruginosa* (+1.94%; p=0.009). In contrast, *H. influenzae* and *S. marcescens* decreased in frequency over the years, although the trends were not statistically significant (−1.51%; p=0.186 and−0.81%; p=0.260 respectively).

Table 4 summarizes the average annual change (AAC) of bacterial resistances to tetracycline, trimethaprim/sulfamethoxazole (TMP/SMZ), ciprofloxacin, gentamicin, tobramycin, erythromycin, cefazolin, and oxacillin.

Table 3 Average biennial change (ABC) and 95% confidence interval (CI) for the top six isolates, from 1997–1998 to 2007–2008

	ABC (%)	95% CI	*P* value
Gram-positive:			
S. aureus	2.78	1.08, 4.48	0.011
S. pneumoniae	0.87	0.43, 1.31	0.005
S. viridans	1.55	0.70, 2.39	0.007
Gram-negative:			
H. influenzae	−1.51	−4.14, 1.12	0.186
P. aeruginosa	1.94	0.82, 3.16	0.009
S. marcescens	−0.81	−2.53, 0.91	0.260

Table 4 Average annual change (AAC) of antibiotic resistances from 1997 to 2008

	AAC (%)	95% CI	*P* value		AAC (%)	95% CI	*P* value
Tobramycin				Ciprofloxacin			
Gram-pos	−0.96	−1.44, −0.48	0.0012	Gram-pos	1.60	0.74, 2.46	0.0020
Gram-neg	0.40	−0.13, 0.92	0.1270	Gram-neg	1.51	0.39, 2.63	0.0131
S. aureus	0.36	0.10, 0.61	0.0106	S. aureus	2.57	1.45, 3.69	0.0005
Gentamicin							
Gram-pos	−0.57	−1.17, 0.03	0.0612	Tetracycline			
Gram-neg	0.36	−0.19, 0.91	0.1714	Gram-pos	5.01	4.41, 5.62	<0.0001
S. aureus	0.36	0.10, 0.61	0.0106	Gram-neg	7.41	6.50, 8.32	<0.0001
				S. aureus	1.42	−1.98, 4.82	0.3731
Erythromycin				H. influenzae	2.18	1.82, 2.54	<0.0001
Gram-pos	1.66	1.45, 1.86	<0.0001	S. pneumoniae	0.85	0.69, 1.02	<0.0001
S. aureus	3.74	2.61, 4.87	<0.0001	S. viridans	2.02	1.64, 2.41	<0.0001
S. pneumoniae	0.38	0.29, 0.48	<0.0001				
S. viridans	3.23	2.58, 3.89	<0.0001	Cefazolin			
				Gram-pos	0.68	−0.44, 1.80	0.2043
TMP/SMZ				Gram-neg	0.84	0.78, 0.90	<0.0001
Gram-pos	2.34	1.85, 2.83	<0.0001	S. aureus	4.02	3.53, 4.52	<0.0001
Gram-neg	3.12	2.67, 3.57	<0.0001				
S. aureus	1.23	0.77, 1.69	0.0001	Oxacillin			
H. influenzae	1.39	1.15, 1.62	<0.0001	Gram-pos	4.39	3.69, 5.08	<0.0001
S. pneumoniae	2.66	2.38, 2.95	<0.0001	S. aureus	3.69	3.16, 4.21	<0.0001
S. viridans	−0.26	−1.18, 0.65	0.5374				

Tobramycin was tested on all 12,134 isolates. Figure 2 illustrates the average annual change (AAC) of tobramycin resistance over the 11.5 years. Although there was a decrease in the resistance of the entire gram-positive isolates group to tobramycin (AAC=−0.96%; p=0.0012), *S. aureus* resistance to the antibiotic increased (AAC=+0.36%; p=0.0106). Gram-negative isolates similarly showed an increase in resistance (AAC=+0.40%; p=0.127) with the exception of *H. influenzae*, which displayed a constant low resistance rate of 1–2%.

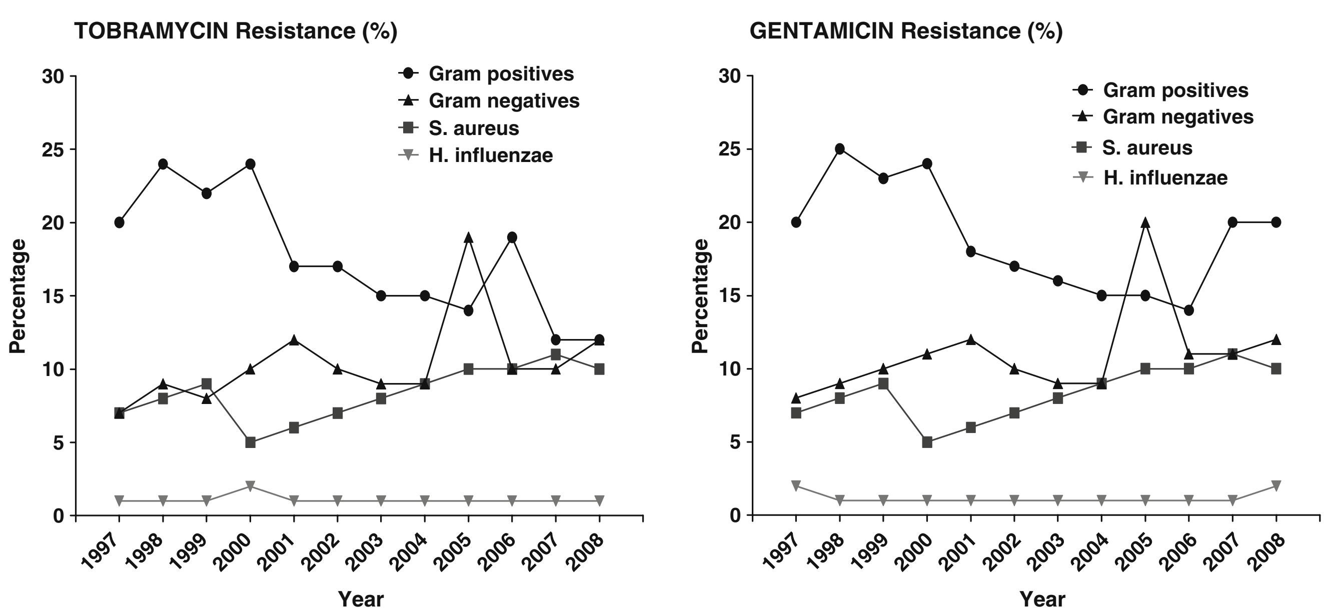

Fig. 2 Trends in resistance of bacterial isolates to the aminoglycosides

Gentamicin was also tested on all 12,134 isolates. Figure 2 illustrates the AAC of gentamicin resistance over the 11.5 years. While gram-positive isolates as a group demonstrated decrease in resistance to the antibiotic (AAC=−0.57%, p=0.061), *S. aureus* resistance to gentamicin increased (AAC=+0.36%, p=0.0106). The gram-negative isolates showed an increased resistance to gentamicin, (AAC=+0.36%, p=0.171), with the exception of *H. influenzae,* which demonstrated a constant low resistance rate of 1–2%.

Erythromycin was tested on gram-positive isolates only (9,290 cultures). Figure 3 shows erythromycin resistance over the 11.5 years. There was a steady increase in resistance to erythromycin of gram-positive isolates (AAC=+1.66%; p<0.0001). This trend was particularly significant in *S. aureus* (AAC=+3.74%; p<0.0001).

Ciprofloxacin was tested on all 12,134 isolates. Figure 4 shows ciprofloxacin resistance over the 11.5 years. There was a steady increase in ciprofloxacin resistance of the entire gram-positive isolates group (AAC=+1.60%; p=0.0020), with *S. aureus* again showing the most significant increase (AAC=+2.57%; p=0.0005). Resistance of the entire group of gram-negative isolates increased also (AAC=+1.51%; p=0.0131). *H. influenzae* and alpha streptococci were exceptions, demonstrating a steady low resistance less than 8% throughout the 11.5 years.

Testing for gatifloxacin and moxifloxacin resistance commenced in 2003 for gram-positive and gram-negative isolates, and was performed on 6,801 isolates. Figure 5 shows gatifloxacin and moxifloxacin resistance over the 5 years. For the gram-positive pathogens, resistance stayed constant at 3–5% between 2003 and 2008, then abruptly increased to15% in 2008. A more gradual increase in resistance was observed for gram-negative isolates (3–6% between 2003 and 2008). *S. aureus* resistance to gatifloxacin and moxifloxacin increased from 0% to 4% and from 0% to 5% respectively, between 2003 and 2008.

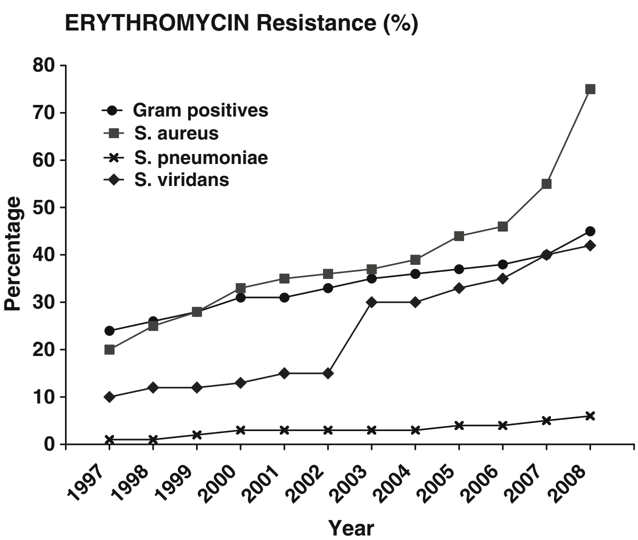

Fig. 3 Trends in resistance of bacterial isolates to erythromycin

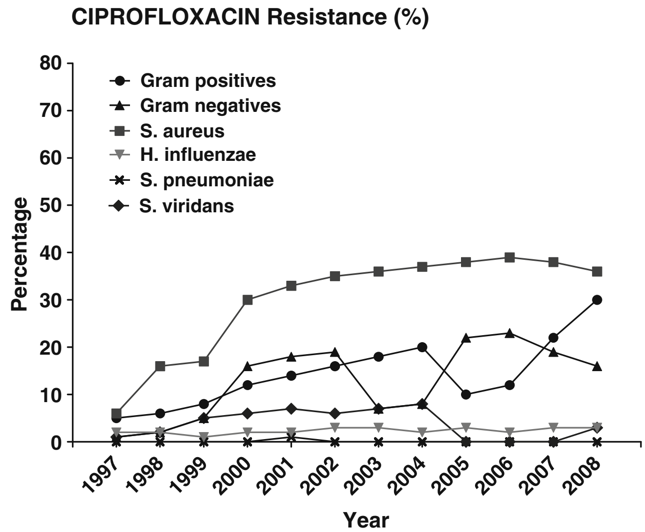

Fig. 4 Trends in resistance of bacterial isolates to ciprofloxacin

Trimethoprim/sulfamethoxazole (TMP/SMZ) was tested on all 12,134 isolates. Figure 6 shows TMP/SMZ resistance over the 11.5 years. There was an increase in resistance of gram-positive (AAC=+2.34%; p<0.0001) and gram-negative (AAC=+3.12%; p<0.0001) isolates to TMP/SMZ, particularly notable in *S. pneumoniae, H. influenzae*, and *S. aureus* (AAC=+2.66%, p<0.0001; AAC=+1.39%, p<0.0001; AAC=+1.23%, p<0.0001 respectively). Only *S. viridans* showed a decrease in resistance to TMP/SMZ, but the finding was not statistically significant (AAC=−0.26%, p-value=0.5374).

Tetracycline was tested on all 12,134 isolates. Figure 7 shows tetracycline resistance over the 11.5 years. There was an increase in resistance of all gram-positive (AAC=+5.01%; p<0.0001) and gram-negative (AAC=+7.41%; p<0.0001) isolates to tetracycline, most prominent in *H. influenzae* and *S. viridans* (AAC=+2.18%, p<o.0001; AAC=+2.02%, p<0.0001 respectively). *S. aureus* showed a statistically insignificant overall increase in tetracycline resistance in 11.5 years (AAC=+1.42, p=0.3731). This organism displayed a bimodal resistance pattern, however, with rapid increase from 5% to 62% between 1999 and 2000, followed by a more gradual decline in resistance to 22% in 2008.

At NYEE, imipenem is tested against gram-negative pathogens only (2,844 isolates). Imipenem resistance remained 0%–1% over the course of 11.5 years (Fig. 8).

Cefazolin was tested on all 12,134 isolates. Figure 9 shows cefazolin resistance over the course of 11.5 years. There was an increase in resistance of both gram-positive and gram-negative isolates to this antibiotic (AAC=+0.68%; p=0.2043 and AAC=+0.84%; p<0.0001 respec-

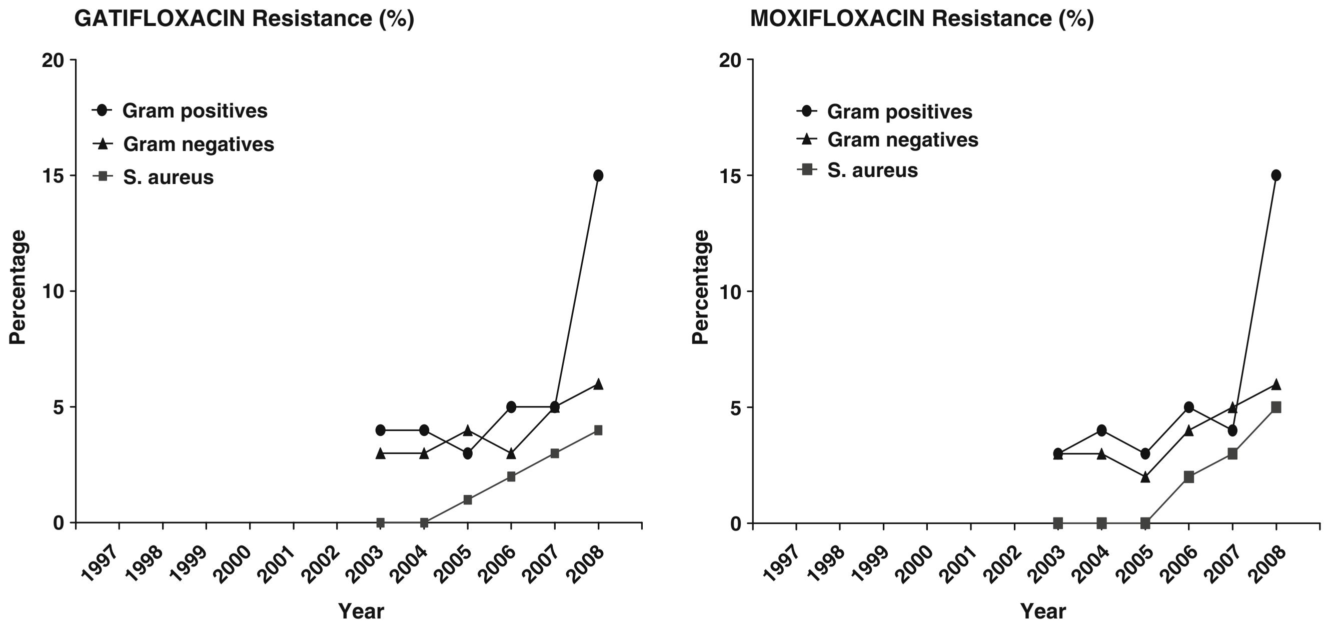

Fig. 5 Trends in resistance of bacterial isolates to the fourth generation fluoroquinolones

tively). *S. aureus* showed greatest increase in cefazolin resistance (AAC=+4.02%; $p<0.0001$).

Oxacillin was tested against gram-positive isolates only. Figure 10 shows oxacillin resistance over the course of 11.5 years. There was a steady increase in oxacillin resistance of all gram-positive pathogens (AAC=+4.39%; $p<0.0001$). Methicillin-resistant *S. aureus* (MRSA) was found in 2,632 of 9,290 isolates (28.3%). The frequency of MRSA isolates steadily increased throughout the 11.5 years (ACC=+3.69%; $p<0.0001$).

Vancomycin resistance was tested on gram-positive pathogens only; they were 100% sensitive to the antibiotic.

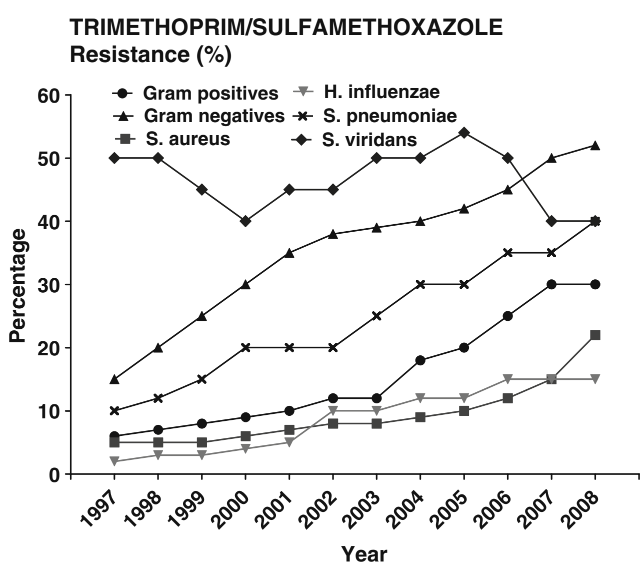

Fig. 6 Trends in resistance of bacterial isolates to trimethoprim/sulfamethoxazole

Discussion

We observed several significant trends in the prevalence of conjunctival bacterial isolates and in their resistance to various antibiotics over the past decade at the New York Eye and Ear Infirmary. The ratio of gram-positive to gram-negative isolates increased significantly ($p=0.004$). High frequencies of *S. aureus, S. viridans, S. pneumoniae, H. influenzae, P. aeruginosa*, and *S. marcescens* were noted, similar in finding to previously reported studies [11–13].

Gram-positive isolates group demonstrated greater resistance to aminoglycosides than the gram-negative isolates in the late 1990s. The resistance of gram-positive isolates group to these antibiotics decreased significantly in the course of

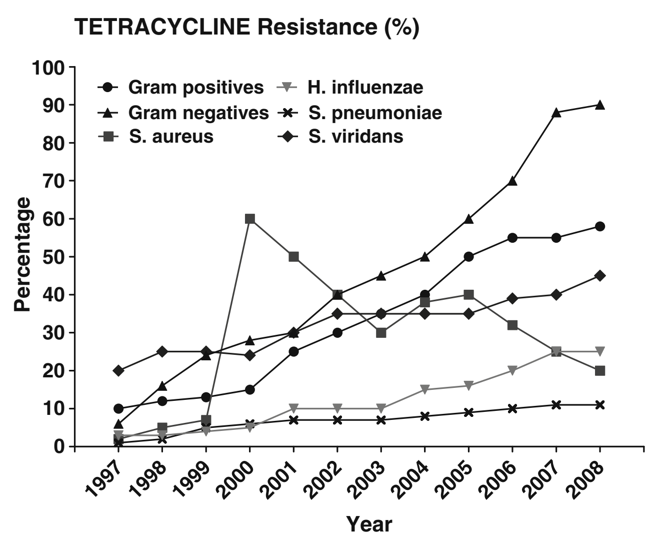

Fig. 7 Trends in resistance of bacterial isolates to tetracycline

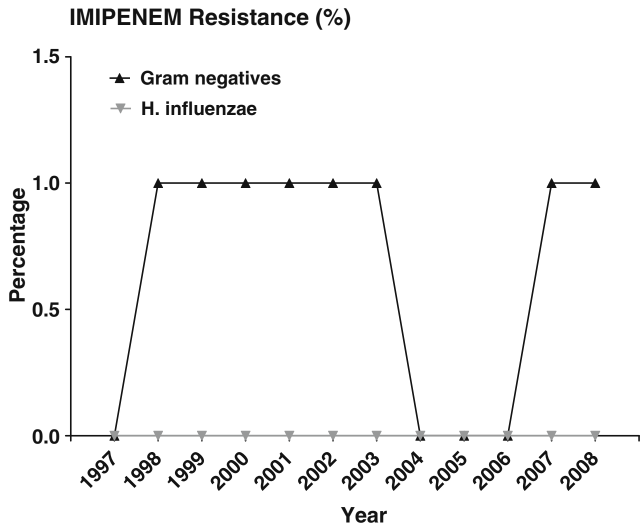

Fig. 8 Trends in resistance of bacterial isolates to imipenem

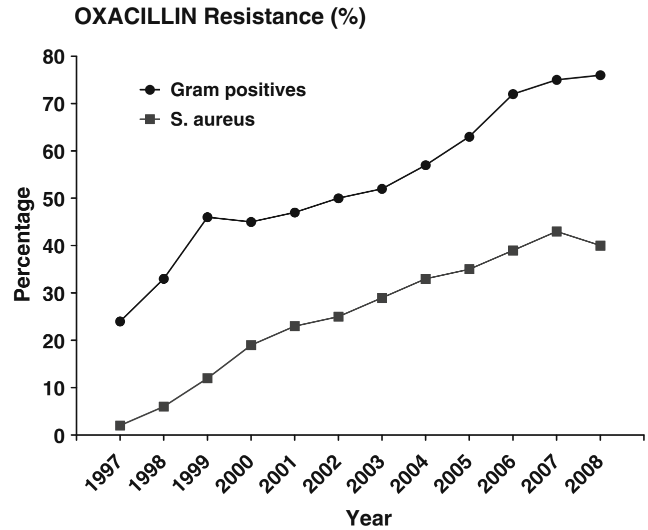

Fig. 10 Trends in resistance of bacterial isolates to oxacillin

10 years, whereas gram-negative organisms demonstrated an increase in resistance, albeit statistically insignificant. These trends are comparable to the previously reported studies on antibiotic susceptibilities of ocular isolates, and probably reflect increased frequency of aminoglycosides selection for presumed and culture-proven gram-negative infections [11, 12, 14].

Despite a steady increase in resistance of gram-negative pathogens to aminoglycosides, data from 2008 show that resistance rate is still relatively low. Overall, 12% of gram-negative isolates were resistant to aminoglycosides in the past year, and *H. influenzae* resistance was as low as 2%. Similarly, 12% of the gram-positive isolates group were resistant to tobramycin and 20% to gentamicin. It is noteworthy that *S. aureus* showed relatively low resistance

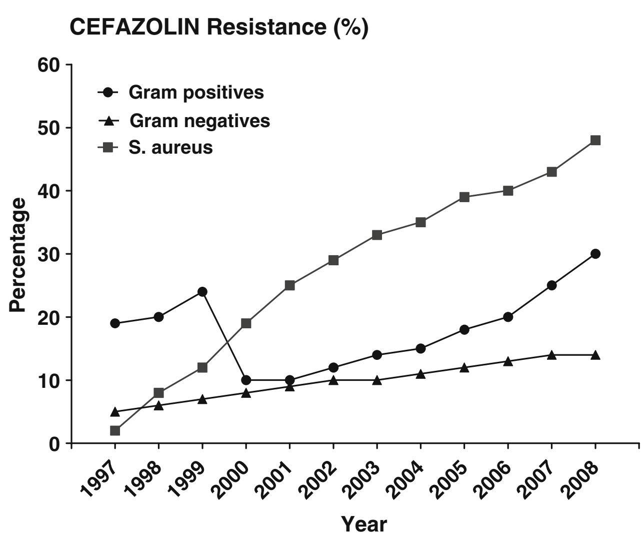

Fig. 9 Trends in resistance of bacterial isolates to cefazolin

rates to tobramycin (10%) and gentamicin (12%). These findings suggest that both aminoglycosides are still reasonably good treatment options for bacterial conjunctivitis.

Erythromycin, the only macrolide in the study, was tested only on gram-positive isolates. There was an overall 2-fold increase in resistance (24–45%) to erythromycin over 11.5 years, with the most significant increases observed in *S. aureus* (AAC=+3.74%; $p<0.0001$) and *alpha-Streptococci* (AAC=+3.23%; $p<0.0001$). These findings are similar to those reported by Cavuoto et al. [12]. Data from 2008 demonstrated that nearly a half of gram-positive isolates were resistant to erythromycin, suggesting that this medication is currently not an ideal choice for empiric antibiotic coverage.

Fluoroquinolones are frequently used for treating conjunctivitis and other ocular infections. We observed a 6-fold increase in resistance of the gram-positive isolates group to ciprofloxacin (5–30%; AAC=+1.60%; $p=0.002$), while the gram-negative isolates group had a less significant increase in resistance (1–16%; AAC=+1.51%; $p=0.0131$). Streptococci and *H. influenzae* maintained a consistently low level of ciprofloxacin resistance (2–6%). All isolates demonstrated low resistance to gatifloxacin and moxifloxacin (0–6%) until the last year, during which a 4- to 5-fold increase in resistance of the gram-positive isolates to the latest generation of quinolones was observed. With the exception of imipenem, moxifloxacin and gatifloxacin had the lowest resistance rates among gram-negative isolates. The two aforementioned antibiotics also have the lowest resistance rates for gram-positive isolates after vancomycin. Of note, *S. aureus* demonstrated low resistance rates to gatifloxacin and moxiflocxacin (4% and 5% respectively). These findings are similar to those of Jensen et al. [9]. The observation of uniformly low resistance makes 4thgeneration quinolones the best choice for empiric broad-spectrum antibiotic coverage. On the other hand, a 4-fold increase in the resistance of gram-positive isolates to these antibiotics in the past year may signal the beginning of an increasing resistance trend.

There was an overall 5-fold increase in the resistance of gram-positive isolates, and 3.5-fold increase in the resistance of gram-negative pathogens to TMP/SMZ. Of all isolates, S. pneumoniae showed the greatest increase at AAC (+2.66%). The increase in resistance in the recent years is greater than values reported by Cavuoto et al. [12]. The discrepancy may reflect inclusion of more recent data in our study. This is supported by the fact that the resistance rates were comparable in the overlapping years of both studies. Additionally, the difference in resistance rates could be attributable to the disparity in the geographic setting of the two studies.

Tetracycline showed an overall 6-fold increase in resistance of gram-positive isolates, and a 15-fold increase in resistance of gram-negative isolates. The data from recent years showed resistance levels up to 90% for gram-negative isolates, a trend that could explain why tetracycline has become an unpopular antibiotic for treatment of bacterial conjunctivitis [15]. Notably, it continues to be effective against *S. pneumoniae* (10% resistance in 2008). *S. aureus'* resistance to tetracycline gradually declined from 60% in 2000 to 20% in 2008, likely reflecting tetracycline's reduced use [15].

Imipenem, tested only against gram-negative pathogens in this study, showed a negligible resistance of 0–1% throughout the years. This low resistance is probably due to the fact that imipenem is not currently commercially formulated for ophthalmic use. Imipenem has the potential of becoming an effective ocular antibiotic in the future.

There was a 1.5-fold increase in gram-positive isolate resistance and about 3-fold increase in gram-negative pathogen resistance to cefazolin. *S. aureus* showed a most prominent increase in resistance, similar to the observations of Chalita at al. [11]. Gram-positive pathogens demonstrated higher levels of cefazolin resistance than gram-negative isolates, probably due to the fact that cefazolin is used more often for suspected and culture-proven gram-positive infections [16].

Oxacillin, a penicillinase-resistant antibiotic often reserved for detection of MRSA, exhibited an increase in resistance of 2%–40% for *S. aureus*, reflecting a significant increase in prevalence of MRSA at our institution. This finding is also similar to those reported in previous studies [12, 17–19].

There was no resistance of any gram-positive pathogens to vancomycin, which makes it an ideal antibiotic for MRSA. It is advisable to limit vancomycin use to MRSA at the present time to minimize the risk of resistance [20].

It is to be acknowledged that the in vitro susceptibility tests in this study were based on serum antibiotic concentrations, and may not reflect the efficacy of the antibiotic in the eye [21, 22]. It is, therefore, possible that in vivo resistances are actually different from what we have demonstrated in in vitro assays. It must also be noted that this study only includes data from the New York Eye and Ear Infirmary laboratory, and that this does not represent a regional or national trend.

With the treatment of acute bacterial conjunctivitis, one should be reminded that most cases resolve spontaneously. While clinical remission is significantly observed early in the course of treatment (days 2–5), the benefit decreases to marginal for later remission (days 6–10) [23].

In summary, this study outlines the prevalence trends in most common conjunctival bacterial isolates and the trends in their resistance rates to the selected antibiotics in the Northeast United States over the past decade. Our study demonstrated that gram-positive organisms have become more frequently identified as etiologic agents of bacterial conjunctivitis. The conjunctival bacterial isolates showed high levels of resistance against tetracycline, erythromycin, and TMP/SMZ, suggesting that these antibiotics are not the ideal choices for empirical broad-spectrum coverage. Moxifloxacin and gatifloxacin currently offer the best broad-spectrum coverage, and aminoglycosides are the second best option. However, a marked increase in resistance to fluoroquinolones in the recent years prompts cautious use of these antibiotics. Vancomycin continues to be the best antibiotic for MRSA coverage.

References

1. McDonnell PJ (1988) How do general practitioners manage eye diseases in the community? Br J Ophthalmol 72:733–736
2. Hovding G (2008) Acute bacterial conjunctivitis. Acta Ophthalmol 86(1):5–17
3. Ostler HB (1993) Conjunctival infections and inflammations. In: Ostler HB (ed) Diseases of the External Eye and Adnexa: A Text and Atlas. Williams & Wilkins, Baltimore, pp 67–136
4. Tarabishy AB, Jeng BH (2008) Bacterial conjunctivitis: a review for internists. Cleve Clin J Med 75(7):507–512
5. Morrow GL, Abbott RL (1998) Conjunctivitis. Am Fam Physician 57:528–529
6. Sheikh A, Hurwitz B (2008) Bacterial conjunctivitis. In: Roy FH, Fraunfelder FW, Fraunfelder FT (eds) Roy and Fraunfelder's Current Ocular Therapy, 6th edn. Elsevier, Philadelphia, pp 332–334
7. Leibowitz HM (1991) Antibacterial effectiveness of ciprofloxacin 0.3% ophthalmic solution in the treatment of bacterial conjunctivitis. Am J Ophthalmol 112(4):29–33
8. Gigliotti F, Hendley JO, Morgan J, Michaels R, Dickens M, Lohr J (1984) Efficacy of topical antibiotic therapy in acute conjunctivitis in children. J Pediatr 104(4):623–626
9. Jensen HG, Felix C, In Vitro Antibiotic Testing Group (1998) In vitro antibiotic susceptibilities of ocular isolates in North and South America. Cornea 17(1):79–87

10. Alvarenga LS, Ginsberg B, Mannis MJ (2008) Bacterial conjunctivitis. In: Tasman W, Jaeger EA (eds) Duane's Clinical Ophthalmology. Vol 4. Lippincott, Williams & Wilkins, Philadelphia, pp 1–17
11. Chalita MR, Hofling-Lima AL, Paranhos A Jr, Schor P, Belfort R Jr (2004) Shifting trends in in vitro antibiotic susceptibilities for common ocular isolates during a period of 15 years. Am J Ophthalmol 137:43–51
12. Cavuoto K, Zutshi D, Karp CL, Miller D, Feuer W (2008) Update on bacterial conjunctivitis in South Florida. Ophthalmology 115(1):51–56
13. Alexandrakis G, Alfonso EC, Miller D (2000) Shifting trends in bacterial keratitis in South Florida and emerging resistance to fluoroquinolones. Ophthalmology 107(8):1497–1502
14. Suh DW (2008) Escherichia coli. In: Roy FH, Fraunfelder FW, Fraunfelder FT (eds) Roy and Fraunfelder's Current Ocular Therapy, 6th edn. Elsevier, Philadelphia, pp 28–29
15. Jansen HG, Perry HD, Donnenfeld ED (2008) Antibacterials. In: Albert D, Miller J, Azar D, Blodi B (eds) Albert & Jakobiec's Principles and Practice of Ophthalmology, vol 1, 3rd edn. Elsevier, Philadelphia, pp 207–214
16. to hereGarat M, Moser CL, Alonso-Tarres C, Martin-Baranera M, Alberdi A (2005) Intracameral cefazolin to prevent endophthalmitis in cataract surgery: 3-year retrospective study. J Cataract Refract Surg 31(11):2230–2234
17. Asbell PA, Sahm DF, Shaw M, Draghi DC, Brown NP (2008) Increasing prevalence of methicillin resistance in serious ocular infections caused by Staphylococcus aureus in the United States: 2000 to 2005. J Cataract Refract Surg 34(5):814–818
18. Hautala N, Koskela M, Hautala T (2008) Major age group-specific differences in conjunctival bacteria and evolution of antimicrobial resistance revealed by laboratory data surveillance. Curr Eye Res 33(11):907–911
19. Freidlin J, Acharya N, Lietman TM, Cevallos V, Whitcher JP, Margolis TP (2007) Spectrum of eye disease caused by methicillin-resistant Staphylococcus aureus. Am J Ophthalmol 144(2):313–315
20. Sakoulas G, Moellering RC Jr (2008) Increasing antibiotic resistance among methicillin-resistant Staphylococcus aureus strains. Clin Infect Dis 46(S5):S360–S367
21. Baum J, Barza M (2000) The evolution of antibiotic therapy for bacterial conjunctivitis and keratitis: 1970–2000. Cornea 19 (5):659–672
22. Block SL, Hedrick J, Tyler R et al (2000) Increasing bacterial resistance in pediatric acute conjunctivitis (1997–1998). Antimicrob Agents Chemother 44:1650–1654
23. Sheikh A, Hurwitz B (2005) Topical antibiotics for acute bacterial conjunctivitis: Cochrane systematic review and meta-analysis update. Br J Gen Pract 55:962–964