BACTERIAL CONJUNCTIVITIS OF ADULTS: CAUSES AND OPHTHALMIC ANTIBIOTIC RESISTANCE PATTERNS FOR THE COMMON BACTERIAL ISOLATES

ABSTRACT

Background: Bacterial conjunctivitis is often observed in newborns as well as in other age groups. It has been associated with several organisms that differed in their relative importance and varied in their response to ophthalmic antibiotic.

Objectives: The purpose of this study was to investigate bacterial conjunctivitis of adult patients by determine the specific bacterial causes and determine the ophthalmic antibiotic resistance patterns for the bacterial isolates from conjunctivitis patients in Sana'a city, Yemen.

Methods: All bacterial swabs taken from adult patients with suspected bacterial conjunctivitis presenting to the ophthalmology clinics in the tertiary hospitals in Sana'a city, Yemen between September 2016 and October 2017 were investigated for bacteriological agents and antibiotic susceptibility . The clinical samples culturing, and microbiology diagnosis were done at National Center of Public Health laboratories Sana'a (NCPHL).

Result: Five hundred and twenty one swab results from conjunctiva were performed, of which 206 (39.5%) were deemed positive for bacterial culture. The isolation rate by bacteria species ranged from 0.5% to 28.2%. The most common bacteria isolate was *Branhamella catarrahalis* with 28.2% of the total isolates, followed by *Staphylococcus aureus* at 27.7%, while *Haemophilus influenza* and *Staphylococcus epidemidis* counted only 9.2% of total isolates. In *Staphylococcus aureus* isolates, ophthalmic antibiotic resistance varied from 10.5% for polymaxin B to 66.7% for erythromycin. In *Branhamella catarrahalis* isolates, ophthalmic antibiotic resistance ranged from 3.4% for levofloxacin to 69% for erythromycin. In *Haemophilus influenzae* isolates, ophthalmic antibiotic resistance varied from 0.0% for ciprofloxacin and polymaxian B to 42.1% for erythromycin and azithromycin.

Conclusion: The most common causative organisms in adult age groups were *Branhamella catarrahalis* and *Staphylococcus aureus*. Obviously, there is no single drug that treats these various types of bacteria. Therefore, bacteriological culture and sensitivity in the laboratory to ophthalmic antibiotics should be performed as much as possible. But if laboratory facilities are not available, some generalizations can be made as guidelines for treating conjunctivitis.

Keywords: Adult, bacterial conjunctivitis, causes, ophthalmic antibiotic resistance, Sana'a, Yemen

INTRODUCTION

Conjunctivitis is a group term for a variety of diseases described by conjunctivitis[1]. The most common cause of infectious conjunctivitis is a viral infection (about 70% of cases), followed by bacteria (about 30% of cases). The non-infectious forms are allergic, mechanical / irritant / toxic, immunogenic, and neoplastic are less common than viral and bacterial infections [1,2]. According to the assessment of the prevalence of positive culture in adult patients presenting to their general practitioner with red eyes, purulent (mucous) or prickly secretions in the eyelids; It was found that approximately 32% of them have bacterial causes. It is known that bacterial conjunctivitis is usually unilateral, but it can sometimes affect both eyes [3,4,5]. The most common pathogens for bacterial conjunctivitis in adults is staphylococcal species, followed by *Streptococcus pneumoniae* and *Haemophilus influenza* [6,7].

In children, bacteria are responsible for 50-75% of cases of conjunctivitis, which are most often caused by *S. pneumoniae*, *Haemophilus influenzae*, or *Moraxella catarrhalis* and the very severe form of bacterial conjunctivitis is caused by either *Neisseria gonorrhoeae* or *Chlamydia trachomatis*. Ophthalmologists should delay the use of broad-spectrum topical antibiotics as there is no evidence to show the superiority of any topical antibiotic agent for its use because methicillin-resistant *staphylococcal* conjunctivitis (MRSA) accounts up to 64% of the causes. This requires management by an ophthalmologist with antibiotics effective against MRSA, such as bisifloxacin ophthalmic suspension [1,2,8,9]. However, inappropriate antimicrobial use is associated with an increase in bacterial resistance, and in recent years a global push has been found to limit antimicrobial prescribing as chloramphenicol has decreased prescribing for conjunctivitis among general practitioners in the United Kingdom but its use has increased several times when it became the first antibiotic available without Prescription[3,4]. Surveillance of causative organisms and resistance susceptibility patterns are important in guiding antimicrobial selection. While large studies in the USA [6,10] have investigated trends in bacterial resistance to antimicrobials over the last decade, these have limited application in the UK as chloramphenicol, an antibiotic very commonly used in the UK, is not used in the USA due to the rare purported association between topically administered chloramphenicol and aplastic anaemia.

To the best of our knowledge this is the first report of this kind from Yemen. The purpose of this study was to investigate adult bacterial conjunctivitis by identified bacterial causes and determine the ophthalmic antibiotic resistance patterns for the bacterial isolates from conjunctivitis patients in Sana'a city, Yemen.

SUBJECTS AND METHODS

All bacterial swabs taken from adult patients with suspected bacterial conjunctivitis presenting to the ophthalmology clinics in the tertiary hospitals in Sana'a city, Yemen between September 2016 and October 2017 were investigated for bacteriological agents and antibiotic susceptibility. The clinical samples culturing, and microbiology diagnosis were done at National Center of Public Health laboratories Sana'a (NCPHL). Conjunctiva samples were collected using cotton swabs from the inferior conjunctival fornix as per local protocol. Samples were inoculated onto chocolate agar, Columbia agar with 5% blood and MacConkey agar plates, and placed in a 5% CO2 incubator at 37 ^{o}C or in air at 37 ^{o}C (MacConkey agar plate). Plates were examined after 24 and 48 hours of incubation for the presence of pathogens associated with conjunctivitis. Organisms were identified by standard laboratory methods. A negative result was defined as a scanty growth of bacteria. Each separate morphological colony species was counted using a digital colony counter after incubation. All identical individual colonies were also handled for Gram staining, and pure cultures were obtained and also used for identification. All specimens were operated according to the procedures of Clinical Microbiology Laboratory Standard Operating Procedures [11].

Antibiotic sensitivity tests

Antimicrobial susceptibility testing was carried out using the Kirby-Bauer disk diffusion method on Muller-Hinton agar according to CLSI guidelines. Antimicrobial susceptibility have been determined using commercial antimicrobial discs (Oxoid, UK). We selected ten antibiotics for ocular infections . with a wide range of mechanisms of action, including drugs that target the cell wall, DNA, and protein (Tables 2). After incubation, the antimicrobial effectiveness was determined by measuring the diameter of the inhibition zones. The bacterial strains were classified as Sensitive (S), Intermediate (I), or Resistant (R) according to the diameter of the inhibition zone[12].

ETHICAL APPROVAL

The ethical approval was obtained from the Medical Research and Ethics Committee at the Faculty of Medicine & Health Sciences at Sana'a University with Document No. 412 dated July 1, 2019. All data, including patient identification, have been kept confidential.

RESULTS

Five hundred and twenty one swab results from conjunctiva were performed, of which 206 (39.5%) were deemed positive for bacterial culture. The isolation rate by bacteria species ranged from 0.5% to 28.2% (Table 1). The most common bacteria isolated was *Branhamella catarrahalis* with 28.2% of the total isolates, followed by *Staphylococcus aureus* at 27.7%, while *Haemophilus influenza* and *Staphylococcus epidemidis* counted only 9.2% of total isolates. Other bacteria as *Pseudomonas aeruginosa, Escherichia coli, Streptococcus pneumonia* were counted 3.4%, 3.9% and 3.4% respectively. There was also a low rate of isolation for other Gram negative and Gram positive bacteria. All organisms isolated have been listed in Table 1. Table 2 shows the sensitivity patterns of major bacteria isolated from conjunctivitis patients to the various antibiotics commonly used for ophthalmic infections. In *Staphylococcus aureus* isolates, ophthalmic antibiotic resistance varied from 10.5% for polymaxin B to 66.7% for erythromycin. In *Branhamella catarrahalis* isolates, ophthalmic antibiotic resistance ranged from 3.4% for levofloxacin to 69% for erythromycin. In *Haemophilus influenzae* isolates, ophthalmic antibiotic resistance varied from 0.0% for ciprofloxacin and polymaxian B to 42.1% for erythromycin and azithromycin. In *Staphylococcus epidemidis* isolates, the rate of resistance to the ophthalmic antibiotic ranged from 10.8% for ofloxacin, moxifloxacin, polymyxin B, chloramphenicol and fusidic acid to 47.3% for erythromycin and azithromycin.

DISCUSSION

The positive for bacterial culture eye swab in the current study was 39.5% , this result is higher than that reported in adult patients presenting to their general practitioner with red eyes, purulent (mucous) or prickly secretions in the eyelids; It was found that approximately 32% of them have bacterial causes [2]. But this study bacterial rate was higher than the low-positive isolation rate of Silvester *et al.* in UK 2016, in which the bacterial rate was 15.8% of total conjunctivitis cases. Also other papers have shown variable rates of positive isolates[13,14.] This difference might be explained by the inclusion of all bacteria isolated in some studies rather than pathogenic bacteria only. In addition, our isolation rate might be lower the actual one as bacterial swabs were taken from all patients with suspected conjunctivitis including those with viral conjunctivitis. Many patients present after they have already started topical antibiotic treatment, this may have reduced the positive isolation rate.

In the current study, the most common bacteria isolated was *Branhamella catarrahalis* with 28.2% of the total isolates, followed by *Staphylococcus aureus* at 27.7%, while *Haemophilus influenzae* was less common. The results of the present study differ from those reported by Azari and Barney 2013; and Smith and Waycaster (2009) in the USA where the most common pathogens of bacterial conjunctivitis in adults *were staphylococcus aureus*, followed by *Streptococcus pneumoniae* and *Haemophilus influenzae* [2,7]. Similar to what has been reported in studies from the US and Britain, [5,6,10] *Staphylococcus aureus* was the most common organism. The high infection rate of *Staphylococcus aureus* is likely associated with cross-infection as reported by other workers.

Although antibacterial agents have not been indicated in viral conjunctivitis, given the difficulty of distinguishing between bacterial and viral causes, it is not unreasonable to prescribe broad-spectrum antimicrobials before obtaining the results of the bacterial culture. Table 2 shows the sensitivity patterns of major bacteria isolated from conjunctivitis patients to the various antibiotics commonly used for ophthalmic infections with high rates of resistance to ophthalmic antibiotics e.g *Staphylococcus aureus* isolates, ophthalmic antibiotic resistance varied from 10.5% for polymaxin B to 66.7% for erythromycin. For this reason, there is clearly no single drug that treats these various types of bacteria. Therefore, as much as possible, bacteriological culture and sensitivity in the laboratory to antibiotics should be done. In the absence of laboratory facilities, some generalizations can be made as guidelines for treating conjunctivitis in adults, as fusidic acid and neomycin can be administered and they will be effective against most bacteria isolated in this age group, depending on the results of this study. Alternatively, moxifloxacin and polymaxin B may be used. Chloramphenicol can be used in all age groups after the neonatal period, as the dominant causative organisms isolated in these age groups, namely *S. pneumoniae* and / or *Haemophilus influenzae*, were sensitive to chloramphenicol. However, ophthalmic formulations of this drug are absorbed into the blood and are known to cause aplastic anemia [15]. Therefore, short-term use of chloramphenicol should be restricted to infections resistant to less serious agents. *Pseudomonas* -eye infections may require systemic and topical treatment with appropriate antimicrobials[16]. In non-ophthalmic infections, excessive and inappropriate use of antimicrobials increased resistance of organisms[8] . Hence, monitoring of antimicrobial susceptibility and trends of resistance is important for ophthalmic antibiotics and antibiotics in general.

CONCLUSION

The commonest causative organisms in the adult age groups were *Branhamella catarrahalis and Staphylococcus aureus* . Obviously there is no single drug that will treat these varied species of bacteria; therefore bacteriological culture and *in vitro* sensitivity to ocular antibiotics should be sought as much as possible. Where laboratory facilities are not available, certain generalizations could be made as guidelines for treatment of conjunctivitis. Prescription of antibiotics should be delayed until a bacterial etiology is confirmed, and educational pamphlets should be distributed to general and emergency care practitioners. Development of novel agents with broad-spectrum antimicrobial activity may offer potential new approaches without the drawback of resistance.

AUTHORS' CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

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The clinical samples culturing, and microbiology diagnosis were done at National Center of Public Health laboratories Sana'a (NCPHL).

CONFLICT OF INTEREST

"No conflict of interest associated with this work".

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Table 1. Pathogens isolated from 512 adult patients of various adult age groups (16 years to 52 years) with conjunctivitis.

Pathogens	**Number**	**percentage**
Staphylococcus aureus	57	27.7
Staphylococcus epidemidis	19	9.2
Streptococcus pneumonia	7	3.4
Streptococcus viridians	2	0.97
Streptococcus pyogenes	3	1.5
Lancefield Group C *streptococci*	1	0.5
Streptococcus faecalis	2	0.97
Non-hemolytic *streptococci*	1	0.5
Branhamella catarrahalis	58	28.2
Haemophilus influenza	19	9.2
Pseudomonas aeruginosa	7	3.4
Escherichia coli	8	3.9
Enterobacter species	2	0.97
Klebsiella species	3	1.5
Serratia marcescens	3	1.5
Proteus species	3	1.5
Moraxella species	7	3.4
Candida albicans	4	1.9
Total non-significant growth	315	60.5
Total positive growth	206	39.5
Total tested for eye swab culture	521	100

Table 2: The susceptibility patterns of the main bacterial isolated from conjunctivitis patients towards the different commonly used antibiotics for ocular infections.

Antibiotics	Resistant							
	Staphylococcus aureus n=57		*Branhamella catarrahalis* n=58		*Haemophilus influenza* n=19		*Staphylococcus epidemidis* n=19	
	No.	%	No.	%	No.	%	N0	%
Ciprofloxacin	16	28	3	5.2	0	00	3	15.8
Ofloxacin	13	22.8	4	6.8	1	5.2	2	10.8
Levofloxacin	16	28	2	3.4	1	5.4	3	15.8
Moxifloxacin	15	26.3	4	6.8	1	5.4	2	10.8
Tobramycin	27	47.3	15	25.8	2	10.8	5	26.3
Gentamicin	25	43.8	13	22.4	2	10.8	3	15.8
Erythromycin	38	66.7	40	69	8	42.1	9	47.3
Azithromycin	36	63.2	36	62	8	42.1	9	47.3
Bacitracin	22	38.6	20	34.5	6	31.6	4	21
Polymixin B	6	10.5	3	5.2	00	00	2	10.8
Neomycin	25	43.8	3	5.2	1	5.2	3	15.8
Chloramphenicol	24	42.1	12	20.7	3	15.8	2	10.8
Fusidic Acid	7	12.2	6	10.3	3	15.8	2	10.8