Assessment and Comparison of Microbiological Efficacy of Moxifloxacin plus Vancomycin Combined Therapy with Fortified Vancomycin in Bacterial Conjunctivitis

Ahmad Abdullah¹, S. N. Askari², Shamim Ahmad², Yasir Alvi³

ABSTRACT

Background: Bacterial Conjunctivitis or red eye being highly communicable need to be tackle at the earliest. Newer antibiotics may kill bacteria more rapidly. Thus, we aim to assess and compare microbiological efficacy of Moxifloxacin (0.5%) plus Vancomycin (2.5%) combined therapy to Fortified Vancomycin (5%) in relation to organism isolated in positive culture of bacterial conjunctivitis.

Methods: The present study was conducted on patients who presented at Ophthalmology OPD, Jawaharlal Nehru Medical College Hospital, Aligarh and Gandhi Eye Hospital, Aligarh. The patients with bilateral conjunctivitis were included in the study. Right eyes were instilled moxifloxacin plus vancomycin combination therapy and Left eyes were instilled fortified vancomycin. Microbiological outcomes were recorded on first visit and on follow up visits during course of treatment.

Results: A total of 35 patients were included in the study. At first visit, 14 cases were positive with coagulase negative Staphylococcus (CoNS) being the most common organisms. All the positive smears became negative in first follow-up (3rd day) in both the groups. No significant difference was found in microbiological study outcome between the two-study groups.

Conclusions: We conclude that both the drugs, i.e. moxifloxacin (0.5%) plus vancomycin (2.5%) combined therapy and fortified vancomycin (5%) had good efficiency in microbial elimination in cases of bacterial conjunctivitis with equivalent outcome and can be considered as an alternative to other antimicrobial therapy in bacterial conjunctivitis.

Keywords: Bacterial Conjunctivitis, moxifloxacin, fortified vancomycin, microbiological efficacy

INTRODUCTION

Bacterial ocular surface infections are one of the most common infections of the body. Among all the ocular infections, bacterial conjunctivitis or red eye is predominant one which involves inflammation of the conjunctival mucosa. It is more common in young children and elderly than in other age groups[1]. The common causal pathogens in bacterial conjunctivitis are S. aureus, S. pneumoniae, and H. influenza, Staphylococcus epidermidis, Enterococcus spp., Moraxella spp., streptococci viridans group, Escherichia coli, Serratia marcescens, Pseudomonas aeruginosa.[1,2,3] Symptoms of bacterial conjunctivitis include mucopurulent discharge, redness and burning or stinging sensation. To maintain a strategic distance from there spread and to prevent further complications, bacterial ocular surface infections need to be tackle at the earliest possible stage. Pathogenesis of bacterial conjunctivitis involves release of toxins and degradative enzymes damaging the integrity of ocular tissues and may cause sight-damaging sequelae, early use of antibiotics for these infections is routine. Studies have shown rapid emerging resistance in bacterial conjunctivitis,[3] therefore development of bacterial resistance to specific antibiotics is an important consideration.
for treating ocular infections. Excessive and injudicious use of antibiotics has aggravated the problem of antibiotic resistance. Therefore, proper selection of antibiotic for these ocular surface infections remains a challenge for clinicians as well as microbiologists. Although clinical resolution of bacterial conjunctivitis occurs without any treatment in most of the patients by 7 days, treatment with topical antibiotics accelerates the rate of clinical resolution and decreases the risk of contagious spread.

Moxifloxacin is a fourth-generation synthetic fluoroquinolone antibacterial agent. It is a broad-spectrum antibiotic that has activity against both Gram-positive and Gram-negative bacteria. This compound appears to cover bacterial resistance to second-and third-generation fluoroquinolones. Clinical examinations have demonstrated that treatment results with fluoroquinolone monotherapy are comparable with combination therapy of fortified antibiotics.[4]

Vancomycin is a semi synthetic member of the beta lactamide resistant penicillin family. It is bactericidal to most gram-positive bacteria by binding to both structural precursors of the bacterial cell wall. Vancomycin is, in fact, a potent agent when multiresistant bacteria proliferate. Topical Vancomycin has been utilized effectively to treat methicillin resistant *Staphylococcal* blepharo-conjunctivitis.[5] Unfortunately economically accessible types of Vancomycin are not accessible for the treatment of bacterial ocular infections.[6] Studies indicate that advanced-generation fluoroquinolones may kill bacteria more rapidly, leading to a faster resolution of ocular infection in the eye than with older topical ocular antibiotics and thereby reducing the risk of ocular drug resistance.[7,8]. Clinical studies have shown that treatment outcomes with fluoroquinolone monotherapy compare favorably with conventional combined therapy of fortified antibiotics.[9] However, authors have not come across any study comparing Moxifloxacin (0.5%) plus Vancomycin (2.5%) combined therapy to Fortified Vancomycin (5%) on reviewing English literature on the topic. Therefore, the present study is planned with the objectives to assess and compare microbiological efficacy of Moxifloxacin (0.5%) plus Vancomycin (2.5%) combined therapy to Fortified Vancomycin (5%) in relation to organism isolated in positive culture of bacterial conjunctivitis.

METHODS

2.1 Study setting and population

The present study was conducted on patients who presented at ophthalmology OPD, Jawaharlal Nehru Medical College Hospital and Institute of Ophthalmology, Gandhi Eye Hospital, Aligarh. The procedures included in the study were explained to the patients and only those patients or guardians in case of minors, who agreed to join the study after written consent, were enrolled for the study. Clinically proven cases of bilateral conjunctivitis with age more than one year were included in the study. Patients with history of hypersensitivity to Moxifloxacin or Vancomycin, pregnant females, history of ocular surgery within 6 weeks, children less than one year and patients not willing to participate in the study or unable to give informed consent were excluded.

2.2 Study groups:

To eliminate investigator and patient’s related bias, Right eyes of all the patients were instilled combination therapy with moxifloxacin (0.5%) plus vancomycin (2.5%) (labeled as Group A) whereas Left eyes of them were instilled fortified vancomycin (5%) (labeled as Group B). In the present study Group A and Group B eye drops were used in Right and Left eye of patients respectively six times a day for 10 days.

Study procedure

Sterile transport cotton swab with polypropylene stick (pw 009) marketed by HIMEDIA Laboratory Pvt. Limited, Mumbai, India, was used for collecting incofums from conjunctival sac before starting topical antibiotics. The swab was moistened with 1-2 drops of normal saline and incofums were collected from lower Conjunctival fornix with 360° rotation of the swab stick. Culture media employed were Blood agar and Chocolate. The pure colonies were identified and characterized on the basis of culture and morphological characteristic including gram staining and biochemical tests. Follow up of the patients was done at visit 1 (day 0) and repeated at visit 2 (day 3), visit 3 (day 6) and visit 4 (day 10). Microbial outcome was documented as either positive or negative for bacterial culture and organism isolated.

2.4 Data Management and Statistics

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) Version 20[9]. The categorical variables were represented by percentage (%). The statistical significance was tested by chi square test. All tests were two tailed, and a p- value of ≤ 0.05 was considered significant.

2.5 Ethics

The study was approved by the board of studies and Institutional Ethics and Research Advisory Committee, JN Medical College, AMU, Aligarh. An informed consent was obtained from each participant (guardians in case of minors) prior to study. The participants were ensured about the privacy and confidentiality of the exercise. Before preceding the study, each patient was informed briefly about the study and given free will to participate and appropriate health education, counselling and referral were provided to all the patients.

RESULTS

A total of 35 (70 eyes) patients were included in the study. As shown in the Table 1, majority of cases were from age group 11-50 years of age. Males outnumbered females in a ratio of 4:1.

The conjunctival smear from all patients of bacterial conjunctivitis were prepared and out of total 70 conjunctival swabs, positive bacterial growth was obtained in 14 swabs (20%) leaving no bacterial growth observed in 56 swabs. While comparing frequency of positive cultures in both the groups on first visit, 9 (25.7%) out of 35 in group A, and 5 (14.3%) out of 35 in group B were positive bacterial smear. No statistical significant difference was seen in positivity of bacterial smear (x² = 1.428, p=0.232) (Table 2). *Coagulase negative Staphylococcus* (CoNS) was the most common organisms in both the study groups (Table 3).

All the positive smears became negative in first follow-up (3rd day) in both the groups. No difference was found in microbiological study outcome between the two-study groups.
Table 1. Demographic and microbiological profile of the study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Male</th>
<th>Female</th>
<th>Sex Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td>28 (56 eyes)</td>
<td>7 (14 eyes)</td>
<td>35 (70 eyes)</td>
</tr>
<tr>
<td>&lt;10 years</td>
<td>5 (10 eyes)</td>
<td>23 (46 eyes)</td>
<td>28 (56 eyes)</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>7 (14 eyes)</td>
<td>0 (0 eyes)</td>
<td>7 (14 eyes)</td>
</tr>
<tr>
<td>Positive bacterial growth</td>
<td>14 eyes</td>
<td>56 eyes</td>
<td>70 eyes</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Staph. aureus</td>
<td>coagulate negative Staphylococcus (CoNS)</td>
<td>Streptococcus spp.</td>
</tr>
<tr>
<td>No</td>
<td>3 eyes</td>
<td>10 eyes</td>
<td>1 eye</td>
</tr>
</tbody>
</table>

Table 2. Baseline culture positivity of study population in two study groups

<table>
<thead>
<tr>
<th>Eye/Group</th>
<th>Conjunctival Swabs Showing Positive Bacterial Growth n (%)</th>
<th>Conjunctival Swabs Showing No Bacterial Growth n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right eye / Group A</td>
<td>26 (74.3)</td>
<td>9 (25.7)</td>
<td>35</td>
</tr>
<tr>
<td>Left eye / Group B</td>
<td>30 (85.7)</td>
<td>5 (14.3)</td>
<td>35</td>
</tr>
</tbody>
</table>

\[ x^2 = 1.428, p=0.232 \]

Table 3. Distribution of isolated organisms in two study groups

<table>
<thead>
<tr>
<th>Eye/Group</th>
<th>Total No. of Eyes</th>
<th>Positive Culture</th>
<th>Organisms Isolated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CoNS</td>
<td>SA</td>
</tr>
<tr>
<td>RE/Group A treated</td>
<td>35</td>
<td>9</td>
<td>07</td>
</tr>
<tr>
<td>LE/Group B treated</td>
<td>35</td>
<td>5</td>
<td>03</td>
</tr>
</tbody>
</table>

\[ x^2 = 0.954, p=0.328 \]

Table 4. Effect of drugs on Bacterial Conjunctival Flora on follow-up visits in two study groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>Day 3</th>
<th>Day 6</th>
<th>Day 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>9</td>
<td>35</td>
<td>0</td>
<td>35</td>
</tr>
<tr>
<td>B</td>
<td>5</td>
<td>35</td>
<td>0</td>
<td>35</td>
</tr>
</tbody>
</table>

DISCUSSION

The aim of treating bacterial conjunctivitis is to rapidly decrease disease transmission, shorten symptom duration and minimize the emergence and spread of resistant bacteria.

In present study 17 out of 35 (48.5%) patients of bacterial conjunctivitis were less than 30 years of age. 2 out of 35(6%) patients of bacterial conjunctivitis were more than 70 years of age. Similar results have been reported in a study by Hovding[11] in 2008 who observed that bacterial conjunctivitis is more common in young population.

In the present study, only 14 out of 70 (20%) of the conjunctival swab for bacterial conjunctivitis showed organism on Gram stain on Day 0 (1st visit). This may be attributed to excessive use of over the counter topical antibiotic in our study population before reaching our hospital. Although much higher rates were reported by Cavuoto et al[3] in 2008 with 52.5% and by Gangopadhyay et al[10] in 2000 with 40% culture proven cases.

In present study most common causal pathogens were coagulate negative Staphylococcus (CoNS) (71%), S. aureus (22%) and Streptococcus spp. (7%). 100% of isolated causative pathogens were Gram Positive. This reflects geographical variation of microbial spectrum in bacterial conjunctivitis. In 2008, Hovding, Bartlett et al and cavuoto et al[1,2,3] found in their studies that most common causal pathogens in bacterial conjunctivitis were S. aureus, S. pneumoniae, and H. influenzae. Also S. epidermidis, Enterococcus spp., Moraxella spp., S. viridans group, Escherichia coli, Serratia marcescens, P. aeruginosa, and Proteus mirabilis were isolated less frequently from bacterial conjunctivitis samples. Staphylococcal infections were more common in adults, while S. pneumoniae and H. influenzae were more common in children.

In the present study, in Group A, 9 out of 35 (25.7%) samples were reported as culture positive on day 0. Group A eye drop was found to be highly effective in eradication of causative micro-organisms in the patients of bacterial conjunctivitis as confirmed by smear examination and microbial culture. Group A drug had eliminated all the bacteria causing conjunctivitis by Day 3 (2nd visit) in the study. In Group B, 5 out of 35 (14.2%) samples were reported as culture positive on day 0. Group B eye drop was also found to be highly effective in eradication of causative micro-organisms in the patients of bacterial conjunctivitis as confirmed by smear examination and microbial culture. Group B drug eliminated all the bacteria causing conjunctivitis by Day 3 (2nd visit) in the study.

All the positive smears became negative in first follow-up (3rd day) in both the groups. No significant difference was found in microbiological study outcome between the two-study groups. To the best of our knowledge, this study is the first study that compares the above mention drugs among bacterial conjunctivitis.
We conclude that both the drugs, i.e. moxifloxacin (0.5%) plus vancomycin (2.5%) combined therapy and fortified vancomycin (5%) had good efficiency in microbial elimination in cases of bacterial conjunctivitis with equivalent outcome and can be considered as an alternative to other antimicrobial therapy in bacterial conjunctivitis.

CONCLUSION

In the present study, moxifloxacin (0.5%) plus vancomycin (2.5%) combined therapy and fortified vancomycin (5%) were evaluated in bacterial ocular surface infections. Their microbiological response in conjunctivitis was comparable and it may be considered as an alternative to other antimicrobial therapy in drug resistant cases. We also conclude that both the drugs, i.e. moxifloxacin (0.5%) plus vancomycin (2.5%) combined therapy and fortified vancomycin (5%) are highly effective in eradication of causative organism in the patients of bacterial conjunctivitis as confirmed by smear examination and microbial culture.

REFERENCES