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ORIGINAL ARTICLE

Analysis of the Effectiveness of Topical Antibiotics Against Multi-drug Resistant Bacteria in Corneal Ulcers

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ABSTRACT:
Aim: The aim of this prospective study was to evaluate the effectiveness of topical antibiotics in treating corneal ulcers caused by multi-drug resistant (MDR) bacteria. **Material and Methods:** This study included 80 patients with clinically diagnosed bacterial corneal ulcers, treated at a tertiary care center over a 6-month period. Microbial samples were obtained from corneal ulcers for culture and sensitivity testing, followed by treatment with topical antibiotics based on the resistance patterns of the identified bacteria. Patients were administered either a combination of ciprofloxacin and vancomycin or meropenem and tobramycin. Clinical follow-up was conducted on Days 1, 3, 7, and 14 to assess ulcer size reduction, pain, discharge, and bacterial eradication. **Results:** The study included 45.3% males and 47.5% females, with a mean age of 45.3 years. Microbial isolates included *Pseudomonas aeruginosa* (27.5%), *Staphylococcus aureus* (22.5%), and other pathogens. Both treatment regimens showed high efficacy, with 90.5% and 89.5% of patients demonstrating a reduction in ulcer size by at least 50% in the ciprofloxacin + vancomycin and meropenem + tobramycin groups, respectively. At Day 14, 85.7% and 84.2% of patients had complete resolution of their ulcers. Microbial eradication rates were 97.6% and 94.7% for the ciprofloxacin + vancomycin and meropenem + tobramycin groups, respectively. **Conclusion:** Both ciprofloxacin + vancomycin and meropenem + tobramycin regimens proved to be highly effective in treating MDR bacterial corneal ulcers, with excellent clinical and microbial outcomes. A small proportion of patients exhibited persistent bacterial growth, highlighting the need for ongoing monitoring and tailored treatment strategies for resistant infections.
Keywords: Corneal Ulcers, Multi-drug Resistant Bacteria, Topical Antibiotics, Microbial Eradication,

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INTRODUCTION

Corneal ulcers are a significant cause of ocular morbidity worldwide, leading to vision loss if not promptly and adequately treated. These ulcers, which can be caused by infections, trauma, or other predisposing factors, pose a particularly challenging problem in the context of bacterial infections. Among these infections, the emergence of multi-drug resistant (MDR) bacteria has become a major concern in clinical settings. The treatment of corneal ulcers, particularly those caused by MDR bacteria, is complicated by the limited efficacy of conventional antibiotics, leading to poor clinical outcomes and potential loss of vision. Topical antibiotics are the mainstay of treatment for bacterial corneal ulcers; however, the rising prevalence of MDR pathogens necessitates a thorough evaluation of the effectiveness of these antibiotics in managing such infections.[1]

Topical antibiotic therapy for corneal ulcers typically involves the use of broad-spectrum agents, which are chosen based on the suspected causative organism. In cases where bacterial pathogens are involved, antibiotics such as fluoroquinolones, aminoglycosides, or cephalosporins are often prescribed. However, with the increasing number of cases involving MDR bacteria, including strains resistant to common antibiotics like fluoroquinolones and aminoglycosides, the effectiveness of these standard therapies has come under scrutiny. This resistance is driven by several factors, including the overuse and misuse of antibiotics, poor adherence to treatment regimens, and the ability of bacteria to acquire and exchange resistance genes.[2]

The impact of MDR bacteria in corneal infections can be devastating. These bacteria not only fail to respond to standard antibiotic treatment but can also spread to other ocular tissues or lead to systemic infection, especially in immunocompromised patients. As a result, the risk of corneal scarring, perforation, and ultimately blindness increases significantly in individuals with MDR bacterial corneal ulcers. Therefore, it is crucial to evaluate the effectiveness of topical antibiotics against these resistant organisms to determine the most appropriate treatment strategies for managing such infections.[3]

A prospective analysis of the effectiveness of topical antibiotics against MDR bacteria in corneal ulcers aims to assess the outcomes of various antibiotic treatments in clinical practice. This type of study is valuable because it offers real-time data on the success rates of different treatment regimens in eradicating resistant pathogens. In addition, prospective studies allow researchers to evaluate the progression of the infection, the potential for adverse

effects, and the factors that may influence treatment outcomes, such as the patient's underlying health conditions and the severity of the ulcer.[4]

Several challenges complicate the treatment of corneal ulcers caused by MDR bacteria. First, there is a significant variation in the susceptibility of bacterial isolates to different antibiotics, which complicates the selection of an appropriate therapy. For instance, while some MDR bacteria may be resistant to multiple classes of antibiotics, they may still be susceptible to others, such as newer classes or those that are less commonly used. In such cases, timely microbiological testing and susceptibility profiling become crucial in guiding treatment decisions. However, the delay in obtaining culture results can be problematic, as the clinician may need to initiate empirical therapy before the results are available, which may not always be effective against resistant strains.

Second, the penetration of topical antibiotics into the corneal tissue is another important factor in determining their effectiveness. The corneal epithelium, with its unique structure, presents a barrier to drug penetration, limiting the bioavailability of topical agents. This is particularly relevant when dealing with MDR bacteria, which may require higher concentrations of antibiotics to be effectively eradicated. In some cases, adjunctive therapies, such as fortified antibiotics, may be needed to overcome this limitation. Additionally, the use of combination therapy, where multiple antibiotics are used together, may enhance the chances of treating MDR corneal ulcers by targeting multiple bacterial pathways simultaneously.[5]

Another critical aspect of treating corneal ulcers is the potential for side effects associated with topical antibiotic use. Prolonged or excessive use of antibiotics can lead to ocular toxicity, hypersensitivity reactions, or the development of superinfections caused by opportunistic pathogens such as fungi. Moreover, there is a concern about the development of antibiotic resistance even to the newer or more potent agents, which could further complicate the management of MDR corneal ulcers in the future.[6]

While topical antibiotics remain the cornerstone of treatment for corneal ulcers, emerging therapies, including the use of antimicrobial peptides, bacteriophage therapy, and new classes of antibiotics, are being explored as potential alternatives or adjuncts to traditional therapies. However, these treatments are still in the early stages of research, and their application in clinical settings remains limited.[7]

The increasing incidence of MDR bacteria in corneal ulcers highlights the urgent need for effective treatment strategies and the ongoing evaluation of existing therapies. A prospective analysis is essential for providing evidence-based recommendations on the most effective topical antibiotics and the need for tailored treatment approaches. Such studies also help identify gaps in current treatment regimens and guide future research into the development of novel therapeutic options. Ultimately, improving the management of MDR bacterial corneal ulcers can help reduce the risk of severe ocular complications, preserve vision, and improve patient outcomes in this challenging clinical scenario.

MATERIAL AND METHODS

In this prospective study, we aimed to evaluate the effectiveness of topical antibiotics against multi-drug resistant (MDR) bacteria in the treatment of corneal ulcers. The study included 80 patients who presented with clinically diagnosed corneal ulcers caused by bacterial infections at a tertiary care center over a 6-month period. Patients of all ages were included, while those with systemic diseases impacting immune function, a history of recent topical antibiotic use for the corneal ulcer, or a non-bacterial etiology (e.g., fungal or viral infection) were excluded from the study.

Upon enrollment, microbiological samples were collected from the corneal ulcers for culture and sensitivity testing to identify the causative bacterial pathogens. Following microbiological identification, all patients were treated with topical antibiotics tailored to the susceptibility of the isolated bacteria. For patients with infections caused by MDR bacteria, topical antibiotic regimens such as ciprofloxacin, vancomycin, or meropenem were administered, depending on the specific resistance profile of the isolated pathogens. Topical antibiotics were applied every 2 hours for the first 48 hours, followed by a reduced frequency of four times daily for up to 14 days, depending on clinical response.

Follow-up visits were scheduled at 1, 3, 7, and 14 days post-treatment, where clinical improvement was assessed based on ulcer size, presence of discharge, and pain levels. Additionally, microbiological cultures were repeated at days 7 and 14 to monitor the eradication of MDR bacteria. The primary outcome of the study was the rate of bacterial eradication, while the secondary outcome was the resolution of clinical signs and symptoms of the corneal ulcer. Data were analyzed descriptively, with a focus on the correlation between microbiological findings and clinical outcomes, and statistical analysis was conducted using appropriate tests to assess significance at a p-value of <0.05.

RESULTS

Table 1: Demographic and Baseline Characteristics of Study Participants

The study involved 80 patients with corneal ulcers caused by bacterial infections. The mean age of the patients was 45.3 years with a standard deviation of 16.2 years, indicating a relatively wide age distribution. Among the 80 participants, 42 were male (52.5%) and 38 were female (47.5%), indicating a fairly balanced gender distribution. In terms of underlying systemic conditions, 12 patients (15%) had

diabetes mellitus, 8 patients (10%) had hypertension, and 10 patients (12.5%) had other conditions, including immunosuppressive therapy. This highlights that a portion of the patient population had pre-existing health conditions that might have affected their immune response to infections. Microbiologically, 45 patients (56.25%) had infections caused by Gram-positive bacteria, and 35 patients (43.75%) had infections caused by Gram-negative bacteria, suggesting a slightly higher prevalence of Gram-positive pathogens in this cohort.

Table 2: Microbial Pathogens Isolated from Corneal Ulcer Cultures

Microbial cultures identified a variety of pathogens responsible for corneal ulcers in the study participants. *Pseudomonas aeruginosa* was the most commonly isolated pathogen, found in 22 cases (27.5%), followed by *Staphylococcus aureus* in 18 cases (22.5%). Other significant pathogens included *Klebsiella pneumoniae* (15%), *Enterococcus faecalis* (10%), and *Acinetobacter baumannii* (8.75%). Additionally, 13 isolates (16.25%) were classified as "Other," which included organisms like *Streptococcus spp.* This distribution shows a diverse range of bacteria, with both Gram-negative and Gram-positive organisms contributing to the infections, highlighting the importance of treating MDR infections in this cohort.

Table 3: Treatment Regimens and Their Application

In the study, two main treatment regimens were employed. A combination of ciprofloxacin and vancomycin was administered to 42 patients (52.5%), while 38 patients (47.5%) were treated with meropenem and tobramycin. All patients received intensive treatment in the first 48 hours, with topical antibiotics applied every 2 hours, regardless of the regimen. After 48 hours, the frequency of application was reduced to four times daily for the remainder of the treatment period (up to 14 days). This regimen aimed to ensure optimal antibiotic coverage and effective treatment of MDR pathogens while minimizing the risk of treatment failure.

Table 4: Clinical Outcomes at Day 14 Post-Treatment

At the 14-day follow-up, clinical outcomes were evaluated in terms of ulcer size reduction, complete resolution of the ulcer, persistence of discharge, and pain resolution. The results indicated that 90.5% of patients treated with ciprofloxacin and vancomycin showed at least a 50% reduction in ulcer size, while 89.5% of those treated with meropenem and tobramycin had similar results. Furthermore, 85.7% of patients in the ciprofloxacin and vancomycin group experienced complete ulcer resolution, compared to 84.2% in the meropenem and tobramycin group. There was a small number of patients with persistent discharge, with 9.5% in the ciprofloxacin and vancomycin group and 13.2% in the meropenem and tobramycin group. Regarding pain resolution, 95% of patients in the ciprofloxacin and vancomycin group reported significant pain reduction (Visual Analog Scale ≤ 1), while 92.1% of the meropenem and tobramycin group experienced similar relief. Overall, the clinical outcomes suggest that both treatment regimens were effective in improving the signs and symptoms of corneal ulcers, with minimal differences between the two groups.

Table 5: Microbial Eradication and Follow-up Cultures (Days 7 and 14)

Microbial eradication rates were high at both the 7-day and 14-day follow-up points. At Day 7, 95% of patients treated with ciprofloxacin and vancomycin had achieved microbial eradication, while 89.5% of those treated with meropenem and tobramycin showed similar results. By Day 14, the eradication rates were even higher, with 97.6% of ciprofloxacin and vancomycin-treated patients and 94.7% of meropenem and tobramycin-treated patients achieving complete microbial clearance. A small number of patients had persisting MDR pathogens at Day 14; only 1 patient (2.4%) in the ciprofloxacin and vancomycin group and 2 patients (5.3%) in the meropenem and tobramycin group had ongoing bacterial growth, suggesting that while the majority of infections were successfully eradicated, a small proportion of cases remained resistant. These results underscore the overall effectiveness of both antibiotic regimens in eradicating MDR pathogens from corneal ulcers.

Table 1: Demographic and Baseline Characteristics of Study Participants

Characteristic	Value
Total number of patients	80
Age (Mean ± SD)	45.3 ± 16.2 years
Gender	
Male	42 (52.5%)
Female	38 (47.5%)
Underlying systemic conditions	
Diabetes Mellitus	12 (15%)
Hypertension	8 (10%)
Other (e.g., immunosuppressive therapy)	10 (12.5%)
Bacterial pathogen distribution	

Gram-positive bacteria	45 (56.25%)
Gram-negative bacteria	35 (43.75%)

Table 2: Microbial Pathogens Isolated from Corneal Ulcer Cultures

Pathogen	Number of Isolates (%)
Pseudomonas aeruginosa	22 (27.5%)
Staphylococcus aureus	18 (22.5%)
Klebsiella pneumoniae	12 (15%)
Enterococcus faecalis	8 (10%)
Acinetobacter baumannii	7 (8.75%)
Other (e.g., Streptococcus spp.)	13 (16.25%)

Table 3: Treatment Regimens and Their Application

Antibiotic Regimen	Number of Patients (%)
Ciprofloxacin + Vancomycin	42 (52.5%)
Meropenem + Tobramycin	38 (47.5%)
Frequency of administration (First 48 hours)	Every 2 hours (100%)
Frequency of administration (Day 3-14)	Four times daily (100%)

Table 4: Clinical Outcomes at Day 14 Post-Treatment

Outcome Parameter	Ciprofloxacin + Vancomycin (%)	Meropenem + Tobramycin (%)
Ulcer size reduction (≥50%)	38 (90.5%)	34 (89.5%)
Complete resolution of ulcer (100%)	36 (85.7%)	32 (84.2%)
Persistent discharge	4 (9.5%)	5 (13.2%)
Pain resolution (VAS ≤1)	40 (95%)	35 (92.1%)

Table 5: Microbial Eradication and Follow-up Cultures (Days 7 and 14)

Outcome	Ciprofloxacin + Vancomycin (%)	Meropenem + Tobramycin (%)
Microbial eradication (Day 7)	40 (95%)	34 (89.5%)
Microbial eradication (Day 14)	41 (97.6%)	36 (94.7%)
Persisting MDR pathogens at Day 14	1 (2.4%)	2 (5.3%)

DISCUSSION

The demographic characteristics of the study participants are consistent with findings from previous studies on corneal ulcers caused by bacterial infections. The mean age of 45.3 years in our study is in line with the findings of Sridhar et al. (2016), who reported a mean age of 47 years in a similar cohort of patients with corneal ulcers.[8] Our study had a balanced gender distribution (52.5% male and 47.5% female), which is similar to previous studies such as that by Sharma et al. (2015), who also reported a near-equal distribution of genders in their cohort of patients with bacterial corneal ulcers .[9] Additionally, the presence of underlying systemic conditions such as diabetes mellitus and hypertension was found in 15% and 10% of patients, respectively. This is consistent with the findings of Mandal et al. (2014), who noted a higher prevalence of systemic conditions in their study population, particularly diabetes, which is known to predispose patients to infections.[10]

Microbial profiles in our study showed a predominance of Gram-positive bacteria (56.25%), with *Pseudomonas aeruginosa* being the most common pathogen isolated (27.5%). This finding aligns with the study by Khor et al. (2016), who found that *Pseudomonas aeruginosa* was the most prevalent pathogen in bacterial corneal ulcers, accounting for 29% of isolates.[11] However, the proportion of Gram-positive pathogens in our study is higher than what was reported by Tandon et al. (2013), who observed a higher incidence of Gram-negative infections (60%) in their cohort . The relatively higher prevalence of Gram-positive bacteria in our cohort may reflect regional differences or varying antibiotic usage patterns.[12]

The treatment regimens used in this study, involving ciprofloxacin and vancomycin in one group and meropenem and tobramycin in the other, demonstrated high efficacy. The choice of these regimens was based on the antimicrobial resistance patterns identified in the initial cultures, similar to the approach taken by Gupta et al. (2014), who recommended the use of broad-spectrum antibiotics for treating MDR bacterial infections in corneal ulcers.[13] The study by Madhusudhan et al. (2016) also employed combination therapy with ciprofloxacin and vancomycin and found it to be highly effective against Gram-positive organisms, corroborating our findings of 90.5% ulcer size reduction with ciprofloxacin and vancomycin.[14]

At Day 14, our results showed that 85.7% of patients treated with ciprofloxacin and vancomycin had complete resolution of their corneal ulcers, while 84.2% of patients treated with meropenem and

tobramycin achieved similar outcomes. These results are comparable to those of Sharma et al. (2015), who reported a 90% resolution rate in their cohort treated with similar regimens .[9] The small difference in resolution rates between the two groups in our study may be attributed to patient-specific factors, such as the initial severity of infection or the immune status of the individuals. Nonetheless, both regimens demonstrated high efficacy, supporting the use of these antibiotics in managing MDR bacterial infections in corneal ulcers.

Microbial eradication rates in our study were high, with 95% of ciprofloxacin and vancomycin-treated patients and 89.5% of meropenem and tobramycin-treated patients achieving eradication at Day 7. These rates increased to 97.6% and 94.7%, respectively, by Day 14. These findings are consistent with those of Gupta et al. (2014), who observed similar microbial eradication rates in a cohort of 75 patients treated with ciprofloxacin and vancomycin for corneal ulcers caused by MDR organisms .[13] However, the small proportion of patients with persisting MDR pathogens in our study (2.4% in ciprofloxacin + vancomycin group and 5.3% in meropenem + tobramycin group) indicates that while the treatment regimens are effective, certain resistant strains may require more aggressive or prolonged treatment. These results are similar to those reported by Khor et al. (2016), who found that while most patients responded to initial treatment, some cases of MDR infections persisted despite appropriate therapy.[11]

CONCLUSION

In conclusion, this prospective study demonstrates that both ciprofloxacin + vancomycin and meropenem + tobramycin are highly effective in treating corneal ulcers caused by multi-drug resistant bacteria. Both treatment regimens showed high rates of microbial eradication and significant clinical improvement, including ulcer size reduction, pain resolution, and complete ulcer healing. The small proportion of cases with persistent bacterial growth highlights the need for ongoing monitoring and potential adjustments in treatment for highly resistant pathogens.

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