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Original Article

A COMPARATIVE STUDY TO EVALUATE EFFICACY AND SAFETY OF TOPICAL CIPROFLOXACIN V/S FORTIFIED GENTAMICIN-CEFTAZIDIME IN BACTERIAL KERATITIS" AT A TERTIARY CARE CENTRE IN TELANGANA

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ABSTRACT

Objective: To compare the efficacy and safety of topical ciprofloxacin v/s fortified gentamicin-ceftazidime in bacterial keratitis.

Methods: This was a randomized control trial done on 60 subjects with 30 subjects in each group. The clinical signs and symptoms are recorded in two groups of bacterial keratitis patients at baseline and after 2 w of treatment using ciprofloxacin ophthalmic solution and standard therapy regimen of fortified gentamicin-ceftazidime using scoring of ocular signs and symptoms (1=minimum, not present), (5=maximum, severe) with a study period of 3 mo

Results: The group administered with fortified ceftazidime+gentamicin demonstrated superior clinical and statistical efficacy compared to ciprofloxacin in treating bacterial keratitis. This regimen led to a substantial alleviation of symptoms and minimized ocular discomfort to a greater extent. Notably, the calculated p-value for the day 14 score, standing at 0.02 (below the 0.05 threshold), underscores the significant superiority of fortified ceftazidime+gentamicin in symptom reduction.

Conclusion: We conclude that fortified ceftazidime+gentamicin is better than ciprofloxacin for the treatment of bacterial keratitis.

Keywords: Ceftazidime, Gentamicin, Fortified, Ciprofloxacin, Bacterial keratitis

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INTRODUCTION

Blindness continues to be one of the major public health problems in developing countries [1]. According to the World Health Organization, corneal opacity is among the major causes of vision impairment in the world today [2]. Scarring of the cornea because of infective keratitis has been reported as an important cause of preventable blindness in many studies [3-5]. Globally it is estimated that ocular trauma and corneal ulceration result in 1.2 to 2 million new cases of corneal blindness annually. Causes of blindness worldwide list corneal scarring second only to cataracts as the major etiology of blindness and visual disability in many of the developing nations in Asia, Africa, and the Middle East [6]. The incidence of microbial keratitis is 2.5 to 799 per 1 lakh population [7, 8]. Corneal blindness is a major problem in India as it adds a substantial burden to the community in general and health care resources and further. Individuals with corneal blindness are usually of a younger age group compared with those suffering from cataracts. Hence the impact of corneal blindness is greater in terms of total blind years [9]. According to the World Health Organization, corneal diseases are among the major causes of vision loss and blindness in the world today, after cataracts and glaucoma. In India, it is estimated that there are approximately 6.8 million people who have vision less than 6/60 in at least one eye due to corneal diseases; of these, about a million have bilateral involvement.

According to the National Programme for Control of Blindness (NPCB) estimates, there are currently 120,000 corneal blind persons in the country. According to this estimate, there is an addition of 25,000-30,000 corneal blindness cases every year in the country. The burden of corneal disease in our country is reflected by the fact that 90% of the global cases of ocular trauma and corneal ulceration leading to corneal blindness occur in developing countries. Microbial keratitis is an infection of the cornea. Corneal opacities, which are frequently due to microbial keratitis, remain among the top five causes of blindness worldwide. Microbial keratitis disproportionately affects low-and middle-income countries. Studies indicate that the incidence of microbial keratitis may be up to [10] times higher in countries like Nepal and India compared to the United States [11]. Many cases with corneal ulceration end up with corneal blindness or still disastrous outcomes such as corneal perforation, endophthalmitis, and phthisis bulbi. About 60 to 70% of corneal scars or adherent leucoma are the result of neglected or improperly treated corneal ulcers. Thus, corneal blindness is a major public health problem and its status is expected to increase. Treatment for corneal infections is based on appropriate antimicrobial therapy, which requires knowledge of the local antimicrobial susceptibility patterns of various antibiotics. Since microbial resistance patterns can vary by year and geographical region, local annual surveys are important in guiding the empiric treatment of bacterial keratitis.

The objective of our study is to compare clinical signs and symptoms in two groups of bacterial keratitis patients at baseline and after 2 w of treatment using ciprofloxacin ophthalmic solution and standard therapy regimen of fortified gentamicin-ceftazidime and to compare safety based on any adverse effects or events occurring during study.

MATERIALS AND METHODS

Study design

The study is a prospective and comparative study with a study tool of scoring Ocular signs and symptoms (1=minimum, not present), (5=maximum, severe).

Study subjects

Patients diagnosed with Bacterial keratitis by Ophthalmologist were included in our study after taking written informed consent; the study was ethically approved by the Institutional Ethics Committee,

Osmania Medical College, Koti, Hyderabad with Reference no: IEC/OMC/2022/M. No. (12) Acad-122.

Sample size

Based on the prevalence statistics obtained from Sarojini Devi Eye Hospital which is 6 patients per day of Bacterial keratitis, I have calculated the Sample size using formula $4PQ/E^2$ around "60".

Where,

- P= Prevalence of bacterial keratitis in Hyderabad is 15%
- Q=100-P
- E= allowable error (10%)

Therefore the Sample size calculated according to the above formula is 51, so we approximated it to be 60

The study is a randomized control trial done for 3 mo in the Department of Ophthalmology, Sarojini Devi Eye Hospital, Hyderabad

Inclusion criteria

We included patients who were clinically diagnosed with bacterial keratitis by an ophthalmologist and were willing to give consent and informative content for the study and Patients who could understand and be able to adhere to dosing and visit schedule. we included patients of both genders and in the age group of 8-60 y.

Exclusion criteria

We excluded patients allergic to any of the study agents or preservatives used in the formulation and Patients with fungal and viral keratitis patients with any other ocular infections. Pregnant women and women of childbearing age who were not taking adequate birth control measures were not enrolled.

Data collection

This is a randomized controlled trial on 60 subjects who were randomly allocated into Group A and Group B with 30 subjects in each group after written informed consent. Group A included subjects whose treatment was with ciprofloxacin ophthalmic solution 0.3% while Group B with a standard therapy regimen of fortified gentamicin-ceftazidime with a double blinding technique.

Each patient receiving a set of masked medications (two bottles of ciprofloxacin or one bottle of fortified gentamicin and one bottle of ceftazidime) is labeled with a unique patient number. The patient has to dose the two masked drugs 5 min apart, following the same dosing regimen with each drug.

The following dosing regimen is shown to the patient by the investigator: Instill 2 drops every 30 min for 6 h and then 2 drops every hour on day 1, 1 drop every hour on days 2 and 3, 1 drop every 2 h on days 4 and 5, 1 drop every 4 h on days 6 through 14. After day 14, the dosing schedule is at the discretion of the investigator. Physician impressions and evaluation of signs and symptoms will be performed on treatment day 1, day 2, day 4, day 7, and day 14. If dosing was continued past day 16, a final evaluation will be made when the instillation of the drug is ceased. The physician evaluated the patient's overall clinical condition and made one of five possible judgments (cured, improved, improving, unchanged, or worse) regarding the response of the corneal ulcer to therapy at each follow-up.

Table 1: Definition of physicians' judgement of corneal ulcer response to therapy

Outcome	Category	Description
Clinical success	Cured	No evidence of active bacterial infection, re-epithelization complete, and inflammation resolved (score = 1)
	Improved	No evidence of active bacterial infection, re-epithelization complete, and inflammation reduced relative to day 1 (score = 2)
	Improving	No evidence of active bacterial infection, re-epithelization progressing but not complete, and inflammation is still evident (score = 3)
Treatment failure	Unchanged	No clinically significant improvement relative to day 1 (score = 4)
	Worse	Progressing infection with worsening inflammation (score = 5)

Statistical analysis

The data were entered in the Microsoft Excel 2019 version. Data were analyzed using Microsoft Excel, SPSS Version 16. Descriptive and inferential statistical analyses were used in the present study

RESULTS

The mean age of the study subjects was 50.3±12.2 in Group A and 52.8±12.7 in Group B. No significant difference was noticed (p=0.96). The majority were males in both group A and group B, with 60% and 70% respectively.

The age and gender distribution of the study population are given below:

In group A, 8 people were less than 40 y old and 22 people were more than 40 y old. In group B, 5 people were less than 40 y old and 25 people were more than 40 y old.

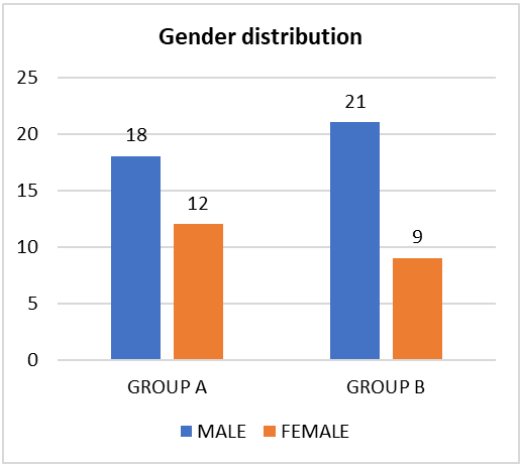

Fig. 1: Showing the gender distribution

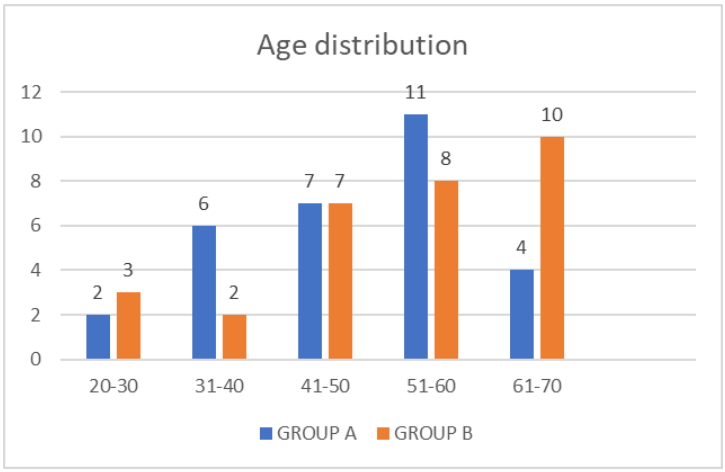

Fig. 2: Showing the age distribution

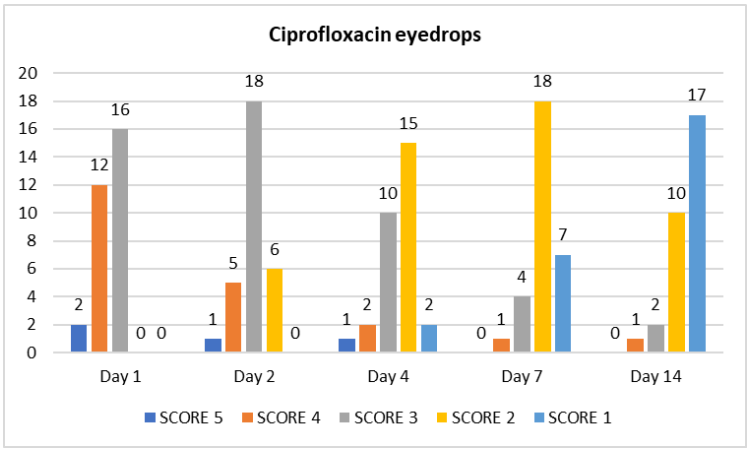

Fig. 3: Scoring of signs and symptoms with ciprofloxacin eye drops

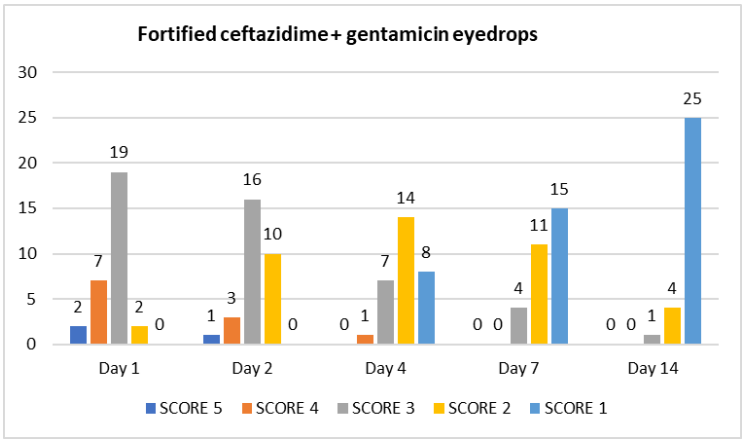

Fig. 4: Scoring of signs and symptoms with fortified ceftazidime and gentamicin eye drops

Table 2: Independent sample t-test comparing mean scores of ciprofloxacin and fortified ceftazidime+gentamicin groups across different days

Timeline	t	df	Std. error difference	95% Confidence interval of the difference		p-value
				Lower	Upper	
Day 1	1.36	58	0.17	.57782	.11115	0.18
Day 7	1.80	58	0.19	.74073	.03744	0.08
Day 14	2.11	58	0.17	.72076	.01916	0.02

The p-value calculated for a score on day 1 was 0.18, which is non-significant, whereas for day 14 the p-value calculated was 0.02 (less than 0.05) is significant, which indicates fortified ceftazidime+gentamicin has a better reduction of symptoms.

The mean scores of group A on day 1 was 3.53, day 2 was 3.03, day 4 was 2.5, day 7 was 1.97, and day 14 was 1.57. Whereas the mean scores of group B on day 1 was 3.3, day 2 was 2.83, day 4 was 2.03, day 7 was 1.63 and day 14 was 1.2.

The mean reduction in scores from day 1 to day 14 was 1.96 in group A and 2.1 in group B.

DISCUSSION

Topical antibiotics remain the first-line treatment for bacterial keratitis [12]. According to Pragya *et al.*, a significantly higher proportion of ulcers that had been treated with gatifloxacin exhibited complete healing compared with those that had been treated with ciprofloxacin (P =0.042); however, the mean time to healing of the ulcer was similar in both groups. Gatifloxacin had a significantly better action against gram-positive cocci both *in vitro* and *in vivo* when compared with ciprofloxacin [13]. According to Hyndiuk *et al.*, Topical ciprofloxacin monotherapy is similar to the standard therapy regimen of fortified antibiotics. No statistically significant differences were noted in the resolution of the clinical signs and symptoms (P>0.08) or the time to cure (P = 0.55) [14].

The present study shows that fortified ceftazidime+gentamicin is superior clinically and statistically to ciprofloxacin for treating bacterial keratitis. It produces a significant reduction of symptoms and gives lesser ocular discomfort. The p-value calculated for a score on day 14 was 0.02 (less than 0.05) is significant, which indicates fortified ceftazidime+gentamicin has a better reduction of symptoms. Nevertheless, we believe our findings are important because there is no data currently available on the comparative efficacy of ciprofloxacin and fortified ceftazidime+gentamicin in the therapy of bacterial keratitis.

The limitations of this study were the inclusion of less number of eyes for the study and fewer cases of severe keratitis.

CONCLUSION

In this study, we conclude that fortified ceftazidime+gentamicin is better than ciprofloxacin for the treatment of bacterial keratitis. It produces a significant reduction of symptoms and gives lesser ocular discomfort. Thus we suggest fortified ceftazidime+gentamicin should replace ciprofloxacin as first-line monotherapy in bacterial keratitis

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AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICTS OF INTERESTS

Declared none

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