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Original article

Comparison of Tobramycin and Moxifloxacin eye drops in acute bacterial conjunctivitis: An open label randomized controlled institutional study from Kolkata

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Abstract

Topical antibiotics are used empirically to hasten the clinical cure and prevent transmission. Tobramycin and Moxifloxacin eye drops are frequently prescribed but head to head clinical comparison was not documented from eastern India. This study was aimed to compare the efficacy and safety of both antibiotics in suspected acute bacterial conjunctivitis. This study was conducted from February 2019 to May 2019. 150 patients with suspected bacterial conjunctivitis were randomized into two groups to receive either Tobramycin sulphate 0.3% W/V or Moxifloxacin 0.5% W/V eye drops 4 times daily in the effected eye for a period of seven days in an open label manner. All participants were allowed to simultaneously apply tear substitute (Carboxymethylcellulose sodium 0.5% W/V) in both eyes thrice daily. Efficacy was measured on day 3 and 7 in terms of clinical cure rate which was defined as absence of any eye sign of conjunctivitis. Safety of the drugs was assessed by the overall ocular adverse events reported by the patients. 61 patients from Tobramycin group and 66 from Moxifloxacin group completed the full study. High clinical cure rates were achieved with both agents although it was slightly higher with Moxifloxacin on day 3 (56.06% versus 47.54%; p=0.37) as well as on day 7 (93.94% versus 88.52%; p=0.52) of follow up. A single case of slight blurring of vision was reported with Tobramycin, while another patient complained of mild irritation on eyes from Moxifloxacin group. Overall ocular adverse effects were very mild and comparable. Both Tobramycin sulphate 0.3% W/V and Moxifloxacin 0.5% W/V eye drops are equally effective as empirical therapy when used in acute bacterial conjunctivitis for seven days four times daily with causing negligible side effects.

Key words: Bacterial conjunctivitis, Tobramycin, Moxifloxacin

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Bacteria are the common causative organisms for conjunctivitis in up to 50 % adult cases and 70 to 80% cases in children[1]. The disease is contagious in nature and doesn't spare any age group or geographical region[2]. It can also cause epidemics among people living in close vicinity like quarters, nursery, schools and student populations[3].

Spontaneous recovery is noted among milder cases without pharmacotherapy in 2 to 5 days time[4]. Systemic involvement is rare; though otitis media may develop in 25% children with *H influenzae* conjunctivitis[5] and systemic meningitis may complicate primary meningococcal conjunctivitis in 18% of people[6].

Empirical usage of topical antibiotics in suspected bacterial conjunctivitis has proved to hasten the clinical cure and microbiological resolution[7]. They also have role in prevention of re-infection and disease transmission[8]. The options of topical antibiotics are largely restricted to aminoglycosides and fluroquinolones. Due to the emergence of antimicrobial resistance against the older generation agents, newer drugs like Moxifloxacin and Tobramycin are now the frontline choices. In recent times however, no head to head clinical comparison was documented from eastern India between these two agents. Hence, the objective of this study was to compare and evaluate the efficacy and safety of Tobramycin and Moxifloxacin eye drops in acute bacterial conjunctivitis on a hospital based population of eastern India.

Materials and methods

It was an open-label, randomized-controlled, active comparator study conducted in a Government owned teaching cum referral hospital of Kolkata from February 2019 to May 2019. After obtaining ethical approval from the Institutional Ethics Committee (Permission no: RKC/Ethics/145; dated 08/01/2019) patients of all age groups of either sex who attended the Ophthalmology out patients department with suspected acute bacterial conjunctivitis were screened for the study. Voluntary written informed consent form was obtained from all participants after explaining the detailed study-protocol. Legal guardian provided the consent if the participant was less than 18 years of age. After initially screening of 157 patients, finally 150 patients were randomized into two groups to received either Tobramycin sulphate 0.3% W/V or Moxifloxacin 0.5% W/V eye drops 4 times daily in the affected eye for a period of seven days in an open label manner. All participants were allowed to simultaneously apply tear substitute (Carboxymethylcellulose sodium 0.5% W/V) in both eyes thrice daily for the same duration of time. Each participant was asked to follow up twice; on day 3 and day 7 to assess the prognosis. Detailed ocular examination was performed during initial as well as on all subsequent visits by qualified ophthalmologists. Efficacy was measured in terms of clinical cure rate which was defined as absence of any eye sign of conjunctivitis. Safety of the drugs was assessed by the overall ocular adverse events reported by the patients during the course of antibiotic therapy.

Statistical analysis

All the outcome data was documented in excel sheet. To deduce the statistical significance of the differences, Student's t-test was performed in case of continuous variables whereas Fisher exact test was used for categorical values.

Results

Out of 150 randomized patients, 127 finally appeared on both follow up dates and thus considered for final analysis of this study. Rest 23 patients were lost to follow up. The detailed patients flow pattern during the study period is shown in figure 1.

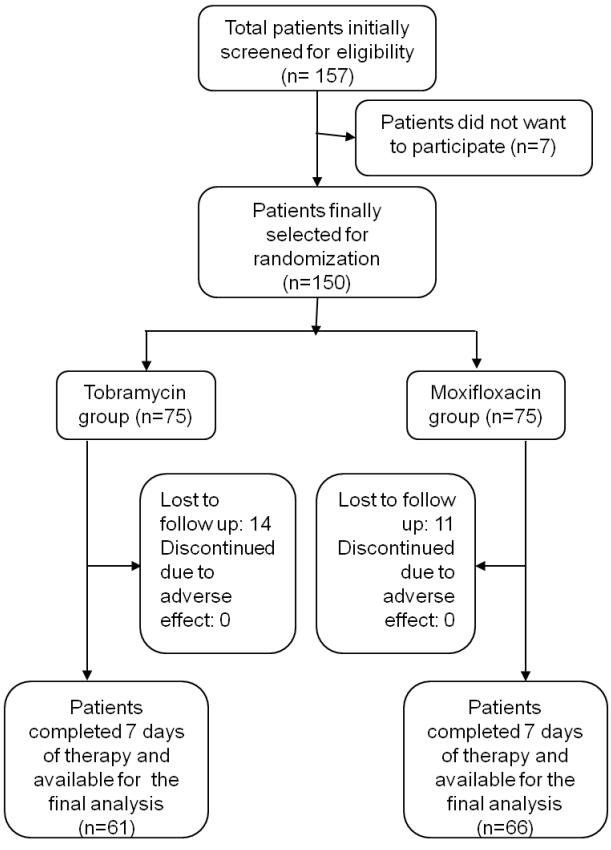

Fig 1. Patients flow during the study

Baseline demographic features of all 127 patients who completed the full study duration are displayed in table 1.

Table 1: Baseline characteristics of all patients of the study (n=127)

Gender	Male (%)	75 (59)
	Female (%)	52 (41)
Age group (years)	4–18	57
	18-40	44
	>40	26
Mean duration of complain (days)		2.7±1.5

Table 2: Comparison of efficacy and safety on day 3 and day 7

	Tobramycin (n=61)	Moxifloxacin (n=66)	*p* value
Age (years)	18.32±14.97	22.85±15.82	0.1*
Clinically cured patients on day 3	29 (47.54%)	37 (56.06%)	0.37^
Clinically cured patients on day 7	55 (88.52%)	62 (93.94%)	0.52^
Overall ocular adverse effects	1 (1.64%)	1 (1.51%)	1.0^

*Student's t-test, ^Chi-square test

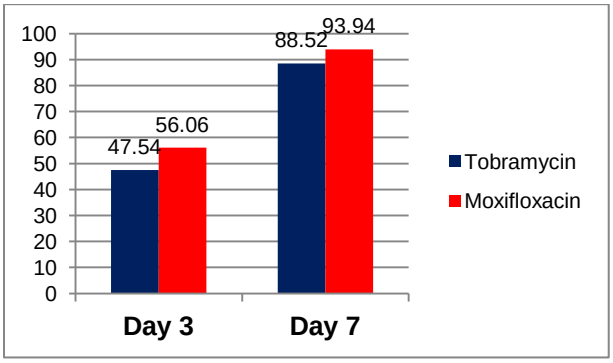

Fig 2. Comparison of clinical cure rates on day 3 and day 7

Table 2 depicts the comparison of demographic detail with efficacy and safety of the two study groups. On day 3, 29 patients from Tobramycin group and 37 patients with Moxifloxacin group achieved clinical cure. Later on day 7, 55 patients from Tobramycin group and 62 patients with Moxifloxacin group were clinically cured. Although slightly higher rates of clinical cure were reported from the patients of Moxifloxacin group; there was no statistical significance on either occasion. A single case of slight blurring of vision was reported after application of Tobramycin, while another patient complained of mild irritation on eyes from Moxifloxacin group. No significant differences could be drawn in terms of overall adverse effect related to the eyes. Figure 2 displays the diagrammatic representation of clinical cure rates observed with both study drugs on day 3 and 7.

Discussion

Suspected or culture-proven acute bacterial conjunctivitis are self-limiting in nature within 1 to 2 weeks in at least 60% of cases[9]. However according to large systemic review topical antibiotics were found to be effective in causing clinical and microbiological cure in patients with culture-proven bacterial conjunctivitis and microbial cure rate was in the group of patients with clinically suspected bacterial conjunctivitis[10]. A large meta-analysis consisting of 11 randomized controlled trials also suggested approximately 10% increase in the rate of clinical improvement compared with that for placebo for patients who received either 2 to 5 days or 6to 10days of antibiotic treatment[8]. On the contrary, no significant differences of clinical cure rates were noted in many earlier observations[10,11].

Therefore, mixed consensus exists regarding the antibiotics usage in acute conjunctivitis owing to the marginal benefit they provide. Despite this, topical antibiotics are frequently prescribed in an empirical way to provide symptomatic relief to the patients before the bacteriological culture report becomes available. Therefore clear knowledge about the extent of clinical efficacy and toxicity of such antibiotics becomes crucial especially in an institution-based practice.

At the end of current observation, substantially higher clinical cure rates among acute bacterial conjunctivitis patients were achieved with both Moxifloxacin and Tobramycin eye drops after 7 days of administration. The differences nevertheless were statistically insignificant on both day 3 and day 7 between them. Selection of appropriate patient, early arrival to hospital and simultaneous application of artificial tear substitute were the possible explanation for overall higher clinical cure rates. An earlier observation on the same topic by Koul et al however suggested Moxifloxacin to be a better agents causing a more rapid and effective clinical cure[2].

Although the present study included patients across all ages, the final clinical cure rate with Moxifloxacin was 93.94%, which was slightly higher than that of 89.2% observed among children by Koul et al[2]. In adult cases, *Staphylococcus* species are the most common pathogens, followed by *Streptococcus pneumoniae* and *Haemophilus influenza*[12,13.] On the other hand organisms like *H. influenzae*, *S. pneumoniae* and *Moraxella catarrhalis* are responsible for acute conjunctivitis among children[14,15]. Moxifloxacin a fourth generation fluroquinolone, acts by interfering with bacterial DNA replication process is known to be highly effective against both gram positive and negative organisms, which explains the higher clinical success rate. Another observation involving various fluroquinolones revealed the remission rate to be 91% with Moxifloxacin, which closely matched with that of the present one[16].

Though the response rate with Tobramycin eye drop was comparatively lesser in the current study, it was more than what was observed by Koul et al[2]. It is a bactericidal drug which acts by primarily inhibiting protein synthesis. Due to coverage against wider ranges of bacteria the drug is useful in controlling both superficial and deep infections of the eye and ocular adnexa[17]. A previous literature on antibiotics resistance among bacterial conjunctival pathogens also pointed out small yet significant reduction in resistance among *S. aureus* to Tobramycin[18].

It was especially valuable in children for two reasons. First, the predominance of Gram negative organisms in acute bacterial conjunctivitis in children which demands the use of an aminoglycoside antibiotic. It is noteworthy that among contact lens users, gram-negative bacteria like *Pseudomonas aeruginosa* are frequently found[13]. Secondly, it is preferred over fluroquinolones in order to avoid the possible adverse effect on growing musculoskeletal system in children. Though the real possibility of such an effect is debatable considering the minimal systemic absorption of an eye drop.

Development of resistance against antibiotics by the bacteria poses the biggest challenge in any chemotherapy. Irrational usage, wide-spread marketing practice and non-adherence among the patients were the key reasons cited by previous author[19]. Beside this, the difficulty in clinically differentiating between viral and bacterial conjunctivitis was often blamed for unnecessary prescription of antibiotics. A recent study revealed very high degree of antimicrobial resistance; especially against Fluroquinolones among the bacteria causing conjunctivitis[19]. In spite of these challenges, treatment failure rates were rather low in the present study, indicating judicious selection of overall empirical antibiotics and identification of right patient in the institution. A detailed study in future focusing on culture sensitivity pattern of the bacteria obtained from conjunctival swab would give more insight.

Both the agents displayed excellent safety profiles throughout the study and appeared comparable in terms of overall ocular adverse effects. One case of each of very mild eye irritation and blurred vision were reported with the application of Moxifloxacin and Tobramycin respectively. They were self-limiting in nature and did not lead to withdrawal of therapy. These findings related to the toxicities were in concurrence with earlier observations and further strengthens the safety records of these two agents[2,20].

Limitations

Firstly a single centre based study involving a relatively smaller sample size might lack statistical power. Secondly, both antibiotics were administered empirically without doing a prior bacterial culture sensitivity of the patients. Thirdly, there was chance of observer-bias while determining clinical cure from the disease by visual examination only. A standardized scoring system to evaluate the clinical prognosis could have given a more precise result. Fourthly, the open–label nature of the study could be a source of bias in the final analysis.

Conclusion

Both Tobramycin sulphate 0.3% W/V and Moxifloxacin 0.5% W/V eye drops are equally effective as empirical therapy when used in acute bacterial conjunctivitis for seven days four times a day. High rates of clinical cure were achieved with both agents with negligible side effects.

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