

Clinical Outcome in the Treatment of Fungal Keratitis Receiving 1% Voriconazole and 5% Natamycin

Bharati Gogoi¹, Emeeg Gogoi²

¹Professor, Regional Institute of Ophthalmology, Gauhati Medical College and Hospital, Guwahati, India

²Post Graduate Trainee, Regional Institute of Ophthalmology, Gauhati Medical College and Hospital, Guwahati, India

Abstract: ***Aim:** To conduct a therapeutic and exploratory clinical trial comparing the visual outcome following treatment with topical 5% Natamycin vs 1% topical Voriconazole for fungal keratitis. **Method:** 70 cases of initially suspected fungal keratitis patients were taken for treatment but 9 out of them did not come for follow up and excluded from the study. Two groups of minimum 30 patients each of isolated fungal keratitis were taken. One group received 5% Natamycin and the other group received 1% Voriconazole. Detailed histories of the patients were taken followed by thorough general and ocular examination. Blood investigations including Gram stain, Koh and Culture and Sensitivity were done. **Result:** Final visual acuity at 3months follow up improved in both Voriconazole and Natamycin treated patients and the difference was found to be statistically insignificant with p value > 0.05. **Conclusion:** The resultant clinical outcome in terms of visual acuity are same in both the groups treated with 5% Natamycin and 1 % Voriconazole.*

Keywords: Fungal keratitis, Natamycin, Voriconazole, Visual Outcome

1. Introduction

- Fungal keratitis (keratomycosis) is a fungal infection of the cornea. It primarily affects the corneal epithelium and stroma, although the endothelium and anterior chamber of the eye may get involved in more severe disease¹. Vision may be severely affected in fungal keratitis² Despite tremendous advancement of medicine and surgery, ocular infection in our society is increasing.
- It was Prof. Theodor Leber (1879) a German Ophthalmologist who first successfully isolated the fungus *Aspergillus Glaucus* from a corneal ulcer of a farmer's eye sustained injury from oats chaff while working with a threshing machine and enlisted the fungus as one of the etiopathological agent of corneal ulcer³.
- Agostino Bassi³ is rightly acknowledged to be the first to refer the etiology of an animal disease to a microbial infection and is universally regarded as Father Of Mycology.

2. Materials and Methods

This study was an hospital based cross sectional study conducted in Regional Institute of Ophthalmology. The study was conducted to assess the visual acuity and resolution of infiltrate in fungal keratitis patients who were treated with 1% Voriconazole and 5% Natamycin. 70 cases of initially suspected fungal keratitis patients were initially taken for treatment but 9 out of them did not come for follow up and excluded from the study. An informed and written consent was obtained and institutional ethical committee clearance was taken prior to conducting the study.

Inclusion criteria

- Adult patients of more than 20 years of age irrespective of sex.

- Presence of a corneal epithelial defect with stromal infiltrate or exudates, clinically suggestive of fungal ulcer with or without hypopyon.
- Widest diameter of the ulcer needed to be between 2 and 6mm as long as there is no sclera involvement.

Exclusion criteria:

- Evidence of bacteria on gram stain at the time of presentation.
- Evidence of *Acanthamoeba* or herpetic keratitis on stain or on history and examination.
- Bilateral ulcers.
- Impending perforation.
- No light perception in the affected eye.
- History of corneal ulcer in the affected eye.
- Use of antifungal drugs.
- Diabetes.
- Previous penetrating keratoplasty.
- Patient less than 20 years of age.

All subjects were subjected to detailed history and clinical examination and the findings were documented. In all cases, general and systemic examination was done.

Laboratory investigations

Blood for total count, differential leucocyte count, haemoglobin percentage and ESR, blood sugar estimation, 10% KOH, gram stain and culture and sensitivity.

3. Results and Observations

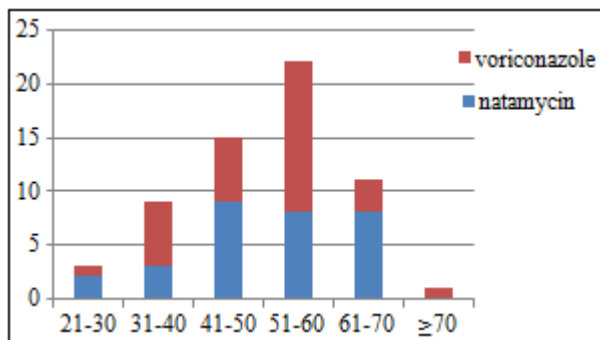


Figure 1: Distribution of patients according to age group and application of 1% Voriconazole and 5% Natamycin on them

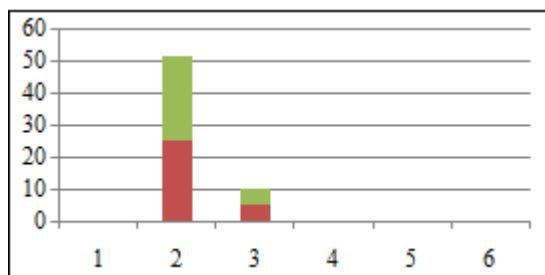


Figure 2: Distribution of patients according to sex and application of 1% Voriconazole and 5% Natamycin on them.

Table 1: Pre – treatment visual acuity at the time of discharge

Visual Acuity	At Time of First Visit	Percentage
Perception of Light	2	3.27%
Hand Movement	3	4.91%
<3/60 - HM	2	3.27%
<6/60 – 3/60	22	36.06%
< 6/18 – 6/60	29	47.54%
<6/12 – 6/18	3	4.91%
6/12 OR better	0	0

Table 2: Visual acuity at 1 month follow up after treatment with 1% Voriconazole and 5% Natamycin

Visual Acuity	Natamycin		Voriconazole	
	Number of Persons	Percentage (%)	Number of Persons	Percentage (%)
Perception of Light	2	6.66%	1	3.22%
Hand Movement	1	3.33%	0	0
<3/60 - HM	2	6.66%	0	0
<6/60 – 3/60	0	0	0	0
<6/18 – 6/60	23	76.66%	22	70.96%
<6/12 – 6/18	2	6.66%	8	25.80%
6/12 OR Better	0	0	0	0
Total	30	100%	31	100%

Table 3: Visual acuity at 3 month follow up after treatment with 1% Voriconazole and 5% Natamycin

Visual Acuity	Natamycin		Voriconazole	
	Improved	Not Improved	Improved	Not Improved
Perception of Light		2		1
Hand Movement		1		
<3/60 - HM		2		3
<6/60 – 3/60				
<6/18 – 6/60	11		3	
<6/12 – 6/18	12		10	
6/12 OR Better	2		4	
Total	25	5	27	4

4. Discussion

- In the present study , visual acuity improved in both the Natamycin and Voriconazole treated patients. The difference between the two groups was found to be statistically insignificant (p value = 0.95).
- Similar observations were made by Prajna et al.⁴In their study, 116 patients were recruited and 112 continued in the study. There was no significant difference in the visual outcome (p value = 0.79).
- Angshu Sharma et al⁵also observed in their study that the two groups of 15 patients each treated with 1% Voriconazole and 5% Natamycin showed that the best corrected visual acuity at the last follow up in each group was 1.46 in group A and 1.80 in group B. Difference was not significant statistically . (p value = 0.749). They also observed that the average time of complete resolution of infiltrate in Group A was 25.86 days and in group B it was 28 days.
- Similar observations were made by SA Iyer et al⁶
- Krishnan T et al⁷ conducted a similar study. In their study they found that the primary analysis showed no significant difference in final visual acuity with voriconazole treatment compared with natamycin. There was no difference in final infiltrate/ scar size or adverse events between the two treated groups.

5. Conclusion

From the present study we came to the conclusion that:

- The cause of fungal corneal ulcer varies in relation to age, sex, occupation and climatic condition of the region.
- In terms of efficacy, both 5% Natamycin and 1% Voriconazole are effective as first line treatment in fungal corneal ulcer.
- The resultant clinical outcome in terms of visual acuity are same in both the groups treated with 1% Voriconazole and 5% Natamycin.

References

- [1] Tuli SS. Fungal keratitis. Clinical Ophthalmology (Auckland , NZ). 2011;5:275
- [2] Chander J, Sharma A. Prevalence of fungal corneal ulcers in northern India Infection. 1994 May 1;22(3): 207-9
- [3] Chnader J. Textbook of medical Mycology. JP Medical Ltd; 2017 Nov 30
- [4] Prajna NV, John RK, Nirmalan PK, Lalitha P, Srinivasan M. A randomized clinical trial comparing 2% Econazole and 5% Natamycin for the treatment of fungal keratitis. British Journal of Ophthalmology.2003 Oct 1;87(10):1235-7.
- [5] Anshu Sharma 1, Sarita Aggarwal 2, Richa Ahluwalia3,Rahul Sahay4,Rimsha5 Clinical study of voriconazole vs. natamycin in treatment of mycotic corneal ulcers 2017/Month: November/Volume:4/ Issue:92/Page:5581-5585
- [6] Iyer SA, Tuli SS, Wagoner RC. Fungal keratitis: emerging trends and treatment outcomes. Eye & Contact lens. 2006 Dec 1;32(6):267-71.

- [7] Krishnan T, Mascarenhas J, Rajaraman R, Prajna L, Srinivasan M, Raghavan A, Oldenburg CE, Ray KJ, ZegansME, McLeod SD. The mycotic ulcer treatment trial: a randomized trial comparing natamycin vs voriconazole. JAMA ophthalmology. 2013 Apr 1;131(4):422-9