ORIGINAL RESEARCH PAPER

Ophthalmology

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

# EFFICACY OF VORICONAZOLE IN TREATMENT OF FUNGAL CORNEAL ULCERS , RCT ON EFFICACY VORICONAZLR V/S NATAMYCIN VORICONAZOLE V/NATAMYCIN

KEYWORDS: fungal corneal ulcer,voriconazole,natamycin

**DR.P.RAJEEVAN**
Associate Professor, Regional Institute of Ophthalmology, Trivandrum, Kerala

**DR.ANITHA.S**
Additional Professor, Regional Institute of Ophthalmolgy, Trivandrum, Kerala

**DR.V.SAHASRANAMAM**
DIRECTOR, RIO TRIVANDRUM

## INTRODUCTION

Corneal disease is second only to cataracts as the most common cause of blindness worldwide, [1]resulting in more than 1.5 million new cases of' vision loss annually[2]. As a consequence of attention being directed towards the management of cataracts, especially in developing countries, strategies for the management of traditional infections that cause blindness have been neglected.

Ophthalmic mycosis is emerging as a major cause of vision loss and morbidity, and can be life threatening. Fungal keratitis is one of the major causes of ophthalmic mycosis accounting for more than 50% of proven ophthalmic mycoses in some countries.[3] Fungal keratitis is usually characterized by a corneal epithelial defect and inflammation of the corneal stroma. If untreated, fungal keratitis can lead to corneal scarring and vision loss.

Fungal keratitis

The first description of fungal keratitis was in the late 1870s Fungal keratitis is most common in tropical regions and developing countries, where it constitutes over 50% of keratitis.In South India, about 44% of corneal ulcers are caused by fungi[4]. Although lower, the prevalence of fungal keratitis is still relatively high in other countries, being 17% in Nepal, 36% in Bangladesh, 38% in Ghana, and 35% in south Florida in the US. In China, the incidence has been increasing in the past decade, By contrast, fungal keratitis generally accounts for only 1%-5% of the keratitis treated in developed countries and temperate regions, such as Britain and the northern US, This also applies to Australia, where the incidence of fungal keratitis at the Royal Victorian Eye and Ear Hospital (RVEEH) in Melbourne was reported at 5%. The RVEEH is a tertiary referral eye hospital responsible for the care ofmost serious corneal infections in a population of about five million across Victoria.

Fungal keratitis is one of the major causes of ophthalmic mycosis and is difficult to treat. The range of common antifungal agents available for fungal keratitis remains inadequate and is generally associated with poor clinical outcomes. Voriconazole is a new generation triazole antifungal agent. Only marketed in systemic formulation and, with broad-spectrum activity and, high intraocular penetration, voriconazole has demonstrated effectiveness against fungal keratitis. 'Systemic voriconazole, however, is not without side effects and is costly[6,7].

Voriconazole eye drops have been prepared extemporaneously and used for the treatment of ophthalmic fungal keratitis. The voriconozole eye drops used are typically of 1% concentration, well tolerated by the eye, and are stable. Despite existing evidence to suggest that the eye drops are effective in the treatment of fungal keratitis, more studies are needed, especially in relation to using the eye drops as first-line and stand-alone treatment, preparation of higher concentrations, and optimal dosing frequency.[7]

Voriconazole is a derivative of Fluconazole,is a new triazole anti fungal agent. Like other triazoles Voriconazole inhibits cytochromp450demethylase which is essential for the synthesis of ergosterol.This adversely affect the permeability of the fungal cell membrane[8]

**Methodology**

Patients fulfilling the inclusion and exclusion criteria and who consent for the study are evaluated using standardized protocol.

Procedure for recruitment —from inpatients

The patients are grouped into 2 those in group I will be treated with Voriconazole [commercially available eye drops]. The concentration of the drug after reconstitution is 1mg/ml with all other supportive measures as per standard regime

The patients in group 2 will be given Topical Natamycin .[5%-commercially available] The patents are followed up during the course hospital admission Follow up visits in the cornea clinic of RIO. For a period 6months on a monthly basis. Data will be collected in the prescribed proforma. Blinding-patients will not know to which group they belong. Data analysis will be done by a bio statistician who also will not know the patient grouping.

This eliminates biases.

**Statistics:** The collected data will be entered into SPSS-18 and analyzed using parametric and non parametric tests. The main outcome variable is no: of days of hospital stay. It is compared in the two groups. Independent t test will be done for significance.

Corneal clarity measured in the 2 groups. Extend& depth of opacity remaining at the end point of study will be compared. Z-test will be done for significance. Best corrected visual acuity at the end point of study in 2 groups will also be compared using Mann Whitney U test. Other parameters will be tested for significance by non parametric tests.

**Probable outcome of the study**

Clinical course of the illness is assessed by slit lamp examination of the anterior segment of the eye to note corneal clarity, presence or absence of complications like corneal perforation spreading of infection into the inner coats of the eye. The status of the eye at the end of 6 weeks of follow up including best corrected visual acuity.

Ulcer healing may be faster than the conventional methods of treatment. Complications may be reduced.

Hospital stay of the patients can be shortened.

**STUDY DESIGN:** Randomized Clinical Trial

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

**STUDY DURATION**

Patients treated for fungal corneal ulcer in our hospital from 08/07/2013 for a period of three years.

**AIMS & OBJECTIVES**

**AIM :-** To find whether reconstituted voriconozole when applied topically in the treatment of laboratory proven mycotic keratitis is more efficacious than topical natamycin.

**PRIMARY:-** To study the efficacy of reconstituted voriconozole when applied topically an effective drug in the management of mycotic keratitis when compared with current regime of natamycin.

**SECONDARY :-** To study the complications of topical application of voriconozole.

**SAMPLE SIZE:-**

At the end point of the study, number of days of hospital stay, corneal status including clarity, best corrected visual acuity, are the main outcome variables. As per available information from literature a proportionate reduction in the number of days of hospital stay of 30% is assumed, being a trial using voriconazole for a follow up of 6 months it is decided to keep the clinically meaning full effect as reduction in number of days of hospital stay of 30%, for an Alfa of 0.05 and a beta of 0.2 giving a power of 80%,for the trial.

Sample size calculation done using the formula
$n=p^1[1-p^1]=p^2[1-p^2]xf(\alpha,\beta)\ /(p^2-p^1)2$ where n = number of patients needed in one arm. $p^1=30\%, p^2=50\%$.

$P^1$ =proportion of reduction of no :of days of hospital stay in the standard therapy group . $p^2$=proportion of no of days of hospital stay in the new drug using group $\alpha$ =5%,$\beta$=20% F[$\alpha$,$\beta$]8.2 this works out be 94.3 patients in one arm.

**Sample expected is 100 patients in one arm.**

**MATERIALS AND METHODS**

**STUDY SETTING**

All patients coming to the department of ophthalmology over the next three year period with a clinical &Iab diagnosis of fungal corneal ulcers will be included in the study. Simple randomization technique will be used for allotting patients the two arms. Coin tossing technique will adopted for allocating patients to the 2 arms of the study. Patients assigned to group-I will be given topical Voriconazole, the new treatment. Patients assigned to group-2 will be given the standard treatment with Natamycin

**Inclusion criteria**

1. Patients with Corneal ulcer (laboratory proven as fungal keratitis)who are willing to participate in the study

**Exclusion criteria**

1. Immune mediated ulcers
2. Patients (not co operative for scraping)
3 Extremes of age
4. Patients who are not willing to participate in the study.

**Procedure**

Under sterile precautions, corneal scrapings will be taken from the base and edges of ulcer under slit lamp using sterile no 15- BP blade after applying topical anesthetic agent done by ophthalmologist
The following microbiological examination techniques will be carried out in the Microbiology lab of RIO to isolate the fungus

Smear and culture to isolate the specific fungus include

**Direct smear** KOH mounting
Gram Staining

Fungal Culture Sabouraud' s Agar,
SA with antibiotics incubation at 23 — 25 degree C & Incubation at 35 —37 degree C

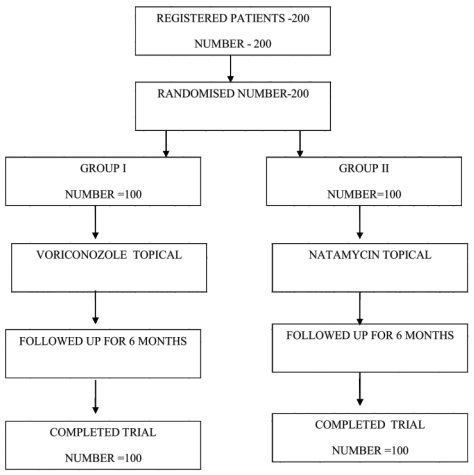
Slide Culture
Special staining techniques may be adopted whenever necessary.

By all these methods the expected fungal isolates are
1. Fusarium, 2. Aspergillus fumigatus.3. Candida albicance

Recent methods of fungal culture and sensitivity testing needs more sophisticated instruments.

Incubator is essential for keeping specimen.

**CLINICAL TRIAL FLOW DIAGRAM**




**RESULTS AND ANALYSIS**

**OBSERVATIONS AND RESULTS**

**Table 1. Age distribution**

| Age | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| < 20 yrs | 5 | 8 | 13 |
| | 5.00% | 8.00% | 6.50% |
| 20 - 29 | 9 | 11 | 20 |
| | 9.00% | 11.00% | 10.00% |
| 30 - 39 | 17 | 12 | 29 |
| | 17.00% | 12.00% | 14.50% |
| 40 - 49 | 24 | 14 | 38 |
| | 24.00% | 14.00% | 19.00% |
| 50 - 59 | 22 | 26 | 48 |
| | 22.00% | 26.00% | 24.00% |
| 60 - 69 | 16 | 21 | 37 |
| | 16.00% | 21.00% | 18.50% |
| >= 70 yrs | 7 | 8 | 15 |
| | 7.00% | 8.00% | 7.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 5.462; P > 0.05 | | | |

It is seen that the mean age of the study participants in Group I 46.91 with SD 15.05.In Group II, 47.95 with SD 17.54.It is comparable in both groups.

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

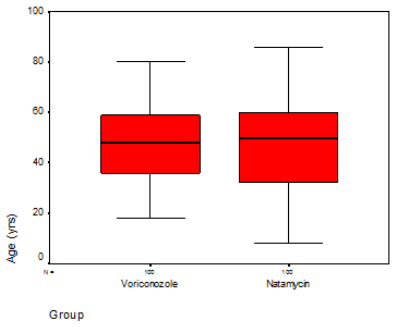
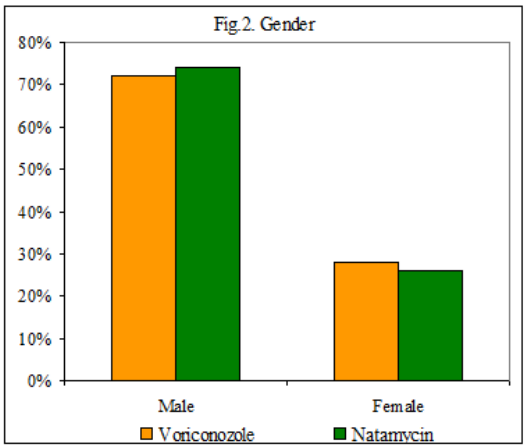



**Table 2. Gender distribution**

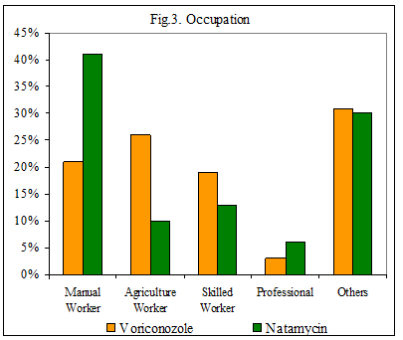
| Gender | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Male | 72 | 74 | 146 |
| | 72.00% | 74.00% | 73.00% |
| Female | 28 | 26 | 54 |
| | 28.00% | 26.00% | 27.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 0.101; P > 0.05 | | | |




In Group I- 72 % were male, 28 % female. In Group II 74% was male and 26% female
It is comparable in both groups. Chi square 0.101, P<0.05

Table 3. Occupation of Patients

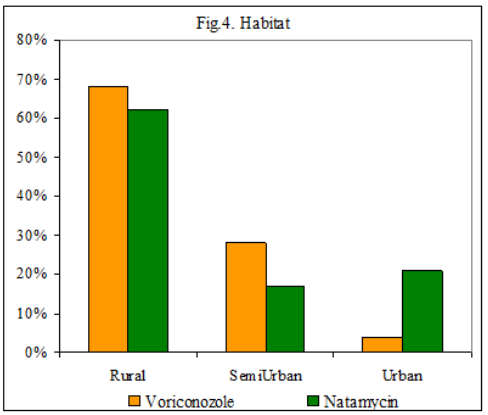
| Occupation | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Manual Worker | 21 | 41 | 62 |
| | 21.00% | 41.00% | 31.00% |
| Agriculture Worker | 26 | 10 | 36 |
| | 26.00% | 10.00% | 18.00% |
| Skilled Worker | 19 | 13 | 32 |
| | 19.00% | 13.00% | 16.00% |
| Professional | 3 | 6 | 9 |
| | 3.00% | 6.00% | 4.50% |
| Others | 31 | 30 | 61 |
| | 31.00% | 30.00% | 30.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 15.704; P < 0.01 | | | |




Of the 100 patients in the Group I 26 % were agricultural workers 21% manual worker 19 % skilled workers 3 % professionals 31 % others.
In the Group II agricultural workers 10%, manual workers 41%,skilled workers 13%,professionals 6% and others 30%.
Shows that total corneal ulcers occurs more in manual labourer and agricultural workers. This is seen worldwide as per literature.

Table 4. Habitat (Place of residence)

| Habitat | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Rural | 68 | 62 | 130 |
| | 68.00% | 62.00% | 65.00% |
| Semi Urban | 28 | 17 | 45 |
| | 28.00% | 17.00% | 22.50% |
| Urban | 4 | 21 | 25 |
| | 4.00% | 21.00% | 12.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 14.526; P < 0.01 | | | |

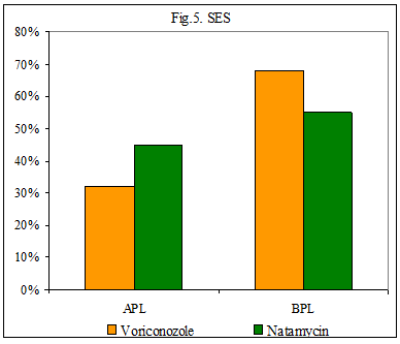



Maximum percentage of patients enrolled for this study was living in rural areas and semi urban areas. This is uncommon in urban habitat. This also agrees with common global scenario as per literature.

Table 5. Socio Economic status

| SocioEconomic Status | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| APL | 32 | 45 | 77 |
| | 32.00% | 45.00% | 38.50% |
| BPL | 68 | 55 | 123 |
| | 68.00% | 55.00% | 61.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 3.569; P > 0.05 | | | |

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

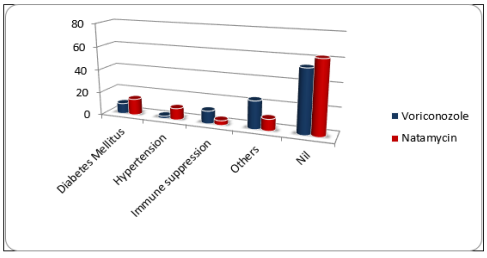



Comparable in both groups

There is no statistical significant. This disease occurs in low socio economic status patients.

Table- 6. PAST MEDICAL HISTORY

| Past Medical History | Voriconozole | Natamycin |
|---|---|---|
| DM | 9 | 14 |
| HYPERTENSION | 2 | 10 |
| IMMUNE SUPPRESSION | 11 | 4 |
| OTHERS | 24 | 10 |
| NIL | 54 | 62 |




Comparable in both groups .No statistical significance

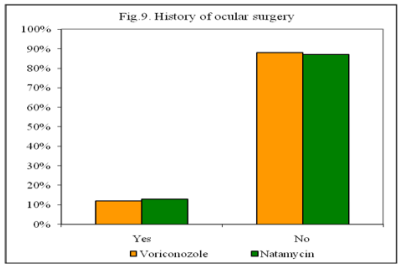
Table- 7. Personal hygiene

| Personal Hygiene | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| very poor | 20 | 33 | 53 |
| poor | 13 | 31 | 44 |
| Good | 43 | 19 | 62 |
| very Good | 24 | 17 | 41 |
| Total | 100 | 100 | 200 |

In Group I- 43% patient's good personal hygiene but in Group II it was in 19%.
Comparable in both groups. No statistical significance

Table- 8. History of ocular surgery

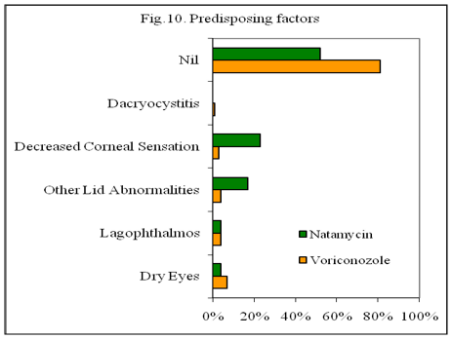
| History of Ocular Surgery | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Yes | 12 | 13 | 25 |
| | 12.00% | 13.00% | 12.50% |
| No | 88 | 87 | 175 |
| | 88.00% | 87.00% | 87.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 0.046; P > 0.05 | | | |




Present in 12% in Group I, 13% in Group II. Absent 88% in Group I , 87% in Group II comparable in both groups. No statistical significance

Table 9.Predisposing factors

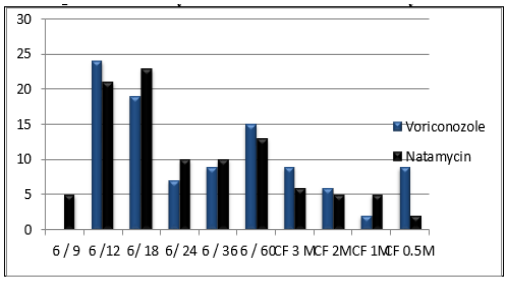
| Predisposing Factors | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Dry Eyes | 7 | 4 | 11 |
| | 7.00% | 4.00% | 5.50% |
| Lagophthalmos | 4 | 4 | 8 |
| | 4.00% | 4.00% | 4.00% |
| Other Lid Abnormalities | 4 | 17 | 21 |
| | 4.00% | 17.00% | 10.50% |
| Decreased Corneal Sensation | 3 | 23 | 26 |
| | 3.00% | 23.00% | 13.00% |
| Dacryocystitis | 1 | | 1 |
| | 1.00% | | 0.50% |
| Nil | 81 | 52 | 133 |
| | 81.00% | 52.00% | 66.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 31.574; P < 0.001 | | | |




Dry eye 7% in Group I and 4% in GroupII. Lagophthalmos 4% in Group I and 4% in Group II. Other lid abnormalities 4% in Group I and 17% in Group II. Decreased corneal sensation 3% in group i and 23 % in group II. Dacryocystitis present 1% in both groups.

Chi square test Value 31.574 p<0.001 statistically significant

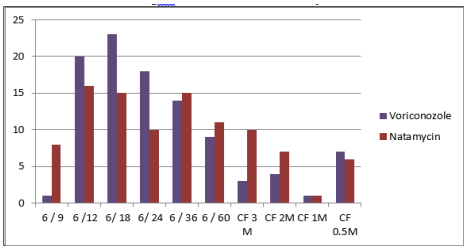
Table: 11-visual acuity at admission: RE
Fig.11visual acuity at admission ulcer affected eye: RE



Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

Table 12. Ocular examination: Left eye

Fig:12 Ocular examination: Left eye




ULCER AFFECTED EYE

Right Eye affected in 43% patients in Group I 56% in Group II.

Left Eye 50% in Group I 44% in Group II ,Both Eye in 7% cases.

Chi square 9.090 p<0.05

| Ulcer Affected | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Right Eye | 43 | 56 | 99 |
| | 43.00% | 56.00% | 49.50% |
| Left Eye | 50 | 44 | 94 |
| | 50.00% | 44.00% | 47.00% |
| Both Eye | 7 | | 7 |
| | 7.00% | | 3.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 9.090; P < 0.05 | | | |

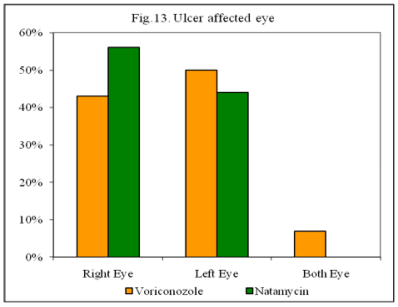
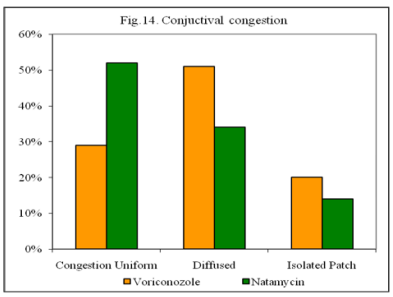



Table-14-Conjunctival congestion

| Conjunctival Congestion | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Congestion Uniform | 29 | 52 | 81 |
| | 29.00% | 52.00% | 40.50% |
| Diffused | 51 | 34 | 85 |
| | 51.00% | 34.00% | 42.50% |
| Isolated Patch | 20 | 14 | 34 |
| | 20.00% | 14.00% | 17.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 10.990; P < 0.01 | | | |




Uniform in 29% in GroupI-and 52% in group II. Diffused congestion 51% in Group I and 34% in group I1

Isolated patch 20% in group I , 14% in Group II

Chi square 10.990 p<0.001

Table.15- Size of ulcer at admission

| Size of Ulcer | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| < 2mm | 24 | 19 | 43 |
| | 24.00% | 19.00% | 21.50% |
| >2mm –< 4mm | 57 | 58 | 115 |
| | 57.00% | 58.00% | 57.50% |
| >4 mnm–< 6mm | 15 | 18 | 33 |
| | 15.00% | 18.00% | 16.50% |
| >= 6mm | 4 | 5 | 9 |
| | 4.00% | 5.00% | 4.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 0.974; P > 0.05 | | | |

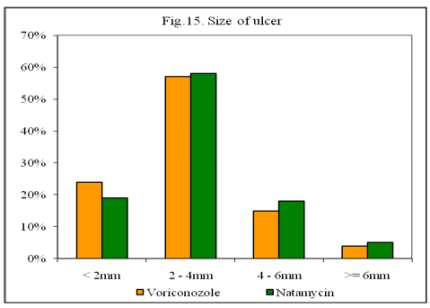



Table. #. Depth of ulcer

| Depth of Ulcer | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Superficial Stromal | 15 | 31 | 46 |
| | 15.00% | 31.00% | 23.00% |
| Mild Stromal | 59 | 43 | 102 |
| | 59.00% | 43.00% | 51.00% |
| Deep Stromal | 26 | 26 | 52 |
| | 26.00% | 26.00% | 26.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 8.075; P < 0.05 | | | |

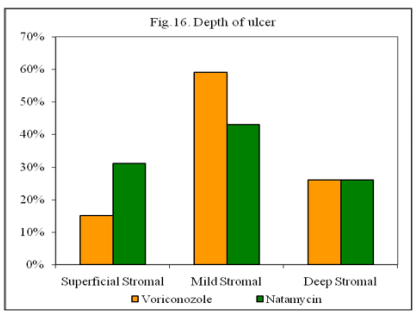



Table. Additional features

| Additional Features | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Vascularization | 51 | 53 | 104 |
| | 51.00% | 53.00% | 52.00% |
| Pigmentation | 42 | 36 | 78 |
| | 42.00% | 36.00% | 39.00% |
| Sclera Involvement | 7 | 11 | 18 |
| | 7.00% | 11.00% | 9.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 1.389; P > 0.05 | | | |

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

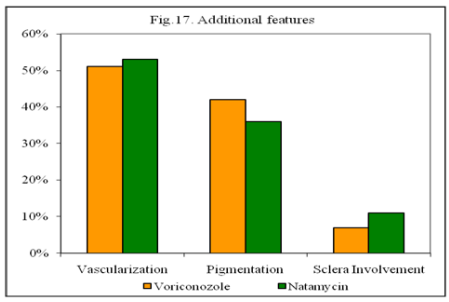



Table #. Duration of hospital stay

| Duration of Hospital Stay | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 1 Week | 52 | | 52 |
| | 52.00% | | 26.00% |
| 2 Week | 48 | 53 | 101 |
| | 48.00% | 53.00% | 50.50% |
| 3 Week | | 37 | 37 |
| | | 37.00% | 18.50% |
| 4 Week | | 7 | 7 |
| | | 7.00% | 3.50% |
| 5 Week | | 3 | 3 |
| | | 3.00% | 1.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 99.248; P < 0.001 | | | |

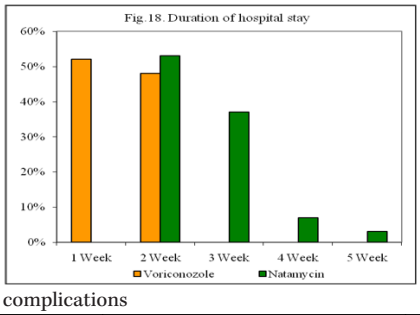



Table #. OE complications

| OE: Complications | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Perforation | 8 | 30 | 38 |
| | 8.00% | 30.00% | 19.00% |
| PseudoCornea | | 38 | 38 |
| | | 38.00% | 19.00% |
| Nil | 92 | 32 | 124 |
| | 92.00% | 32.00% | 62.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 79.769; P < 0.001 | | | |

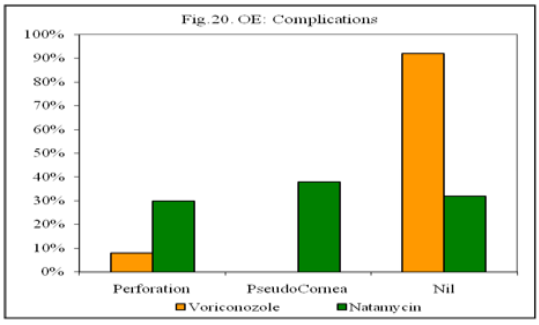



Table Culture and sensitivity

| Culture & Sensitivity | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| *Fusarium* | 24 | 29 | 53 |
| | 24.00% | 29.00% | 26.50% |
| *Aspergillus niger* | 20 | 12 | 32 |
| | 20.00% | 12.00% | 16.00% |
| *Aspergillus flavour* | 10 | 16 | 26 |
| | 10.00% | 16.00% | 13.00% |
| *Aspergillus fumigatus* | 26 | 20 | 46 |
| | 26.00% | 20.00% | 23.00% |
| *Candida* | 10 | 9 | 19 |
| | 10.00% | 9.00% | 9.50% |
| *Basidiobolus* | 3 | 3 | 6 |
| | 3.00% | 3.00% | 3.00% |
| *Pencillium* | 1 | 1 | 2 |
| | 1.00% | 1.00% | 1.00% |
| *Phoma* | 1 | 2 | 3 |
| | 1.00% | 2.00% | 1.50% |
| *Mucor* | 2 | 2 | 4 |
| | 2.00% | 2.00% | 2.00% |
| *Sepctidonium* | 1 | 1 | 2 |
| | 1.00% | 1.00% | 1.00% |
| *Trichoderma* | 1 | 1 | 2 |
| | 1.00% | 1.00% | 1.00% |
| *Aureobacidium* | 1 | 4 | 5 |
| | 1.00% | 4.00% | 2.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 6.825; P > 0.05 | | | |

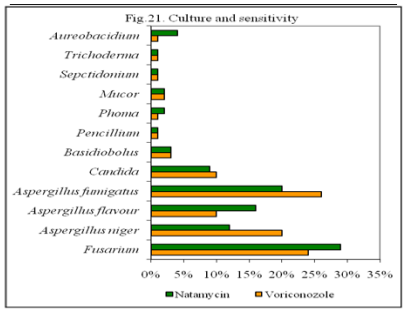



Table # 1 Week Follow Up: RE Vision

| Follow Up: 1 Week: RE Vision | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | | 5 | 5 |
| | | 5.00% | 2.50% |
| 6/12 | 30 | 21 | 51 |
| | 30.00% | 21.00% | 25.50% |
| 6/18 | 18 | 24 | 42 |
| | 18.00% | 24.00% | 21.00% |
| 6/24 | 6 | 11 | 17 |
| | 6.00% | 11.00% | 8.50% |
| 6/36 | 15 | 13 | 28 |
| | 15.00% | 13.00% | 14.00% |
| CF 0.5m | 4 | 3 | 7 |
| | 4.00% | 3.00% | 3.50% |
| 6/60 | 12 | 8 | 20 |
| | 12.00% | 8.00% | 10.00% |

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

| | | | |
|---|---|---|---|
| CF 1m | 5 | 6 | 11 |
| | 5.00% | 6.00% | 5.50% |
| CF 2m | 7 | 8 | 15 |
| | 7.00% | 8.00% | 7.50% |
| CF 3m | 3 | 1 | 4 |
| | 3.00% | 1.00% | 2.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 11.159; P > 0.05 | | | |

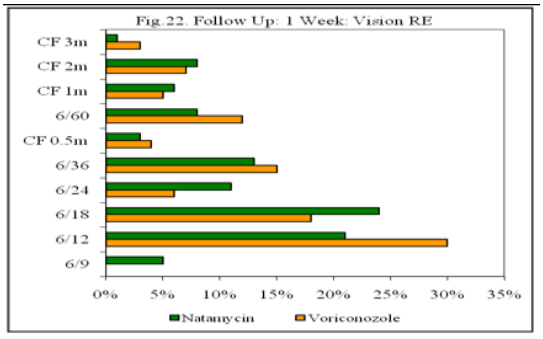



Table #. 1 Week follow up: left eye vision

| Follow Up: 1 Week: LE Vision | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | 1 | 8 | 9 |
| | 1.00% | 8.00% | 4.50% |
| 6/12 | 29 | 16 | 45 |
| | 29.00% | 16.00% | 22.50% |
| 6/18 | 25 | 18 | 43 |
| | 25.00% | 18.00% | 21.50% |
| 6/24 | 17 | 10 | 27 |
| | 17.00% | 10.00% | 13.50% |
| 6/36 | 12 | 22 | 34 |
| | 12.00% | 22.00% | 17.00% |
| CF 0.5m | 1 | 6 | 7 |
| | 1.00% | 7.00% | 3.50% |
| 6/60 | 7 | 1 | 8 |
| | 7.00% | 1.00% | 4.00% |
| CF 1m | 5 | 2 | 7 |
| | 5.00% | 2.00% | 3.50% |
| CF 2m | 2 | 9 | 11 |
| | 2.00% | 9.00% | 5.50% |
| CF 3m | 1 | 7 | 8 |
| | 1.00% | 7.00% | 4.00% |
| HM | | 1 | 1 |
| | | 1.00% | 0.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 34.502; P < 0.001 | | | |

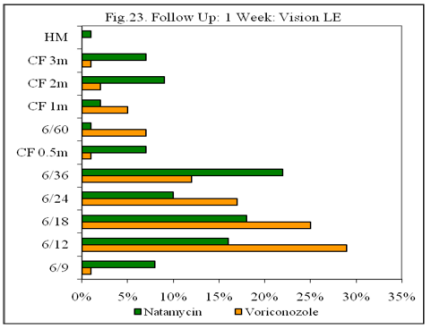



Table. #. 1 Week follow up: Size

| Follow Up: 1 Week: Size | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| < 2mm | 88 | 81 | 169 |
| | 88.00% | 81.00% | 84.50% |
| 2 - 4mm | 12 | 18 | 30 |
| | 12.00% | 18.00% | 15.00% |
| 4 - 6mm | | 1 | 1 |
| | | 1.00% | 0.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 2.491; P > 0.05 | | | |

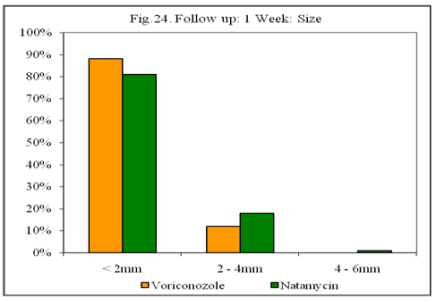



Table #. 1 Week follow up: Depth

| Follow Up: 1 Week: Depth | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Superficial Stromal | 15 | 31 | 46 |
| | 15.00% | 31.00% | 23.00% |
| Mild Stromal | 59 | 43 | 102 |
| | 59.00% | 43.00% | 51.00% |
| Deep Stromal | 26 | 26 | 52 |
| | 26.00% | 26.00% | 26.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 8.075; P < 0.05 | | | |

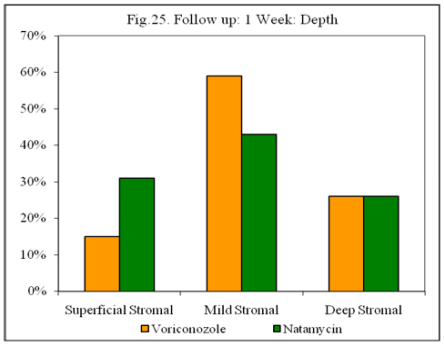



Table #. 1 Week follow up: Edges

| Follow Up: 1 Week: Edges | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Overhanging | | 19 | 19 |
| | | 19.00% | 9.50% |
| Flat | | 50 | 50 |
| | | 50.00% | 25.00% |
| Dwelling | 11 | 25 | 36 |
| | 11.00% | 25.00% | 18.00% |
| Clear | 89 | 6 | 95 |
| | 89.00% | 6.00% | 47.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 146.960; P < 0.001 | | | |

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

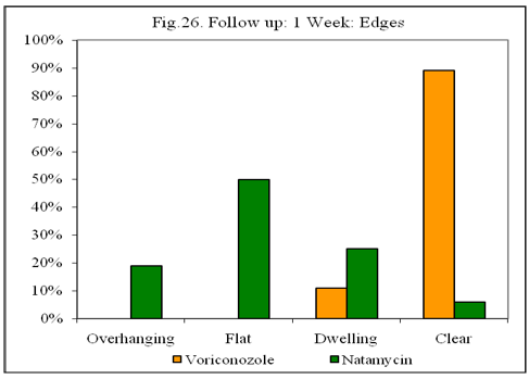



Table #. 1 Week follow up: Base

| Follow Up: 1 Week: Base | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Debris | 11 | 89 | 100 |
| | 11.00% | 89.00% | 50.00% |
| Clear | 89 | 11 | 100 |
| | 89.00% | 11.00% | 50.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 121.680; P < 0.001 | | | |

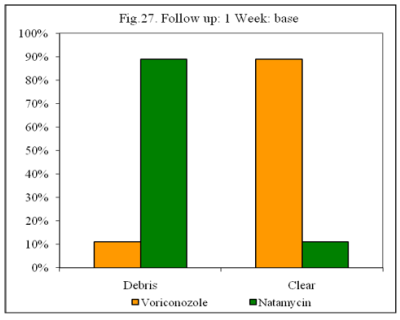



Table. #. 1 week follow up: A/C reaction

| Follow Up: 1 Week: A/C Reaction | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 1 + | 26 | 6 | 32 |
| | 26.00% | 6.00% | 16.00% |
| 2 + | 12 | 7 | 19 |
| | 12.00% | 7.00% | 9.50% |
| 3 + | | 4 | 4 |
| | | 4.00% | 2.00% |
| Nil | 62 | 83 | 145 |
| | 62.00% | 83.00% | 72.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 20.857; P < 0.001 | | | |

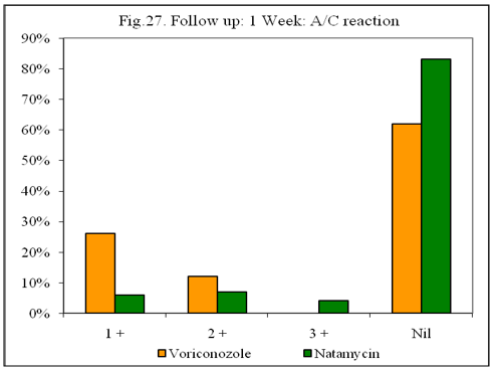



Table #. 1 week follow up: Pupil

| Follow Up: 1 Week: Pupil | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Widely Dilated | 1 | 43 | 44 |
| | 1.00% | 43.00% | 22.00% |
| Semi Dilated | 5 | 57 | 62 |
| | 5.00% | 57.00% | 31.00% |
| Normal | 94 | | 94 |
| | 94.00% | | 47.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 177.704; P < 0.001 | | | |

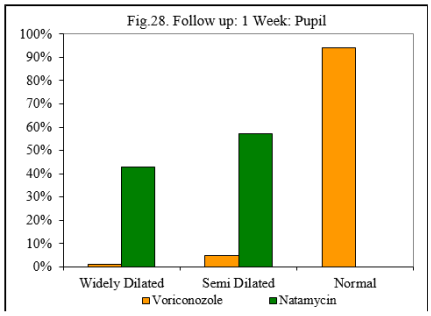



Table.#. 1 Week follow up: Signs of healing

| Follow Up: 1 Week: Signs of Healing | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Healed | 65 | 44 | 109 |
| | 65.00% | 44.00% | 54.50% |
| Not Healed | 35 | 56 | 91 |
| | 35.00% | 56.00% | 45.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 8.892; P < 0.01 | | | |

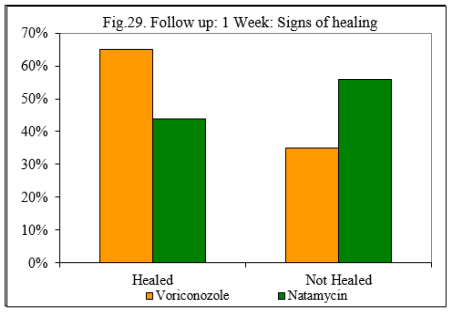



Table #. 1 month follow up: right eye vision

| Follow Up: 1 Month: RE Vision | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | | 5 | 5 |
| | | 5.00% | 2.50% |
| 6/12 | 43 | 21 | 64 |
| | 43.00% | 21.00% | 32.00% |
| 6/18 | 19 | 24 | 43 |
| | 19.00% | 24.00% | 21.50% |
| 6/24 | 11 | 11 | 22 |
| | 11.00% | 11.00% | 11.00% |
| 6/36 | 10 | 13 | 23 |
| | 10.00% | 13.00% | 11.50% |

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

| | | | |
|---|---|---|---|
| CF 0.5m | 6 | 3 | 9 |
| | 6.00% | 3.00% | 4.50% |
| 6/60 | 7 | 8 | 15 |
| | 7.00% | 8.00% | 7.50% |
| CF 1m | | 6 | 6 |
| | | 6.00% | 3.00% |
| CF 2m | 1 | 8 | 9 |
| | 1.00% | 8.00% | 4.50% |
| CF 3m | 3 | 1 | 4 |
| | 3.00% | 1.00% | 2.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 27.046; P < 0.01 | | | |

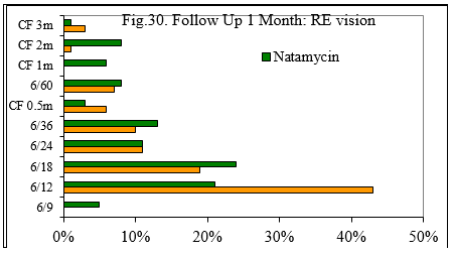



Table #. 1 month follow up: left eye vision

| Follow Up: 1 Month: LE Vision | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | 1 | 8 | 9 |
| | 1.00% | 8.00% | 4.50% |
| 6/12 | 55 | 16 | 71 |
| | 55.00% | 16.00% | 35.50% |
| 6/18 | 19 | 18 | 37 |
| | 19.00% | 18.00% | 18.50% |
| 6/24 | 12 | 10 | 22 |
| | 12.00% | 10.00% | 11.00% |
| 6/36 | 7 | 24 | 31 |
| | 7.00% | 24.00% | 15.50% |
| CF 0.5m | 1 | 4 | 5 |
| | 1.00% | 4.00% | 2.50% |
| 6/60 | 3 | 1 | 4 |
| | 3.00% | 1.00% | 2.00% |
| CF 1m | 1 | 2 | 3 |
| | 1.00% | 2.00% | 1.50% |
| CF 2m | | 9 | 9 |
| | | 9.00% | 4.50% |
| CF 3m | 1 | 7 | 8 |
| | 1.00% | 7.00% | 4.00% |
| HM | | 1 | 1 |
| | | 1.00% | 0.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 54.032; P < 0.001 | | | |

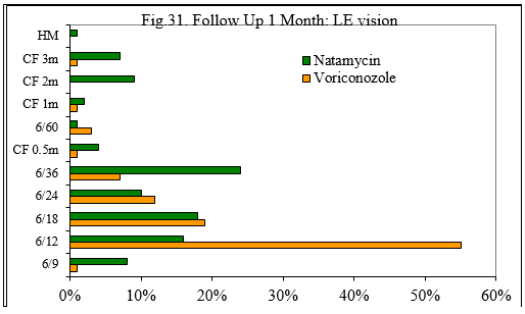



Table #. 1 month follow up: depth

| Follow Up: 1 Month: Depth | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Superficial Stromal | 15 | 31 | 46 |
| | 15.00% | 31.00% | 23.00% |
| Mild Stromal | 59 | 43 | 102 |
| | 59.00% | 43.00% | 51.00% |
| Deep Stromal | 26 | 26 | 52 |
| | 26.00% | 26.00% | 26.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 8.075; P < 0.05 | | | |

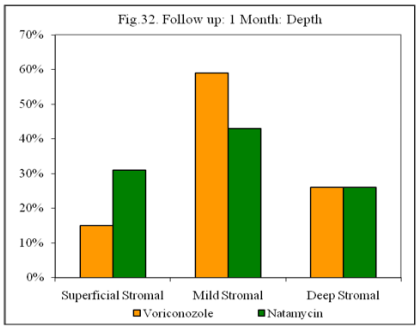



Table #. 1 month follow up: edges

| Follow Up: 1 Month: Edges | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Overhanging | 17 | 18 | 35 |
| | 17.00% | 18.00% | 17.50% |
| Flat | 28 | 32 | 60 |
| | 28.00% | 32.00% | 30.00% |
| Dwelling | 22 | 15 | 37 |
| | 22.00% | 15.00% | 18.50% |
| Clear | 33 | 35 | 68 |
| | 33.00% | 35.00% | 34.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 1.678; P > 0.05 | | | |

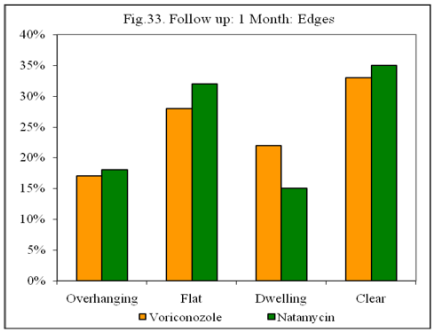



Table #. 1 month follow up: base

| Follow Up: 1 Month: Base | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Debris | | 89 | 89 |
| | | 89.00% | 44.50% |
| Clear | 100 | 11 | 111 |
| | 100.00% | 11.00% | 55.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 160.360; P < 0.001 | | | |

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

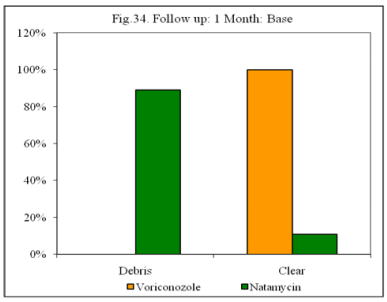



Table #. 1 month follow up: pupil

| Follow Up: 1 Month: Pupil | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Widely Dilated | | 43 | 43 |
| | | 43.00% | 21.50% |
| Semi Dilated | | 57 | 57 |
| | | 57.00% | 28.50% |
| Normal | 100 | | 100 |
| | 100.00% | | 50.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 200.000; P < 0.001 | | | |

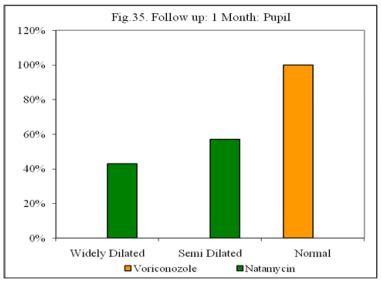



Table #. 1 month follow up: signs of healing

| Follow Up: 1 Month: Signs of Healing | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Healed | 64 | 44 | 108 |
| | 64.00% | 44.00% | 54.00% |
| Not Healed | 36 | 56 | 92 |
| | 36.00% | 56.00% | 46.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 8.052; P < 0.01 | | | |

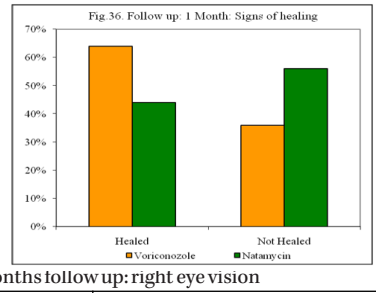



Table #. 3 months follow up: right eye vision

| Follow Up: 3 Months: RE Vision | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | | 5 | 5 |
| | | 5.00% | 2.50% |
| 6/12 | 43 | 21 | 64 |
| | 43.00% | 21.00% | 32.00% |
| 6/18 | 19 | 24 | 43 |
| | 19.00% | 24.00% | 21.50% |
| 6/24 | 11 | 11 | 22 |
| | 11.00% | 11.00% | 11.00% |
| 6/36 | 10 | 12 | 22 |
| | 10.00% | 12.00% | 11.00% |
| CF 0.5m | 6 | 4 | 10 |
| | 6.00% | 4.00% | 5.00% |
| 6/60 | 7 | 8 | 15 |
| | 7.00% | 8.00% | 7.50% |
| CF 1m | | 6 | 6 |
| | | 6.00% | 3.00% |
| CF 2m | 1 | 8 | 9 |
| | 1.00% | 8.00% | 4.50% |
| CF 3m | 3 | 1 | 4 |
| | 3.00% | 1.00% | 2.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 26.237; P < 0.01 | | | |

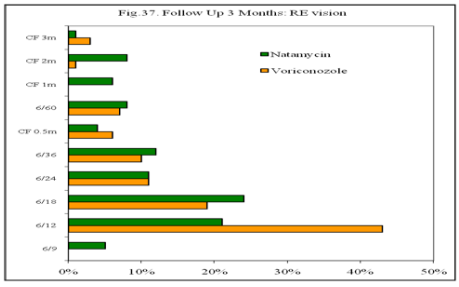
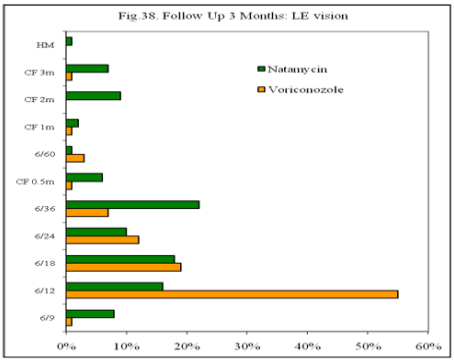



Table #. 3 months follow up: left eye vision

| Follow Up: 3 Months: LE Vision | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | 1 | 8 | 9 |
| | 1.00% | 8.00% | 4.50% |
| 6/12 | 55 | 16 | 71 |
| | 55.00% | 16.00% | 35.50% |
| 6/18 | 19 | 18 | 37 |
| | 19.00% | 18.00% | 18.50% |
| 6/24 | 12 | 10 | 22 |
| | 12.00% | 10.00% | 11.00% |
| 6/36 | 7 | 22 | 29 |
| | 7.00% | 22.00% | 14.50% |
| CF 0.5m | 1 | 6 | 7 |
| | 1.00% | 6.00% | 3.50% |
| 6/60 | 3 | 1 | 4 |
| | 3.00% | 1.00% | 2.00% |
| CF 1m | 1 | 2 | 3 |
| | 1.00% | 2.00% | 1.50% |
| CF 2m | | 9 | 9 |
| | | 9.00% | 4.50% |
| CF 3m | 1 | 7 | 8 |
| | 1.00% | 7.00% | 4.00% |
| HM | | 1 | 1 |
| | | 1.00% | 0.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 54.239; P < 0.001 | | | |



Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

Table #. 3 months follow up: size

| Follow Up: 3 Months: Size | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 0 | | 100 | 100 |
| | | 100.00% | 50.00% |
| < 2mm | 100 | | 100 |
| | 100.00% | | 50.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 200.000; P < 0.001 | | | |

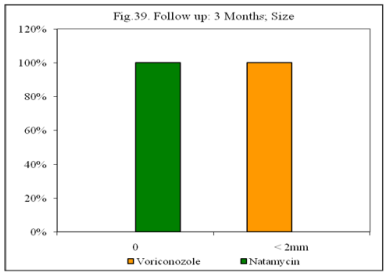



Table #. 3 months follow up: depth

| Follow Up: 3 Months: Depth | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Superficial Stromal | 15 | 31 | 46 |
| | 15.00% | 31.00% | 23.00% |
| Mild Stromal | 59 | 43 | 102 |
| | 59.00% | 43.00% | 51.00% |
| Deep Stromal | 26 | 26 | 52 |
| | 26.00% | 26.00% | 26.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 8.075; P < 0.05 | | | |

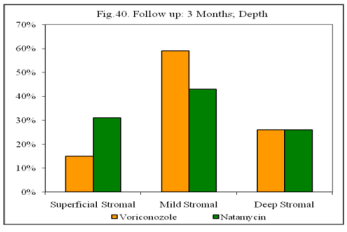



Table #. 3 months follow up: edges

| Follow Up: 3 Months: Edges | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Overhanging | 1 | 18 | 19 |
| | 1.00% | 18.00% | 9.50% |
| Flat | 1 | 20 | 21 |
| | 1.00% | 20.00% | 10.50% |
| Dwelling | | 10 | 10 |
| | | 10.00% | 5.00% |
| Clear | 98 | 52 | 150 |
| | 98.00% | 52.00% | 75.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 56.508; P < 0.001 | | | |

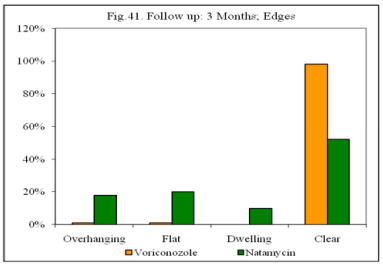



Table #. 3 months follow up: base

| Follow Up: 3 Months: Base | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Debris | 11 | 89 | 100 |
| | 11.00% | 89.00% | 50.00% |
| Clear | 89 | 11 | 100 |
| | 89.00% | 11.00% | 50.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 121.680; P < 0.001 | | | |

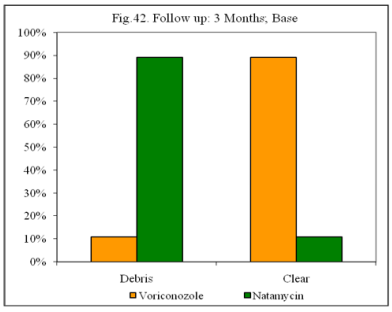



Table #. 3 months follow up: pupil

| Follow Up: 3 Months: Pupil | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Widely Dilated | | 43 | 43 |
| | | 43.00% | 21.50% |
| Semi Dilated | | 57 | 57 |
| | | 57.00% | 28.50% |
| Normal | 100 | | 100 |
| | 100.00% | | 50.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 200.000; P < 0.001 | | | |

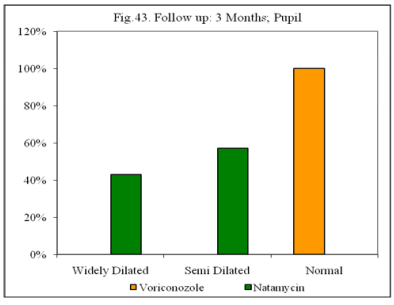
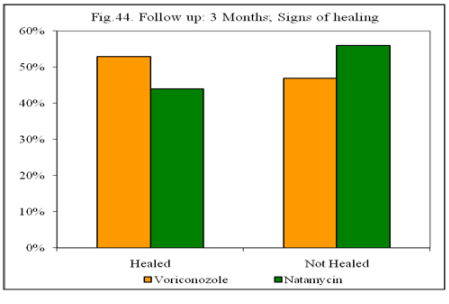



Table #. 3 months follow up: signs of healing

| Follow Up: 3 Months: Signs of Healing | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Healed | 53 | 44 | 97 |
| | 53.00% | 44.00% | 48.50% |
| Not Healed | 47 | 56 | 103 |
| | 47.00% | 56.00% | 51.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 1.621; P > 0.05 | | | |



Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

Table #. 6 months follow up: right eye vision

| Follow Up: 6 Months: RE Vision | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | | 5 | 5 |
| | | 5.00% | 2.50% |
| 6/12 | 43 | 21 | 64 |
| | 43.00% | 21.00% | 32.00% |
| 6/18 | 19 | 24 | 43 |
| | 19.00% | 24.00% | 21.50% |
| 6/24 | 11 | 12 | 23 |
| | 11.00% | 12.00% | 11.50% |
| 6/36 | 10 | 11 | 21 |
| | 10.00% | 11.00% | 10.50% |
| CF 0.5m | 6 | 4 | 10 |
| | 6.00% | 4.00% | 5.00% |
| 6/60 | 7 | 8 | 15 |
| | 7.00% | 8.00% | 7.50% |
| CF 1m | | 6 | 6 |
| | | 6.00% | 3.00% |
| CF 2m | 1 | 8 | 9 |
| | 1.00% | 8.00% | 4.50% |
| CF 3m | 3 | 1 | 4 |
| | 3.00% | 1.00% | 2.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 26.146; P < 0.01 | | | |

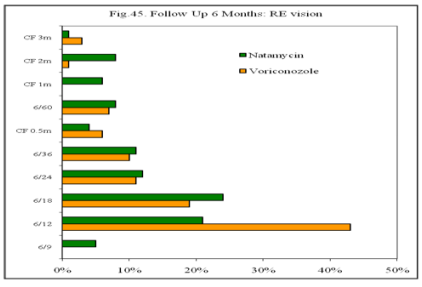



Table #. 6 months follow up: left eye vision

| Follow Up: 6 Months: LE Vision | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | 1 | 8 | 9 |
| | 1.00% | 8.00% | 4.50% |
| 6/12 | 55 | 16 | 71 |
| | 55.00% | 16.00% | 35.50% |
| 6/18 | 19 | 18 | 37 |
| | 19.00% | 18.00% | 18.50% |
| 6/24 | 12 | 10 | 22 |
| | 12.00% | 10.00% | 11.00% |
| 6/36 | 7 | 22 | 29 |
| | 7.00% | 22.00% | 14.50% |
| CF 0.5m | 1 | 6 | 7 |
| | 1.00% | 6.00% | 3.50% |
| 6/60 | 3 | 1 | 4 |
| | 3.00% | 1.00% | 2.00% |
| CF 1m | 1 | 2 | 3 |
| | 1.00% | 2.00% | 1.50% |
| CF 2m | | 9 | 9 |
| | | 9.00% | 4.50% |
| CF 3m | 1 | 7 | 8 |
| | 1.00% | 7.00% | 4.00% |
| HM | | 1 | 1 |
| | | 1.00% | 0.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 54.239; P < 0.001 | | | |

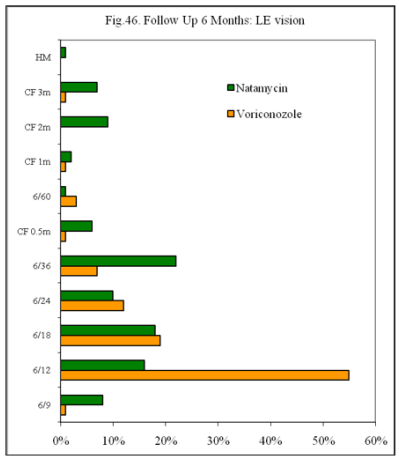



Table #. 6 months follow up: size

| Follow Up: 6 Months: Size | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 0 | | 100 | 100 |
| | | 100.00% | 50.00% |
| < 2mm | 100 | | 100 |
| | 100.00% | | 50.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 200.000; P < 0.001 | | | |

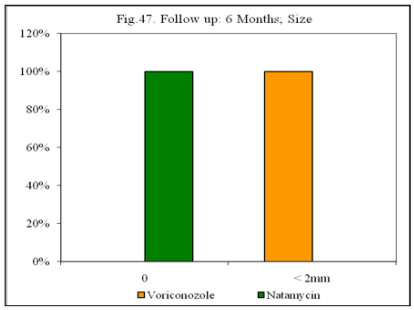
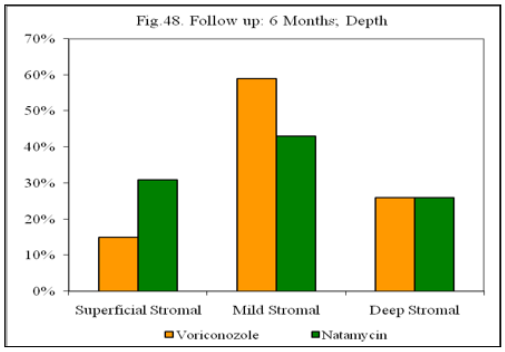



Table #. 6 months follow up: depth

| Follow Up: 6 Months: Depth | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Superficial Stromal | 15 | 31 | 46 |
| | 15.00% | 31.00% | 23.00% |
| Mild Stromal | 59 | 43 | 102 |
| | 59.00% | 43.00% | 51.00% |
| Deep Stromal | 26 | 26 | 52 |
| | 26.00% | 26.00% | 26.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 8.075; P < 0.05 | | | |



Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

Table #. 6 months follow up: edges

| Follow Up: 6 Months: Edges | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Overhanging | 1 | 7 | 8 |
| | 1.00% | 7.00% | 4.00% |
| Flat | 1 | 6 | 7 |
| | 1.00% | 6.00% | 3.50% |
| Dwelling | | 6 | 6 |
| | | 6.00% | 3.00% |
| Clear | 98 | 81 | 179 |
| | 98.00% | 81.00% | 89.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 15.686; P < 0.01 | | | |

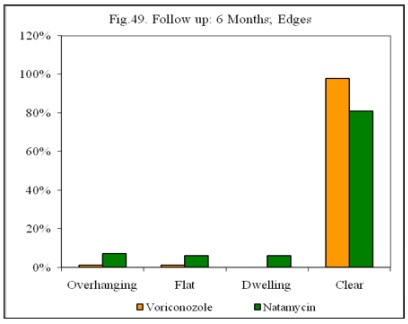



Table #. 6 months follow up: base

| Follow Up: 6 Months: Base | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Debris | 11 | 89 | 100 |
| | 11.00% | 89.00% | 50.00% |
| Clear | 89 | 11 | 100 |
| | 89.00% | 11.00% | 50.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 121.680; P < 0.001 | | | |

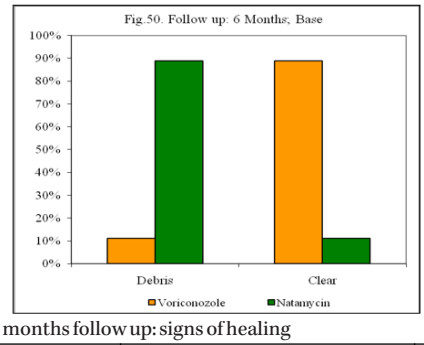



Table #. 6 months follow up: signs of healing

| Follow Up: 6 Months: Signs of Healing | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Healed | 53 | 44 | 97 |
| | 53.00% | 44.00% | 48.50% |
| Not Healed | 47 | 56 | 103 |
| | 47.00% | 56.00% | 51.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 1.621; P > 0.05 | | | |

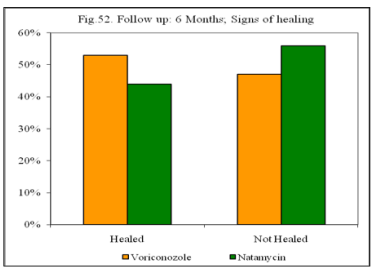



Table #. BCVA right eye

| BCVA: RE | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | | 5 | 5 |
| | | 5.00% | 2.50% |
| 6/12 | 43 | 21 | 64 |
| | 43.00% | 21.00% | 32.00% |
| 6/18 | 19 | 24 | 43 |
| | 19.00% | 24.00% | 21.50% |
| 6/24 | 11 | 11 | 22 |
| | 11.00% | 11.00% | 11.00% |
| 6/36 | 10 | 12 | 22 |
| | 10.00% | 12.00% | 11.00% |
| CF 0.5m | 6 | 4 | 10 |
| | 6.00% | 4.00% | 5.00% |
| 6/60 | 7 | 8 | 15 |
| | 7.00% | 8.00% | 7.50% |
| CF 1m | | 6 | 6 |
| | | 6.00% | 3.00% |
| CF 2m | 1 | 8 | 9 |
| | 1.00% | 8.00% | 4.50% |
| CF 3m | 3 | 1 | 4 |
| | 3.00% | 1.00% | 2.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 26.237; P < 0.01 | | | |

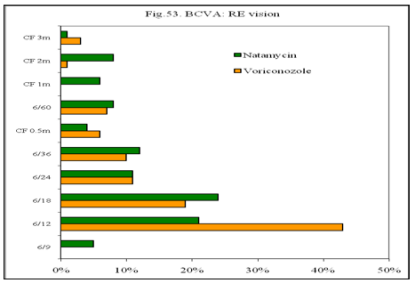



Table #. BCVA left eye

| BCVA: LE | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 6/9 | 1 | 8 | 9 |
| | 1.00% | 8.00% | 4.50% |
| 6/12 | 55 | 16 | 71 |
| | 55.00% | 16.00% | 35.50% |
| 6/18 | 19 | 18 | 37 |
| | 19.00% | 18.00% | 18.50% |
| 6/24 | 12 | 10 | 22 |
| | 12.00% | 10.00% | 11.00% |
| 6/36 | 7 | 24 | 31 |
| | 7.00% | 24.00% | 15.50% |
| CF 0.5m | 1 | 4 | 5 |
| | 1.00% | 4.00% | 2.50% |
| 6/60 | 3 | 1 | 4 |
| | 3.00% | 1.00% | 2.00% |
| CF 1m | 1 | 2 | 3 |
| | 1.00% | 2.00% | 1.50% |
| CF 2m | | 9 | 9 |
| | | 9.00% | 4.50% |
| CF 3m | 1 | 7 | 8 |
| | 1.00% | 7.00% | 4.00% |
| HM | | 1 | 1 |
| | | 1.00% | 0.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 54.032; P < 0.001 | | | |

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

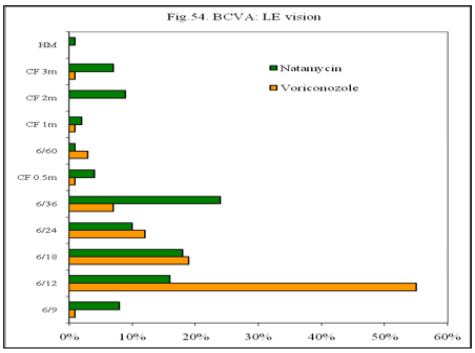



Table #. Size and nature of opacity

| Size and Nature of Opacity | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| 0 | | 100 | 100 |
| | | 100.00% | 50.00% |
| < 2mm | 100 | | 100 |
| | 100.00% | | 50.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 200.000; P < 0.001 | | | |

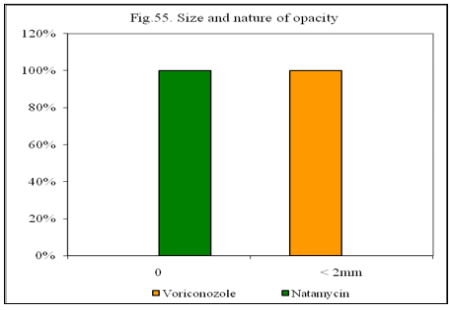



Table #. Vascularisation

| Vascularization | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Yes | 51 | 53 | 104 |
| | 51.00% | 53.00% | 52.00% |
| No | 49 | 47 | 96 |
| | 49.00% | 47.00% | 48.00% |
| Total | 100 | 100 | 200 |
| Chi Square: 0.080; P > 0.05 | | | |

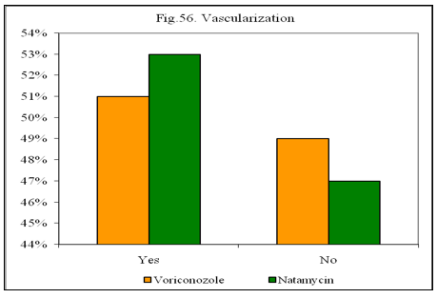
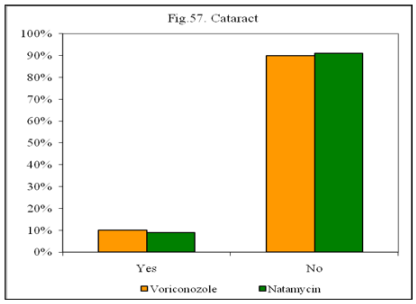



Table #. Cataract

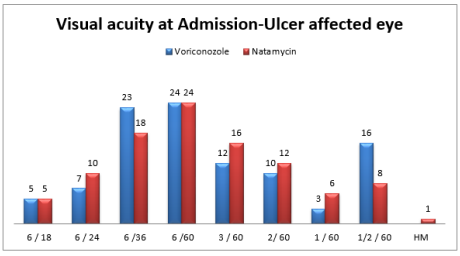
| Cataract | Group | | Total |
|---|---|---|---|
| | Voriconozole | Natamycin | |
| Yes | 10 | 9 | 19 |
| | 10.00% | 9.00% | 9.50% |
| No | 90 | 91 | 181 |
| | 90.00% | 91.00% | 90.50% |
| Total | 100 | 100 | 200 |
| Chi Square: 0.058; P > 0.05 | | | |




Visual Acuity at admission-Ulcer affected eye

| vision | Logmar | Voriconozole | Percentage | Natamycin | Percentage |
|---|---|---|---|---|---|
| 6 / 18 | 0.47 | 5 | 5 | 5 | 5 |
| 6 / 24 | 0.6 | 7 | 7 | 10 | 10 |
| 6 /36 | 0.77 | 23 | 23 | 18 | 18 |
| 6 /60 | 1 | 24 | 24 | 24 | 24 |
| 3 / 60 | 1.3 | 12 | 12 | 16 | 16 |
| 2/ 60 | 1.2 | 10 | 10 | 12 | 12 |
| 1 / 60 | 1.1 | 3 | 3 | 6 | 6 |
| 1/2 / 60 | 0.9 | 16 | 16 | 8 | 8 |
| HM | 1.4 | | | 1 | 1 |

MEAN IN GROUP I AT ADMISSION = 6.708 SD IN GI = 8.063
MEAN IN GROUP II AT ADMISSION= 5.750 SD IN GROUP II=7.188
The visual acuity measured in ulcer affected eye was comparable in both groups.

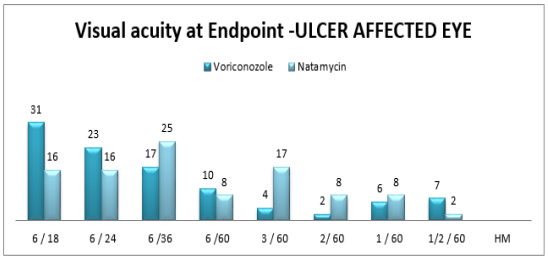



VISION ACUITY AT ENPOINT- ULCER AFFECTED EYE

| vision | Logmar | Voriconozole | Percentage | Natamycin | Percentage |
|---|---|---|---|---|---|
| 6 / 18 | 0.47 | 31 | 31 | 16 | 16 |
| 6 / 24 | 0.6 | 23 | 23 | 16 | 16 |
| 6 /36 | 0.77 | 17 | 17 | 25 | 25 |
| 6 /60 | 1 | 10 | 10 | 8 | 8 |
| 3 / 60 | 1.3 | 4 | 4 | 17 | 17 |
| 2/ 60 | 1.2 | 2 | 2 | 8 | 8 |
| 1 / 60 | 1.1 | 6 | 6 | 8 | 8 |
| 1/2 / 60 | 0.9 | 7 | 7 | 2 | 2 |
| HM | 1.4 | | | | |

MEAN IN GROUP I AT END POINT= 6.70 SD IN GI=9.20
MEAN IN GROUP II AT ENDPOINT= 6.39 SD IN GII=7.64
26% patients in group I improved vision at endpoint of the study 6/18, log mar 0.47

16%patients in Group II improved vision at endpoint of

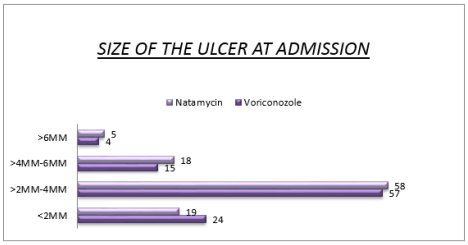


Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

**SIZE OF THE ULCER AT ADMISSION**

| SIZE OF ULCER | Voriconozole | Percentage | Natamycin | Percentage |
|---|---|---|---|---|
| <2MM | 24 | 24 | 19 | 19 |
| >2MM-4MM | 57 | 57 | 58 | 58 |
| >4MM-6MM | 15 | 15 | 18 | 18 |
| >6MM | 4 | 4 | 5 | 5 |

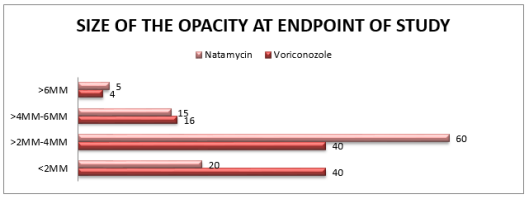
Chi Square: 0.974; P > 0.05




Comparable in both groups.

**SIZE OF THE OPACITY AT ENDPOINT OF STUDY**

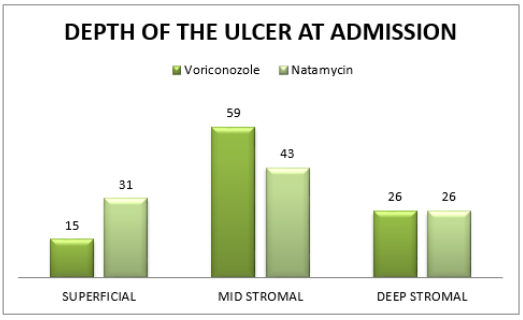
| SIZE OF ULCER | Voriconozole | Percentage | Natamycin | Percentage |
|---|---|---|---|---|
| <2MM | 40 | 40 | 20 | |
| >2MM-4MM | 40 | 40 | 60 | |
| >4MM-6MM | 16 | 16 | 15 | |
| >6MM | 4 | 4 | 5 | |




Chi Square: 200.000; P < 0.001

**DEPTH OF THE ULCER AT ADMISSION**

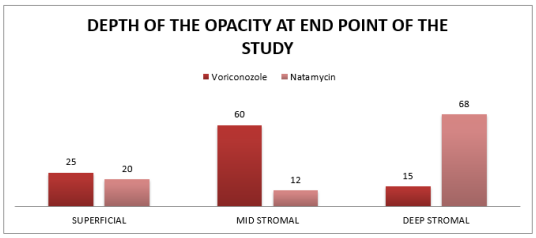
| DEPTH OF ULCER | Voriconozole | Natamycin | Percentage |
|---|---|---|---|
| SUPERFICIAL | 15 | 31 | |
| MID STROMAL | 59 | 43 | |
| DEEP STROMAL | 26 | 26 | |




Chi Square: 8.075; P < 0.05

**DEPTH OF THE OPACITY AT END POINT OF THE STUDY**

| DEPTH OF ULCER | Voriconozole | Natamycin | Percentage |
|---|---|---|---|
| SUPERFICIAL | 25 | 20 | |
| MID STROMAL | 60 | 12 | |
| DEEP STROMAL | 15 | 68 | |




There was improvement in both the groups but more in voriconozole treated group.

**Results**

Age group of study patient's minimum 20 years maximum 70 years. Mean age Group I

We recruited 200 patients randomized into 2 groups Group I patients received new drug voriconozole 1/w/v supplied by aurolab in powder form. Group II patients received natamycin 5%w/v solution commercially available as standard regime. All supportive measures like mydriatric lubricants anti inflammatory drugs were given to all patients in 2 group identically. All patient got admitted in generalward in RIO.Regular follow up with standardized protocol done in all patients after discharge these patients were called for follow up on our research lab,vision and aniterior segment evaluation done as per protocol and data entered into proforma. All patients were followed upto six weeks, 2 weeks ,1 month, 3months and six months . We found that of the 100 patients in group I treatment voriconozole had faster healing of ulcer with short hospital stay.

Out of the 200 patients 48% belong to the age Group of 50-59 years. Mean age of patients in Group I is 46.91 with SD of 15.05 . In group II mean age is 47.95 with SD of 17.54. Chi square value 5.462 , p>0.05. This was not found to be statistically significant.

There were 72 male and 28 females in Group I and 74 male and 26 female in group II comparable in both Groups chi square value 0.101 , p > 0.05 . No statistically significant.

On comparison of occupation it was seemed that 26% patients in group I were agricultural workers. While it was 10% in Group II. Manual workers in Group I is 21% and in Group II it was 41 % . chi square test is 15.704 p< 0.01.

The habitat of study participants were elicited, it was found that 68% in Group I were coming from rural areas while it is 62% in Group II ,28% from Group I from semi urban areas while it was 17% in Group II . 4% in Group I and 21% in group II where from urban areas. Chi square value 14.526,p < 0.01.

The social economic status of the study participant were evaluated. It was found that 32% in Group I belonged to APL while it was 45% in Group II. 68% in Group I belonged to BPL while it was 55% in Group II. There was no statistical significant.

Personal hygiene of the study participants has been evaluated . It was good in 43% patients in Group I while it is 19% in Group II. 33% in Group I and 31% in Group Ii, it was poor. It was very good in 24% in group I and 17% in Group II .It was significant.

History of ocular surgery was noted, it is 12% in Group I and 13 % in Group II . There was no history of ocular surgery 88% in group I and 87 % in group II. Chi square value 0.046. p>0.05. No significance.

There was no predisposing factors in 81% of patients in group I and 52% in group II. Dry eyes were present in 7% in group I and 4% in Group II. Lagophthalmos were present in 4% of patients in both

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

groups. Other lid abnormalities were present in 4% of patients in group I and 17% patients in group II . decreased corneal sensation was present 3% in group I and 23% in group II Dacryocystitis present in one patient in group I.

Visual acuity measured at admission shown 24% patients in group I had 6/12 vision, while in group II it was 21% . 15 % patients in group I had 6/60 and 13% in group II had the same.

Ulcer affected eye 43% in group I had ulcer in the right eye while it was 56% in group II . 50% patients in group I had ulcer in the left eye while 44% in group II . 7 patients in Group I had ulcer in both eyes.

Size of the ulcer at admission 24% in group I had ulcer of ≤ 2mm size and it was 19% in group II. 57% in group I had ulcer of the size 2mm and 58% in Group II it was 2-4mm. 15% in group I had ulcer of the size 4-6 mm and 18% in group II had ulcer of 4-6mm. ulcer of the size >6mms was found in 4 patients in Group I and 5 patients in group II . Chi square value 0.976 . P > 0.05. No significance.

**Additional features noted were**
1.Vascularization 2. Pigmentation 3. Scleral involvement.

It was found that 51% patients in Group I had vascularization and 53% patients in Group Ii had the same . pigmentation was present 42% patients in group I and 36% of patients in Group II and scleral involvement was present in 7% in Group I and 11% in Group II , Chisquare 1.389 p>0.05 . no significance.

**Duration of Hospital stay**
52% of patients in Group I stayed up to 1 week and 48% of patients in Group I stayed up to 2 weeks . In group II 53% of patients stayed for 3 weeks 37% of patients stayed for 3 weeks 7% of patients for 4 weeks 3% of patients for 5 weeks.chi square p> 0.001. Statistically significant.

**Laboratory test of the study participants**
**1. Hemoglobin**
Mean hemoglobin value of patients in Group I was 13.65 with SD 1.52. in Group II it is 13.88 with SD of 1.48 . Comparable in both Group . No significance.

**2. Random blood sugar**
In Group I it was 81.57% with SD 91.63. in Group II it is 109.21 with SD of 49.43

**Fungal isolates**
Fusarium 24% in Group I,29% in Group II
Aspergillus niger 20% in Group I, 12% in Group II
Aspergillus fumigatus 26% in Group I,20% in GroupII
Aspergillus flavour 10% in Group I ,16 % in Group II
Candida 10% in Grroup I, 9% in Group II
Basidiobolus ,3% in Group I& II
Pencillium is 15 in both Groups
Phoma is 1% in Group I 2% in Group II
Mucor is 2% in both Groups
Sepctidonium, 1% in both Groups
Trichoderma ,1% in both Groups
Aureobacidium 1% in Group I and 4% in Group II.

Eventhough there is no statistical significant. Our study found out that more species of fungi produces corneal ulcer world literature says fusarium aspergillus and candida are the main organism produces corneal ulcers our study also find out the same.

All the study participants were followed up to 6 months with standard protocol.

At the end point of study in Group I patients logmar visual acuity recorded with mean of 0.54 and SD of 0.28. in Group II it is 0.63 with SD of 0.22.

At 6 months follow up depth of the corneal opacity noted using slit lamp it was categorized in to three
1. Super ficial stroimal
In Group I 15% and 31 % in Group II
2. Mid stromal
59% in group I and 33% in group II
3. Deep stromal
26% in group I, 26% in group II

Corneal neovascularization was present in 51% in Group I ans 53% in group II. There was no corneal neovascularization in 49% in Group I and 47% in Group II.Chi square value 0.088,P>0.05. not significant.

Cataract was present in 10% patients in Group I and 9% in Group II. This is not related to the ulcer since good number of patient where above 50.

**Complications**
The following complications where present
1. Perforation 8% in Group I and 30% in Group II
2. PseudoCornea formation occurred in 38% of patients in G II only

Other systemic illness from where the patients were suffering was noted by history taking. It was categorized into five items. Major illness were Diabetes Mellitus, Hypertension ,Immune Suppression, others and nil.

**DISCUSSION**
Fungal corneal ulcers is prevalent in both developing and developed countries . This is more in developing and under developed countries. If not treated properly it progresses and leads to complications like perforations, Endophthalmitis and there by loss of sighted eye itself . If identified and properly treated ulcer may heal and patient will regain some amount of vision. With the present regiume of treatment using Natamycin which is an antifungal, antibiotic tracks the disease for no. of days leading to the loss of vision, loss of productivity and economic burden to the family and the patient.

Randomized Clinical Trial is the most powerful tool available for evaluation of efficacy of new therapeutic interventions. As this was the study comparing the efficacy of two therapeutic inventions , randomized clinical trial was chosen as the appropriate design. Natamycin occupied the pride of place as the treatment of choice for fungal corneal ulcers.Reconstituted voriconozole once applied topically has been found to be very useful in the treatment of fungal corneal ulcers.

Voriconozole is an imidazole with inhibitory effects on cellwall synthesis of fungal filaments. It is found to have fungicidal effect. There are theoretical reasons to accept that voriconozole could potentially work for fungal keratitis.

Since there is no much published studies from india we thought off undertaking this study.

Prevalence of fungal corneal ulcers in the district Thiruvananthapuram in kerala in population above the age of 20, 17-36% Out of the corneal ulcers admitted into the General ward of RIO Trivandrum 75%turns out to be fungal in nature.

The sample size for this study was calculated to find out minimum number of hospital stay is needed for patients getting treated with voriconozole when compared with standard treatment using Natamycin which is being followed in our institute. Number of days of hospital stay in voriconozole group from base line of three ,

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

maximum of 21. for alpha of 0.05 and beta of 20% and adjusting for drop out of 5%, the sample size required was found to be 100 patients in each arm. The patients recruited for randomised clinical trial was chosen from these with features of fungal corneal ulcer and laboratory proven fungal filaments. Positive Randomization was done after obtaining written informed consent. The patients were divided into two groups. Group 1 (intervention group) The patients were given voriconozole which was supplied by m/s in powder form with water for reconstitution . The reconstituted 1% solution applied to the eye on an hourly basis during watering hours for the first 48 hrs.

Group2 (control group) patients were given commercially available Natamycin 5% solution applied in the eye on an hourly hours for the first 48 hrs.

Supportive management was exactly similar in both groups.
Baseline characteristic of two groups were comparable.

**SUMMARY**

1. Fungal corneal ulcers is one of the major causes of blindness
2. Everywhere in the world antifungal, antibiotics is the treatment of choice.
3. In India also natamycin eye drops is the primary treatment
4. In Kerala prevalence of fungal corneal ulcers is high
5. In Regional Institute of Ophthalmology Thiruvannathapuram will conducted at pilot study will giving voriconozole eye drops to patients fungal corneal ulcers . results of the study were encouraging
6. Laboratory proven fungal corneal ulcers attending the operation department of Regional institute of ophthalmology has been recruited for the study.
7. 200 patients participated in the study
8. They where randomized in to two groups using simple randomization procedure
9. Group I patients where given voriconozole eye drops Group II patients were given natamycin eye drops.
10. Patients in the two groups where followed up for the period of 6 months
11. All the 200 patients completed the trial.
12. Clinical cure occurred in both the groups
13. Voriconozole groups show faster healing of ulcers and minimum number of days of hospital stay
14. Complications occurred in both the groups but it was more in natamycin group
15. Corneal opacity left behind was larger and denser in natamycin group
16. The clinical trial has shown there is benefit in giving voriconozole reconstituted eye drops in treating mycotic keratitis.
17. The beneficial effect found out in the study this only with smaller sample size.
18. Study with larger sample size is necessary to derive conclusive evidence of the therapeutic effects.

**Limitation of study**

Since our hospital is a tertiary care institute we get patients referred to us from other hospitals on a later stage of the disease, with some treatment history, Many participants had large ulcers: Our hospital being an exclusive eye hospital with no general physician, few participants who had diabetes which became uncontrolled were taken to nearby GH for metabolic control during that time ulcer became large and went for perforation and other complications.

**Conclusions**

Laboratory proven fungal corneal ulcers who undergone this clinical trial showed improvement in both groups. With faster healing and minimum number of days of hospital stay in the voriconozole treated group. Healing was slow to occur and complications more in the natamycin treated groups.

Patientsb in the voriconozole groups got discharge from the hospital wards earliest by 3 days and latest by 21 days in the intervention groups. While patient treated with natamycin were forced to stay in the hospital from minimum of 2 weeks maximum of 6 weeks.

At the endpoint of study 20% of patients in natamycin treated groups still had signs of inflammation.

There was clinically and statistically significant improvement in the corneal pathology in both the groups but more in voriconozole treated groups.

10% of patients in Group I and 9% patients in Group II had cataracts lens changer but it is not due to drug effect.

There was no statistically significance difference in the visual acuity measured in both groups at the endpoint of the study.

Study with larger sample size is necessary to derive efficacy evidence of the therapeutic effect.

**ACKNOWLEDGMENT**

I express my sincere gratitude to Dr.P.S.GIRIJADEVI, Head of the Department of ophthalmology and Director R.I.O, Govt. MedicalCollege, Thiruvananthapuram for her support in carrying out this Project.

I wish to thank Dr.Asha.S,Additional Professor ,Department of Pharmacology for helps and support in the project especially in collecting pharmaco dynamics and kinetics of the new drug voriconozole which we were trying.

I wish to thank Dr.Reena.A,Associate Professor,RIO,Trivandrum in preparing the proforma for the study.

I wish to thank Dr.Anuja Sathar,Assistant Professor ,RIO,Trivandrum for her moral support.

I wish to thank Dr.Anna Cherian, Associate Professor of microbiology at RIO,and staff of microbiology lab for their support in identifying the fungi, fungal culture and lab services.

I wish to thank all post graduates and Residents of RIO,Trivandrum for helping us in completing the study.

I wish to thank Nursing staff of General ward of RIO,Trivandrum for safe keeping of the files of study patients promptly.

I wish to thank store keeper and staff of RIO, Store ,Trivandrum for keeping the drug under trial and prompt supply to study participants.

I wish to thank office staff Mrs.Mridula,Mrs.Sreekala of RIO maintaining the accounts of the project promptly and support for procuring equipments and consumables.

I wish to thank Dr.Jayageetha,Associate professor in biostatistics , Medical college Trivandrum for helps.

I wish to thank Dr.Kurian Abraham,Statistician of My Project for helping us in data analysis.

I wish to thank Auditor Mr.Madhu chartered accountant and staff of his firm for auditing the accounts of our project.

I wish to thank Dr.Vijayakumar,scientific officer KERALA STATE COUNCIL FOR SCIENCE TECHNOLOGY AND ENVIRONMENT ,Pattom who was instrumental in sanctioning the project.

Our sincere gratitude to all staff of KSCSTE.

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96

I wish to thank M/S Aurolab whjo supplied the new drug voriconozole for the clinical trial at subsidized rate.

I wish to express my gratitude to all my patients, who formed the integral part of my study for their cooperation and goodwill extended to me all along for the successful completion.

I thank my wife Dr.Soja .V and My children Renju Rajeev and Rejitha Rajeev for their love and support without which this study would not have been possible.

Above all we are thankful to the LORD ALMIGHTY for the blessings which helped me to conduct this study

**APPENDICES**

**PROFORMA** **Admission Date:**
**Discharge Date:**
**IP No:**

1. Name:
2. Age:
3. Sex:
4. Address with phone number :
5. Occupation: manual labourer/ agriculture worker / skilled worker/professional /others
6. Habitat: rural /semi urban /urban
7. Socio economic status: APL / BPL
8. Complaints:
9. History of present complaint:
10. Past history: D.M /HT /immune suppression/others/Nil.
11. Drug history: on topical medication: Yes / No
12. Personal hygiene: poor /adequate /good
13. Previous history of ocular surgery: Yes/ No
14. Predisposing factors Dry eyes /lagophthalmos /other lid abnormalities /decreased corneal sensation/ dacryo cystitis/Nil.

**GENERAL EXAMINATION:**

**Ocular examination**

Visual acuity - Group A : 6/9-6/24. Group B: 6/24-6/60. Group D : HM - PL+

**Slit lamp Examination**

Conjunctiva - congestion uniform /diffused /isolated patch

Corneal status-detailed description of ulcer-extend and depth of ulcer
Size of ulcer - <2mm, 2-4mm, 4-6mm, >6mm

Depth of ulcer – a. superficial stromal , b. mid stromal c. deep stromal

Additional features if any – vascularisation /pigmentation /sclera involvement

Symptomatic relief- on days 1,2,3,6,10,14,18,22,24 and time of discharge.

Clinical signs-ulcer healing – conjunctival congestion / extend and depth of opacity.

Comnplicatio- secondaryglaucoma/ perforation/ pseudocornea/ Anterior staphyloma

**Lab investigation results:-**

a. Blood – Hb, Tc, Dc FBS
b. Urine :- Alb, sugar, deposit

**Smears**

1. GRAM STAINING
2. KOH MOUNT
3. Culture & sensitivity

**Follow up -**

| | |
|---|---|
| Vision | |
| Size | |
| Depth | |
| Edges | |
| Base | |
| A/c reaction | |
| pupil | |
| Signs of healing | |
| Signs of progression | |

**Late follow up**

**1 month**

| | |
|---|---|
| Vision | |
| Size | |
| Depth | |
| Edges | |
| Base | |
| A/c reaction | |
| pupil | |
| Signs of healing | |
| Signs of progression | |

**3 months**

| | |
|---|---|
| Vision | |
| Size | |
| Depth | |
| Edges | |
| Base | |
| A/c reaction | |
| pupil | |
| Signs of healing | |
| Signs of progression | |

**6 months**

| | |
|---|---|
| Vision | |
| Size | |
| Depth | |
| Edges | |
| Base | |
| A/c reaction | |
| pupil | |
| Signs of healing | |
| Signs of progression | |

**Endpoint**

1. BCVA
2. SIZE& Nature of Opacity
3. Vascularisation
4. Cataract
5. Secondary glaucoma

**REFERENCES**

1. Prajna NV, Krishnan T, Mascarenhas J, Rajaraman R, Prajna L, Srinivasan M, Raghavan A, Oldenburg CE, Ray KJ, Zegans ME, McLeod SD, Porco TC, Acharya NR, Lietman TM; Mycotic Ulcer Treatment Trial Group The mycotic ulcer treatment trial: a randomized trial comparing natamycin vs voriconazole.
2. Margarita I. Echavez, Archimedes Lee D. Agahan, and Noel S. Carino, Fungal Keratitis Caused by Drechslera spp. Treated with Voriconazole: A Case Report

Volume - 7 | Issue - 1 | January - 2017 | ISSN - 2249-555X | IF : 3.919 | IC Value : 79.96


3. Topical and Oral Voriconazole in the Treatment of Fungal Keratitis Sang Joon Lee, MD, Jung Joo Lee, MD, and Shin Dong Kim, MD
4. Prajna NV, Mascarenhas J, Krishnan T, Reddy PR, Prajna L, Srinivasan M, Vaitilingam CM, Hong KC, Lee SM, McLeod SD, Zegans ME, Porco TC, Lietman TM, Acharya NR Comparison of natamycin and voriconazole for the treatment of fungal keratitis.
5. Sharma N, Chacko J, Velpandian T, Titiyal JS, Sinha R, Satpathy G, Tandon R, Vajpayee RB ,Comparative evaluation of topical versus intrastromal voriconazole as an adjunct to natamycin in recalcitrant fungal keratitis.
6. Deoud Al-Badrtyeh, Chin Fen Neoh, Kay Stewart, David CM Kong Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Victoria, Australia. Authors: Daoud Al-Badriyeh, Chin Fen Neoh, Kay Stewart, et al Published Date iy 2010 Volume 2010:4 Pages 391 -
7. Voriconazole for the treatment of refractory Aspercjillus fumiqatus keratitis Hijab Mehta, Hiteridra B Mehta, Prashant Garg, Harish Kodial
8. Antoine Dupuis, Nicolas Tournier,' Gwenael Le Moal, and Nicolas Venissa Centre Hospitalier Universitaire de Poitiers, Poitiers, France, Facuté de Médecine et de Pharmacie, Universite de Poitiers, Poitiers, France .
9. Jhanji V, Sharma N, Mannan R, Titiyal JS, Vajpayee RB Management of tunnel fungal infection with voriconazole.
10. FlorCruz NV, Evans JR. Medical interventions for fungal keratitis.
11. Arora R, Gupta D, Goyal J, Kaur R. Voriconazole versus natamycin as primary treatment in fungal corneal ulcers.
12. Rose-Nussbaumer J, Prajna NV, Krishnan T, Mascarenhas J, Rajaraman R, Srinivasan M, Raghavan A, Oldenburg CE, O'Brien KS, Ray KJ, Porco TC, McLeod SD, Acharya NR, Keenan JD, Lietman TM; Mycotic Ulcer Treatment Trial Group. Risk factors for low vision related functioning in the Mycotic Ulcer Treatment Trial: a randomised trial comparing natamycin with voriconazole
13. Ogawa A, Matsumoto Y, Yaguchi T, Shimmura S, Tsubota K. Successful treatment of Beauveria bassiana fungal keratitis with topical voriconazole.
14. Lee SJ, Lee JJ, Kim SD. Topical and oral voriconazole in the treatment of fungal keratitis
15. Sharma S, Das S, Virdi A, Fernandes M, Sahu SK, Kumar Koday N, Ali MH, Garg P, Motukupally SR. Re-appraisal of topical 1% voriconazole and 5% natamycin in the treatment of fungal keratitis in a randomised trial.