

# Comparative evaluation of topical fluconazole 0.3% eye drops, natamycin 5% ophthalmic suspension and ketoconazole 4% ophthalmic suspension in the management of fungal keratitis

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## Abstract

Aim of the study is to find out the efficacy of Topical Fluconazole 0.3% eye drops, Natamycin 5% ophthalmic suspension and Ketoconazole 4% ophthalmic suspension in the management of Fungal Keratitis. To study comparative efficacy of the above drugs in the treatment of fungal keratitis. To study the side effects of these drugs. In this study 30 adult patients with microbiological proved mycotic keratitis were treated. These patients were divided into three three treatment groups viz. natamycin group, fluconazole group and ketoconazole group. All patients belonged to age group 31-45 years (35.56%) of all patients 22 (73.33/.) were males and 8 (26.63/.) Were females Around 70% given history of work related to agriculture industry and the onset of work related to agriculture industry and onset of keratomycosis was preceded by vegetative trauma in 90% cases.

**Key Words:** Natamycin, Fluconazole,, Ketoconazole, fungal keratitis, agriculture industry.

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antifungals, clinical evaluation of newer drugs is constantly being carried out to obtain highly effective, readily available, relatively safe and well tolerated dosages. So this study aims at finding out the comparative effectiveness of fluconazole 0.3%. Topical eye drops introduced antifungal agents against ketoconazole 4% Ophthalmic suspension which use some time now and natamycin 5%. Ophthalmic suspension first topical drug approved by food and drug administration (F.D.A.) IN USA for topical use.

## INTRODUCTION

Fungal Keratitis refers to a suppurative, usually ulcerative mycotic infection of the cornea which can be a sight threatening infection. Topical antifungals are used to treat this infection. Due to various limitations of available

## MATERIALS AND METHODS

30 patients presenting with symptoms of tinea corporis who were mycologically confirmed for the presence of fungal hyphae. They were randomly divided into three groups of 10 patients in each group: one group received Natamycin (5%), second group received Fluconazole

(3%) and the third group received Ketoconazole 4%. Cases were first clinically diagnosed and fungalaetiology was proved with KOH smear and culture media. Diagnosis of keratomycosis with slit lamp, microscopic examination of corneal scrapings and culture material on sabaroud media, blood sugar, brain heart infusion broth, Fran's staining. The criteria for diagnosis of fungal infections identified hyphae or yeast cells on unstained or

stained smears and confirmation growth on culture media. Patients were followed up on 4th, 14th, 21st and 28th day for assessment of healing of ulcer. On day 14th and 28th smear and culture were repeated. Response to therapy within 7 days considered successful. Treatment duration was for 4 weeks. Evaluation was carried out using the standard clinical parameters on day 4, day 14, day 21 and day 28. Adverse effects were also recorded.

**OBSERVATIONS AND TABLES**

**Table 1 a:** Age wise distribution of cases

Age in years	Frequency	Percentages (%)
21-30	06	18.30
31-40	09	37.56
41-50	10	24.22
51-60	05	20.22
<b>Total</b>	<b>30</b>	<b>100.0</b>

**Table 1b:** Sex wise distribution of Cases

SEX	Frequency	Percentage
Male	22	73.33
Female	08	26.67
<b>Total</b>	<b>30</b>	<b>100 %</b>

**Table 2:** Occupation wise distribution of cases

Occupation	Frequency	percentage
Farmer	19	63.33
Housewife	03	10.00
Others	08	26.67
<b>Total</b>	<b>30</b>	<b>100.0</b>

**Table 3:** Distribution according to type of fungal infection

Types of fungal spp	Study group			Total cases (%)
	Natamycin Cases (%)	Fluconazole Cases (%)	Ketoconazole Cases (%)	
Aspergillus	5(50.0)	5(50.0)	4(40.0)	14(46.66)
Fusarium	3(30.0)	3(30.0)	3(30.0)	9(30.0)
Dematiacious	2(20.0)	1(10.0)	----	3(10.0)
Mixed (bacterium+fungus)	----	1(10.0)	3(30.0)	4(3.34)
<b>Total</b>	<b>10(100)</b>	<b>10(100)</b>	<b>10(100)</b>	<b>30(100)</b>

**Table 4:** Distribution of cases according to severity of ulcer

Severity	Natamycincases(%)	Fluconazole Cases (%)	Ketoconazole Cases (%)	Total Cases (%)
Not severe	7(70.0)	6(60.0)	6(60.0)	
Severe	3(30.0)	4(40.0)	4(40.0)	
<b>Total</b>	<b>10(100)</b>	<b>10(100)</b>	<b>10(100)</b>	<b>30(100)</b>

**Table 5:** Distribution of cases according to response to treatment

Response	Study groups		
	Natamycin Cases (%)	Fluconazole Cases (%)	Ketoconazole Cases (%)
Excellent	5(50.0)	4(40.0)	3(30.0)
Moderate	2(20.0)	2(20.0)	2(20.0)
Poor	3(30.0)	4(40.0)	5(50.0)
<b>Total</b>	<b>10(100)</b>	<b>10(100)</b>	<b>10(100)</b>

**Table 6:** Distribution of cases according to response to treatment by NATAMYCIN

Response to Natamycin	Types of fungal species			
	Aspergilluscases (%)	Fusariumcases (%)	Dematiaceouscases (%)	Mixed cases (%)
Excellent	3(60.0)	2(50.0)	1(100.0)	---
Moderate	---	1(25.0)	---	---
Poor	2(40.0)	1(25.0)	---	---
<b>Total</b>	<b>10(100)</b>	<b>10(100)</b>	<b>10(100.0)</b>	<b>---</b>

**Table 7:** Correlation between type of etiological fungus and overall response (B) fluconazole group

Response to Flucanazol	Aspergilluscases (%)	Fusariumcases (%)	Dematiaceouscases (%)	Mixed cases (%)
Excellent	3(60.0)	2(50.0)	1(100.0)	---
Moderate	2(40.0)	---	---	---
Poor	1(20.0)	2(50.0)	---	---
<b>Total</b>	<b>5(100.0)</b>	<b>4(100.0)</b>	<b>1(100.0)</b>	<b>---</b>

**Table 8:** Correlation between type of etiological fungus and overall response to Ketoconazole

Response to ketoconazol	Aspergilluscase s(%)	Fusariumcases (%)	Dematiaceouscases (%)	Mixed cases (%)
Excellent	32(50.0)	2(50.0)	---	---
Moderate	---	1(25.0)	---	---
Poor	2(50.0)	1(25.0)	---	2(100.0)
<b>Total</b>	<b>4(100)</b>	<b>4(100.0)</b>	<b>---</b>	<b>2(100.0)</b>

**Table 9:** Eradiation rate of etiological fungi

Type of fungal spp	Study groups		
	Natamycincases (%)	Fluconazole Cases (%)	Ketoconazole Cases (%)
Aspergillus	3(42.85)	5(71.42)	4(66.67)
Fusarium	4(66.67)	3(50.0)	4(66.67)
Dematiaceous	2(100.0)	1(100.0)	---
Mixed	---	---	---



**Figure 1:**



**Figure 2:**



**Figure 3:**



**Figure 4:**

## RESULTS AND DISCUSSION

This study includes 30 adult patients with mycotic keratitis. They were divided into 3 treatment groups in random fashion. Table 1,2: As only adult patients were selected 15 years was the lowest age and maximum incidence of keratomycosis was seen in the age group of 31-40 years (37.56). This is most active age group. Of the 30 patients, 22 were male (73.33%) and female (26.67%). Nineteen patients (63.33%) were doing work related to agriculture industry and that was the commonest occupation showing mycotic keratitis. Table 3: In this study, aspergillus sp. Was the commonest fungal isolated observed in 46.66% cases. fusarium species was 2<sup>nd</sup> most common fungal isolate observed in 30% cases. Mixed infections was observed in 4 cases (8.89%) Table no.4: In the present study 60% patients belonged to non severe ulcer group and 40% to severe ulcer group. Table no.5: In natamycin group 50% patients showed excellent response, 20% showed moderate and 30% showed poor response. In fluconazole group 40% patients showed excellent response, 20% showed moderate and 40% showed poor response. In ketoconazole group 30% patients showed excellent response, 20% showed moderate and 50% showed poor response. In all the groups there was direct relationship between no. of severe ulcer cases and poor response. Table no.6 and 7: In the present study in natamycin group aspergillus species was isolated from 5 cases. out of which 3 cases (60%) showed excellent response and 2 cases (40%) showed poor response. So the eradication rate was 42.85%. Fusarium species was isolated from 4 cases out of which 2 cases (50%) showed excellent response, 1 case (25%) moderate response and 1 case (25%) poor response. Thus eradication rate was 66.67%. Dermateous fungi (helminthosporium and curvularia spp.) were isolated from 2 cases. both cases showed excellent response. thus eradication rate was 100%. In fluconazole group aspergillus spp. Was isolated from 6 cases out of which 3 cases (60%) showed excellent, 2 cases moderate and 1 case showed poor response. So eradication rate was 71.42%. fusarium spp. was isolated in 4 cases out of which 2 cases (50%) showed excellent response, no moderate response and 2 cases (50%) showed poor response. so eradication rate was 50%. Dermateous fungi was isolated in 1 case which showed excellent response so eradication was 100%. Mixed infections was present in 1 case which showed poor response. In ketoconazole group aspergillus and fusarium spp. produced 8 cases, 4 cases of each spp. 2 cases of each spp showed excellent response, 1 case showed moderate response and 2 cases of each fungus showed poor response. So eradication rate was 66.67%. Mixed infections was seen in 2 cases and all showed poor

response. Table no.8: In natamycin group 6 cases showed no severe ulcers and all responded excellently. 4 cases showed severe ulceration and out of which 1 case showed moderate response and 3 cases showed poor response. Out of 3 poor responders in 1 case therapeutic keratoplasty was done before eradication of causative fungus but both grafts showed failure. Thus natamycin was effective against superficial keratomycosis. In fluconazole group 6 cases belonged to non severe ulcer group and all of them responded excellently. 4 cases belonged to severe ulcer group out of which 1 case showed moderate response and 3 showed poor response. Out of 3 poor responders 1 case undergo therapeutic keratoplasty to save the integrity of eyeball, 1 showed reinfection and one showed failure. Thus fluconazole was effective against superficial keratomycosis. In ketoconazole group 4 cases showed non severe ulcers and 6 cases showed severe ulcers. all non severe showed excellent response. Out of 6 severe cases 2 showed moderate and 4 showed poor response. Out of 4 poor responders 1 case underwent therapeutic keratoplasty during t/t to prevent perforation of eyeball. Both cases had reinfection which was treated with natamycin. Thus ketoconazole was effective against superficial keratomycosis no severe local side effect were observed in any of the drugs. No significant biomicroscopic ocular surface toxicity was observed with topical ketoconazole. Fluconazole eye drops did not show any side effect.

## CONCLUSION

In natamycin group 50% patients showed excellent response, 20% showed moderate and 30% showed poor response. In fluconazole group 40% patients showed excellent response, 20% showed moderate and 40% showed poor response. In ketoconazole group 30% patients showed excellent response, 20% showed moderate and 50% showed poor response. In all the groups excellent response was seen in cases with superficial keratomycosis. Thus natamycin appears to be most effective in treatment of superficial filamentary keratomycosis. No significant ocular side effects were observed with any of the drugs.

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