

Comparative role of topical natamycin and itraconazole in mycotic keratitis

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Abstract:

Background: To compare the role of topical 5% Natamycin and topical 1% Itraconazole in mycotic keratitis. **Material and Methods:** Total 52 patients of microbial keratitis were enrolled for the study between April 2010 to July 2012. Each of them underwent therapeutic scrapping for 10% KOH mount by a single surgeon and inoculation in Sabouraud's dextrose agar (SDA) and in blood agar by a single microbiologist. If the culture media failed to show growth of any organism after two weeks, the culture plate was discarded. All the KOH positive cases were randomly (computer generated randomization) divided into two groups. The first group received topical 5% natamycin and the second group received 1% Itraconazole drop in identical regimen. Healing time, success rate (defined as complete re-epithelization accompanied by variable amount of stromal scarring along with complete resolution of ciliary flush for two consecutive examinations one week apart) and complication profiles between the two groups were recorded and compared. **Results:** Total 52 cases were enrolled for the study. Mixed etiology was found in 5 cases (9.6%). Majority of cases (n=41, 78.8%) belonged to 20-50 years (range 12-61 years) age group. The average healing time in Natamycin group was 21.4 ± 2.40 days and the same in Itraconazole group was 27.7 ± 1.98 days ($p=1.23$). Resolution of ulcer (success rate of therapy) was 72.2% in Natamycin group as compared to 38.8% in Itraconazole group ($p=.045$). **Conclusion:** Natamycin remains the principal choice in mycotic keratitis.

Keywords: Microbial Keratitis, Mycotic Keratitis, Anti-fungal Drops.

Corneal blindness is a major public health problem in India. It accounts for 20-30% of all blindness in the developing countries including India. Microbial keratitis tops the list especially in south Asia.¹ Among several causes that can elicit severe inflammatory response in cornea, microbial keratitis is the most common cause. The causative organism mainly guides therapy for this potentially sight-threatening ocular infection. Proper health initiatives in the form of early diagnosis and treatment can effectively be curative. This also minimizes the incidence of post-infectious scar in cornea. Microbial keratitis especially mycotic keratitis is very common in the Gangetic West Bengal. Proper detection of the causative fungi along with prompt institution of anti-fungal pharmacotherapy is the main factor to reduce corneal morbidity. Against this background, the current study is undertaken to compare the efficacy of topical natamycin and itraconazole in mycotic keratitis.

Material and methods:

All the cases with mycotic keratitis (diagnosed, suspected and fresh cases) presented to Institutional Cornea Clinic between April 2010 to July 2012 were enrolled for the study. Patients, who are already getting any anti-microbial drops,

are advised to stop them for 2 days. Corneal scrapping was done after 2 days and the samples were subjected to 10% KOH mount and inoculation in Sabouraud's dextrose agar (SDA) and in blood agar. After two weeks, if no growth was obtained, the culture plate was discarded.

All the KOH positive cases were randomly divided into two groups. The first group received topical 5% natamycin and the second group received topical 1% Itraconazole drop. Both the groups had similar drug instillation regimen of one drop at hourly interval for first day followed by one drop at two hourly intervals for next two weeks and then one drop at three hourly intervals thereafter. All the enrolled cases did also get topical atropine sulphate (1%) one drop three times a day along with oral analgesics as required. The healing of ulcer was defined as complete re-epithelization accompanied by variable amount of stromal scarring along with complete resolution of ciliary flush for two consecutive examinations one week apart. Patients primarily presented with desmetocele or perforation, were excluded from the study.

Results:

We initially recruited 57 cases for the study. Five of them were KOH negative or Culture negative or both. Hence, a

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total of 52 cases were enrolled for the study. Mixed etiology was obtained in 5 cases (9.6%). They received topical 0.5% Moxifloxacin drop in addition to the properly designated anti-fungal drop. Majority of cases (n=41, 78.8%) belonged to 20-50 years (range 12-61 years) age group. Out of total cases, 37 were male (71.2%) and rest were female (n=15, 28.8%). Among the male group, three cases showed mixed etiology (8.1%). The same finding among female was seen among two cases (13.3%). The cultivators (n=24, 46.1%) were the commonest occupational group followed by skilled and unskilled workers (n=10, 19.2%), housewives (n=8, 15.6%) and students (n=4, 7.7%). Culture positivity was highest among cultivators (n=15, 62.5%) followed by workers (skilled and unskilled) and housewives.

History of trauma was found in 32 cases (61.5%). Commonest type of trauma was with vegetable matter (n=20, 62.5%) followed by corneal foreign body (n=11, 21.15%) and finger nail (n=1, 1.9%). Besides trauma, other predisposing factors were chronic dacryocystitis (n=4, 7.7%), diabetes mellitus (n=5, 9.61%) and Steven-Johnson's syndrome (n=1, 1.9%). 11 out of 52 cases did not give any significant history of trauma. Among all fungal isolates, *Aspergillus fumigatus* was the commonest (44.5%) followed by *Fusarium species* (40.7%), *Aspergillus flavus* (7.4%) and *Aspergillus niger* (7.4%). Among cases with mixed isolates, *Aspergillus fumigates* (3 cases) was commonest followed by *Fusarium species* (2 cases). Regarding bacterial species of mixed isolates, *E. coli* was found in 2 cases, *pseudomonas sp* in 2 cases and *Diphtheroids sp* in one case. Two cases from Natamycin group developed sloughing corneal ulcer and 1 case developed perforation. Similarly 4 cases from Itraconazole group developed sloughing ulcer and 1 case developed perforation. Excluding the cases which developed complications as mentioned above, 2 cases did not improve in Natamycin group and 7 cases did not improve in Itraconazole group. The average healing time in Natamycin group was 21.4±2.40 days and the same in Itraconazole group was 27.7±1.98 days (p=1.23). Resolution of ulcer (success rate of therapy) was 72.2% in Natamycin group as compared to 38.8% in Itraconazole group (p=.045).

Discussion:

Infectious keratitis remains a major cause of corneal morbidity throughout the world. Roser first reported bacterial ulcer in 1856.² Leber described hypopyon corneal ulcer of mycotic origin.³ Nema et al found 35.3% mycotic keratitis in his study on corneal ulcer in Aligarh.⁴ In our study, *Aspergillus fumigatus* was the commonest (44.5%) followed by *Fusarium species* (40.7%). Jones et al from Florida found *Fusarium species* as the commonest isolate in a series of 38 cases.⁵ Most of the studies of Indian origin had reported *Aspergillus species* as the commonest fungal

isolate.^{6,7,8} Mycotic keratitis is a male dominated disease as they are more prone to outdoor ocular trauma.^{7,9} Like our study, most of the studies cited trauma as the principal predisposing factor.^{10,11} The average healing time, in our study, was better in natamycin group and success of ulcer resolution was higher in natamycin group. These findings were supported by the study conducted by Kalavathy et al.¹² The major drawback of natamycin is that it is not available in systemic form. Though, Itraconazole is mainly active against *Aspergillus species*, natamycin remains the frontline anti-fungal agents in mycotic keratitis.

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