Role of 0.02% Polyhexamethylene Biguanide and 1% Povidone Iodine in Experimental Aspergillus Keratitis

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MATERIALS AND METHODS

A prospective, randomized, case-control study was carried out in a rabbit model. Prior permission for the experimental study was obtained from the institutional animal ethics committee, and the experimental rules set forth in the ARVO resolution on animal experimentation were strictly adhered to. Twenty-four rabbit corneas were inoculated with a human ocular isolate of Aspergillus fumigatus obtained from the Department of Ocular Microbiology of our center.

Production of the Corneal Ulcer

All eyes received prior 0.3% ciprofloxacin ophthalmic ointment twice daily for 2 days to minimize the risk of secondary bacterial infections. Topical 4% Xylocaine drops were instilled three times

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TABLE 1. Perforations in experimental Aspergillus keratitis (n = 24)

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of eyes</th>
<th>Range (d)</th>
</tr>
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<tbody>
<tr>
<td>A (5% natamycin)</td>
<td>0/6</td>
<td>20</td>
</tr>
<tr>
<td>B (0.02% PHMB)</td>
<td>1/6</td>
<td>20</td>
</tr>
<tr>
<td>C (1% povidone iodine)</td>
<td>3/6</td>
<td>19–22</td>
</tr>
<tr>
<td>D (0.5% HPMC)</td>
<td>5/6</td>
<td>19–23</td>
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PHMB, polyhexamethylene biguanide; HPMC, hydroxypropylmethyl cellulose.

RESULTS

The average time to initiation of the ulcer was 3.62 ± 1.87 days and to attaining 4-mm size was 5.4 ± 2.24 days. None of the ulcers perforated in group A, while there was one perforation in group B, three in group C, and five perforations in group D during the course of therapy (Table 1). None of the eyes developed endophthalmitis. There was no significant variability noted between the two examiners.

The average times to rounding of the ulcer margin, decrease in size of the hypopyon, decrease in infiltrates, decrease in corneal edema, and resolution of epithelial defects are depicted in Table 2. The average healing times for the four groups are shown in Table 2. The difference between groups A and B was statistically significant (p < 0.012). Similarly, differences between groups A and C and groups A and D were highly significant (p < 0.001) (Table 3). All corneas healed with scarring, and those with perforation healed with the formation of adherent leucoma. Scarring was noted to be least with natamycin (group A). It was surprising to note that
The lack of efficacy of 1% povidone iodine against *Aspergillus* keratitis as revealed in the current study is discouraging. The discrepancy between in vitro and in vivo studies is again highlighted. The lack of in vivo efficacy of 1% povidone iodine could be explained by poor corneal penetration. Higher concentrations of povidone iodine may be more effective.

The strengths of this study were that it was a double-masked, prospective, randomized, case-control study in which multiple drugs were tested in a controlled environment and cases were seen by two clinicians masked as to which drug each rabbit was receiving. The weaknesses of this study were that higher concentrations of povidone iodine should have been tested and monkeys would have been a more ideal host because of the similarity between monkey and human corneas. A randomized, controlled trial would already conducted using 0.2% chlorhexidine in mycotic keratitis, which showed its efficacy; hence, we felt no need to repeat the studies in an experimental setting.

This study showed that natamycin is superior to the antiseptic agents used in our study for the treatment of *Aspergillus* keratitis. In India, despite the high prevalence of *Aspergillus* keratitis and the high cost of drugs, natamycin still remains the drug of choice over less expensive antiseptic agents. However, the antiseptic agents may be tried as an adjuvant therapy in *Aspergillus* keratitis. Worldwide, there is a need for further research on the role of less expensive and more readily available drugs that are effective against ocular fungal infection. Thus, we may conclude that 0.02% PHMB is a moderately effective drug for *Aspergillus* keratitis, which needs further assessment for regular use. However, 1% povidone iodine is not an effective drug for topical use against *Aspergillus* keratitis. Further assessment with higher concentrations within tolerable limits is warranted.

**REFERENCES**