ABSTRACT

Objective: To test the antibacterial properties of three commercially available nasal corticosteroid preparations containing Mometasone Furoate (MF), Fluticasone Propionate (FP) and Fluticasone Furoate (FF) against S. pneumoniae, S. viridans, S. aureus, H. influenza, P. aeruginosa and E. coli.

Methods:

Study Design: Experimental in vitro study using the disc diffusion method.

Clinical isolates of S. pneumoniae, H. influenzae, S. viridans, S. aureus, P. aeruginosa, and E. coli were inoculated on separate plates. 0.15 ml of nasal corticosteroid preparations containing MF, FP and FF were applied to blank paper discs, then placed on the plates, including an empty disc. Following 24 and 48 hours of incubation, the inhibition zones were measured to the nearest mm from the point of abrupt inhibition of growth.

Results: After 24 and 48 hours of incubation, S. pneumoniae, S. viridans, and S. aureus showed inhibition zones to all three preparations. S. aureus and S. viridans show the largest zones of inhibition at 24 and 48 hours respectively. H. influenza, P. aeruginosa, and E. coli were negative. The inhibition zones of each bacteria were shown to be statistically different. The preparation containing FP had the largest zone of inhibition at 24 and 48 hours, although post hoc tests showed their difference was not significant.

Conclusion: The present study demonstrates possible antimicrobial properties of commercially available nasal corticosteroid preparations. However, it is unclear whether these can be attributed to the steroids, their excipients, or both. Further studies testing each component may offer better insights into their therapeutic use.

Keywords: Mometasone Furoate, Fluticasone Propionate, Fluticasone Furoate, antibacterial, nasal corticosteroids, allergic rhinitis, acute bacterial rhinosinusitis
Health care experts estimate that in the United States, acute and chronic rhinosinusitis affects an estimated 14% of the population. Unfortunately, there is no precise local information. Although nasal corticosteroids are generally not used in acute infections because of adverse effects, their adjunct use in acute sinusitis has been proposed because of their decongestant and anti-inflammatory properties. Double-blind study data have shown that the addition of topical corticosteroids to oral antibiotics have a positive effect in the treatment of acute exacerbations of chronic rhinosinusitis.

In addition to decongestant and anti-inflammatory properties, recent data suggest that corticosteroids may also demonstrate antibacterial properties against common ear, nose, and throat pathogens. In a recent in vitro study, viability of S. pyogenes was reduced by 99.00% by 0.01% Mometasone Furoate (MF), by 99.90% by 0.1% MF, and by 99.99% by 0.5% MF after 24 hours of incubation. In a similar study, Dexamethasone (0.1%) killed S. milleri and A. flavus after incubation periods of 24 to 48 hours. This added property may modify the heretofore adjunct therapeutic role of topical corticosteroids in the management of acute sinusitis and other common ENT infections. A literature search of Ovid, PubMed and HERDIN databases using the terms “Mometasone Furoate,” “Fluticasone Propionate,” “Fluticasone Furoate” yielded no other studies on the possible antibiotic properties of other intranasal corticosteroids such as Fluticasone Propionate (FP) and Fluticasone Furoate (FF).

This study aims to investigate the antimicrobial activity of commercially available nasal corticosteroid preparations containing Mometasone Furoate (MF), Fluticasone Propionate (FP) and Fluticasone Furoate (FF), against common bacteria causing bacterial sinusitis.

Specific Objectives:
1. To measure the zone of inhibition from nasal corticosteroid preparations containing MF, FP and FF on S. pneumoniae, S. viridians, S. aureus, H. influenzae, P. aeruginosa and E. coli at 24 and 48 hours; and
2. To determine if there is a significant difference among the inhibition zones of S. pneumoniae, S. viridians, S. aureus, H. influenzae, P. aeruginosa and E. coli produced by the three preparations containing MF, FP and FF.

METHODS
Bacterial strains from clinical isolates were inoculated and evaluated using the Vitek 2 Compact System (BioMerieux, Inc. Durham, NC, USA) to verify the identity of the bacteria.

Guided by the Manual on Antibacterial Susceptibility Testing, each organism was inoculated on three separate plates, to allow for randomization. Inoculation was done onto the following media: freshly prepared Mueller-Hinton Agar (S. aureus, P. aeruginosa, and E. coli), Sheep Mueller-Hinton Agar (S. pneumoniae, and S. viridans), and commercially prepared Chocolate Agar Plate (H. influenzae).

Disc diffusion susceptibility testing using the Kirby Bauer inoculation method was performed. Using a micropipette, 0.15 ml of commercially prepared intranasal corticosteroids were applied on separate 6.0 mm sterile blank paper discs (Becton, Dickenson & Company, Sparks MD 21152 USA). The preparations used were Mometasone Furoate 0.05% (Nasonex™, Merck & Co), Fluticasone Propionate 0.05% (Flaxiside™, GlaxoSmithKline) and Fluticasone Furoate 27.5 µg/actuation (Avamys™, GlaxoSmithKline).

The discs were placed individually and distributed evenly into each plate. A blank paper disc was included to serve as a control. The plates were placed in a CO2 incubator (Memmert model TV50U, Bavaria, Germany) set to 35 to 37 °C within 15 minutes after the discs were applied.

Following 24 and 48 hours of incubation, the diameter of each zone of inhibition was measured with a ruler from the edges of the last visible colony-forming growth. The results were recorded in millimeters (mm).

Data was verified and tabulated using Excel, version 2007 (Microsoft Corporation), then analyzed using SPSS for Windows version 16.0.2.

RESULTS
After 24 hours of incubation, plates with S. pneumoniae, S. viridians and S. aureus, showed inhibition zones to MF, FP and FF. Plates with H. Influenzae, P. aeruginosa and E. coli were negative for inhibition (Table 1). S. aureus with FP showed the highest difference from baseline (3mm). Consistently, across other specimens, discs containing FP had the largest zones of inhibition at 24 hours (Table 2).

After 48 hours of incubation, plates with S. pneumoniae, S. viridians, and S. aureus showed inhibition zones to MF, FP and FF. Plates with H. Influenzae, P. aeruginosa and E. coli were negative for inhibition (Table 1). S. viridans showed the largest inhibition zone regardless of the steroid. Consistently, FP registered the largest reaction to S. pneumoniae, S. viridans and S. aureus (Table 2).

At 24 hours, ANOVA detected significant differences among the specimens regardless of the corticosteroid preparation (P-value 0.00). Post hoc (Multiple Comparison) test showed H. influenzae, P. aeruginosa, E. coli and the control were similar to each other, but significantly different from the group S. pneumoniae and S. viridans, and that both groups were significantly different from S. aureus.

At 48 hours, ANOVA detected significant differences among the specimens (P-value 0.00). Post hoc test showed that S. viridans has the highest reaction to the corticosteroid preparations at 48 hours, followed
Table 1. Average size of inhibition zones of the steroid preparations on the different bacterial specimens after 24 and 48 hours of incubation

<table>
<thead>
<tr>
<th>Time</th>
<th>Specimen</th>
<th>S. Aureus</th>
<th>S. Viridans</th>
<th>S. Pneumoniae</th>
<th>H. Influenzae</th>
<th>P. Aeruginosa</th>
<th>E. Coli</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 Hrs</td>
<td>Fluticasone Furoate</td>
<td>7.67</td>
<td>6.67</td>
<td>6.33</td>
<td>6.00</td>
<td>6.00</td>
<td>6.00</td>
<td>6.00</td>
</tr>
<tr>
<td></td>
<td>Fluticasone Propionate</td>
<td>9.00</td>
<td>7.33</td>
<td>8.33</td>
<td>6.00</td>
<td>6.00</td>
<td>6.00</td>
<td>6.00</td>
</tr>
<tr>
<td></td>
<td>Mometasone</td>
<td>7.67</td>
<td>7.00</td>
<td>7.00</td>
<td>6.00</td>
<td>6.00</td>
<td>6.00</td>
<td>6.00</td>
</tr>
<tr>
<td>48 hrs</td>
<td>Fluticasone Furoate</td>
<td>8.33</td>
<td>12.67</td>
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<td>6.00</td>
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<tr>
<td></td>
<td>Fluticasone Propionate</td>
<td>9.00</td>
<td>13.33</td>
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<td>6.00</td>
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<tr>
<td></td>
<td>Mometasone</td>
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<td>9.00</td>
<td>7.00</td>
<td>6.00</td>
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</tbody>
</table>

Table 2 - Average difference of inhibition zones from the baseline of 6mm (blank paper disc diameter). The table shows FP registered the largest reaction to S. pneumoniae, S. viridans and S. aureus at 24 and 48 hours (indicated by an asterisk).

<table>
<thead>
<tr>
<th>Time</th>
<th>Specimen</th>
<th>S. Aureus</th>
<th>S. Viridans</th>
<th>S. Pneumoniae</th>
<th>H. Influenzae</th>
<th>P. Aeruginosa</th>
<th>E. Coli</th>
<th>Control</th>
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<td>1.67</td>
<td>0.67</td>
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<td>0.00</td>
<td>0.00</td>
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</tr>
<tr>
<td></td>
<td>Fluticasone Propionate</td>
<td>3.00*</td>
<td>1.33*</td>
<td>2.33*</td>
<td>0.00</td>
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<td>0.00</td>
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</tr>
<tr>
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<td>1.00</td>
<td>1.00</td>
<td>0.00</td>
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<td>0.00</td>
</tr>
<tr>
<td>48 hrs</td>
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<td>2.33</td>
<td>6.67</td>
<td>0.33</td>
<td>0.00</td>
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<tr>
<td></td>
<td>Fluticasone Propionate</td>
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<tr>
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</table>

DISCUSSION

Nasal corticosteroids have been a mainstay of therapy for allergic rhinitis with persistent symptoms.\(^9\) The use of nasal steroids (particularly with intramaxillary instillation) may be beneficial in chronic rhinosinusitis, with no side effects or increased signs of infection.\(^4\) While it is common practice to treat acute bacterial rhinosinusitis empirically with antibiotics,\(^2\) the idea that steroids may play a role in controlling infection as an adjunctive or first-line treatment is novel. Such a role may find application in treating patients suffering from allergic rhinitis and bacterial sinusitis as well as in other ENT infections.

Several locally available, commonly prescribed nasal corticosteroid sprays currently used for allergic rhinitis include MF, FP and FF. This study suggests that these preparations may possess antimicrobial properties against S. pneumoniae, S. viridans, and S. aureus.

Although the mechanism of action of steroids on bacteria is relatively unknown, the results of this, as well as other studies suggest susceptibility of streptococcus and staphylococcus species to corticosteroids. This may be due to the general effects of corticosteroids.\(^3\)

A recent study on dexamethasone suggests that it may have to do with the steroid’s action on the cell wall or cytoplasmic membrane, as well as the transcription and translation machinery of the microorganisms.\(^5\)

To the best of our knowledge, no other studies have investigated the antibacterial properties of FP or FF.

All three preparations tested contain Benzalkonium chloride as an excipient. Benzalkonium chloride is a quarternary ammonium compound commonly used to prevent bacterial contamination as an antimicrobial additive, rendering solutions bacteriostatic or bactericidal according to concentration. Since 1982, Benzalkonium chloride has been approved by the US Food and Drug Administration as an “inactive ingredient” for prescription drugs.\(^14\)

It is not clear whether the antibacterial properties exhibited by all three preparations of intranasal corticosteroids can be attributed to the steroids, the excipient, or both. While the study shows the preparations themselves have antibacterial properties, further studies testing their components separately are in order.
ACKNOWLEDGEMENT
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REFERENCES