Antibacterial Activity of Mometasone Furoate

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**Objective:** To test the antibacterial properties of the topical corticoid mometasone furoate, which is used as a nasal spray.

**Design:** The activity of mometasone (0.01%, 0.1%, and 0.5%) in buffer solution against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Streptococcus pyogenes*, and *Streptococcus milleri* was tested by quantitative killing assays.

**Setting:** In vitro study.

**Main Outcome Measure:** Reduction of viable bacteria and fungi in quantitative killing assays.

**Results:** Mometasone (0.5%) reduced viable counts of *S pyogenes* and *S milleri* by 99.99% and 99.00%, respectively, after 24 hours of incubation, whereas colony-forming units (CFUs) of *S aureus*, *P aeruginosa*, and *E coli* were not affected by the corticoid. Mometasone (0.1%) caused a decrease in CFUs of *S pyogenes* 99.90% to 99.99%, while it led to a 99.00% reduction in CFUs of *S milleri*, but only if low bacterial counts of 1 × 10⁴ CFUs/mL were incubated. By contrast, the use of mometasone at a low concentration (0.01%) demonstrated an increase in CFUs of *S milleri* if the baseline bacterial count was low (1 × 10⁴ CFUs/mL).

**Conclusion:** Mometasone demonstrates antimicrobial activity against streptococci.


**METHODS**

**BACTERIA AND MEDIA**

Bacterial strains of *Staphylococcus aureus* (American Type Culture Collection [ATCC] 29233), *Pseudomonas aeruginosa* (ATCC 27853), *Escherichia coli* (ATCC 11229), *Streptococcus pyogenes* d68 (Sandoz, Vienna, Austria), and *Streptococcus milleri* (clinical isolate), which were deep frozen for storage, were grown overnight on tryptic soy agar or Columbia blood agar (Merck, Darmstadt, Germany). Colonies from the agar were grown in tryptic soy broth (Merck) at 37°C overnight; *S milleri* was incubated in an atmosphere of 3% carbon dioxide.

Bacteria were centrifuged at 1800 g, washed twice in 0.9% sodium chloride, and diluted to a concentration of 1 × 10⁴ to 1 × 10⁷ colony-forming units (CFUs)/mL before use.

**RESULTS**

Recently, topical corticoids have been used in acute infections of the upper airway tract and external auditory canal because of their anti-inflammatory and deswelling properties. In a study on rats, topical application of a 0.05% betamethasone dipropionate solution was found to be the most efficient therapy for experimental external otitis. In a randomized parallel-group multicenter study on humans, treatment of infected external otitis with betamethasone dipropionate solution (group III steroid) was compared with eardrops containing hydrocortisone (group I steroid), oxymetacryl hydrochloride, and polymyxin B. Treatment with betamethasone solution without antibiotics was superior to the group I steroid plus antibiotics. These results might suggest a direct antimicrobial effect of corticoids. Virtually, we could demonstrate antimicrobial activity of dexamethasone phosphate against the ear, nose, and throat (ENT)-relevant pathogens *Streptococcus milleri*, *Aspergillus flavus*, and *Aspergillus fumigatus*. Dexamethasone is known to be resorbed when applied locally, causing systemic adverse effects in long-term and high-dosage use. Therefore, new corticoids with lower resorption rates and less systemic adverse effects have been introduced in otorhinolaryngology. Mometasone furoate is one of the well-tolerated and highly active modern representatives licensed for allergic and chronic rhinosinusitis, but in the clinical routine, it is also used in acute ENT infections, such as sinusitis, as an adjuvant therapy. The aim of this study was to investigate mometasone on antimicrobial activity against bacteria causing ENT infections.
C, Bactericidal activity of mometasone against Streptococcus milleri (colony-forming unit [CFU] count of 1 × 10^4/mL) at 37°C (pH 7.1); buffer solution without mometasone was the control. Data are given as mean (SEM) values of 3 independent experiments. B, Bactericidal activity of mometasone against S. pyogenes at 37°C (pH 7.1); buffer solution without mometasone was the control. Data are given as mean (SEM) values of 3 independent experiments. † Data are given as mean (SEM) values of 2 independent experiments.

**STATISTICAL ANALYSIS**

The t test was used for comparison of paired means of 2 groups of measurements. One-way analysis of variance and the Dunnett multiple comparison test (GraphPad Software Inc, San Diego, California) were applied for evaluation of the significance of 3 or more groups of measurements at single incubation time points.

**RESULTS**

Viability of S. pyogenes was reduced by 99.00% by 0.01% mometasone, by 99.90% by 0.1% mometasone, and by 99.99% by 0.5% mometasone (Figure, A). This was statistically significant for 0.1% and 0.5% concentrations (P < .05 for 24 hours vs control). At a bacterial count of 1 × 10^4 CFU/mL, S. milleri was killed by 0.1% and 0.5% mometasone (reduction of viable counts by ≥99.00% after 24 hours; P < .01 after 24 hours) (Figure, B) and by 0.5% mometasone at a bacterial count of 1 × 10^3 CFU/mL (Figure, C). When used at a low concentration (0.01%), mometasone demonstrated an increase in CFUs of S. milleri after 24 hours if the test was started with a baseline bacterial count of 1 × 10^3 CFU/mL.

Using the other test bacteria (S. aureus, P. aeruginosa, and E. coli), we detected no reduction in colony counts.

**COMMENT**

For their immunosuppressive effects, corticoids are generally not applied in acute infections. In ENT infections, however, the use of corticoids can be justified in acute sinusitis and external otitis because of their decongestant and anti-inflammatory properties. Emgård and Hellstrom demonstrated an improved therapy for infective external otitis with the class III topical corticoid betamethasone compared with a combination of the class I corticoid hydrocortisone and antibiotics in a rat model and in human beings. The antimicrobial activity of corticoids became conceivable because in these studies by Emgård and Hellstrom, as well as in a study on atopic dermatitis, not only were the clinical symptoms removed, but the pathogens were eliminated more rapidly in the test groups.

**MOMETASONE**

Mometasone (pure substance from Chem Swiss AG, Baar, Switzerland) was diluted in 0.01M phosphate-buffered saline (pH 7.1) to final concentrations of 0.01%, 0.1%, and 0.5%. For S. pyogenes and S. milleri, mometasone was dissolved in 50% tryptic soy broth in 0.9% isotonic sodium chloride solution (pH 7.3) (Merck). Solutions were sonicated for 5 minutes in a Sonorex Bandelin water bath (35 kHz, 240 W; BANDELIN electronic GmbH & Co KG, Berlin, Germany). Phosphate-buffered saline (pH 7.1) and 50% tryptic soy broth in 0.9% isotonic sodium chloride solution (pH 7.3), without mometasone, were applied for control experiments.
In a recent study, we demonstrated antibacterial and antifungal activity of a class III corticoid (dexamethasone phosphate) for the first time to our knowledge. Similar to dexamethasone, we found bacterialidal activity of mometasone against streptococci but not against S. aureus, P. aeruginosa, and E. coli. Not only the spectrum but also the antimicrobial activity of both corticoids appeared to be similar. This might indicate that streptococci are particularly susceptible to corticoids due to their general effects. Surprisingly, Nilsson et al. and Emgård and Hellstrom reported therapeutic efficacy in dermatitis and otitis caused mainly by S. aureus and P. aeruginosa, bacteria whose viability was not affected in our tests. Therefore, we cannot prove that these results are connected with antimicrobial activity of corticoids. On the other hand, bacterial killing assays as performed in our study do not exclude some impact on growth or virulence, which might be causative for the efficacy seen in vivo.

The mechanism of antimicrobial action of corticoids is as yet unclear. Because of the relatively slow activity, specific targets are probably involved. The effect appears to be concentration dependent, and high concentrations are needed for sufficient killing. Since mometasone did not dissolve completely in 0.01M phosphate-buffered saline, the free, active concentration was lower than the added 0.01% to 0.5%. Nevertheless, the clinically applied formulation as a nasal spray is also a suspension. It contains 0.05% mometasone, a concentration very close to 0.1%, which demonstrated activity in our study. Repeated application of the spray may be considered to exert some antibacterial activity in vivo.

In conclusion, antimicrobial activity might contribute to the clinical efficacy of corticoids seen in the treatment of bacterial infections. The suitability of mometasone in the treatment of acute ENT infections remains to be proven in clinical studies.

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Author Contributions: Dr Nagl had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Neher and Nagl. Acquisition of data: Neher and Nagl. Analysis and interpretation of data: Neher, Gstöttner, Scholtz, and Nagl. Drafting of the manuscript: Neher, Gstöttner, and Nagl. Critical revision of the manuscript for important intellectual content: Neher, Gstöttner, Scholtz, and Nagl. Statistical analysis: Gstöttner and Nagl. Administrative, technical, and material support: Neher and Nagl. Study supervision: Neher, Gstöttner, Scholtz, and Nagl.

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