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Title of Study
A Proof of Concept Study to Evaluate Effects of Intranasal Salmeterol and Fluticasone Given Alone and in Combination in Allergic Rhinitis

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Study centre(s)
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Publication (reference)
LIPWORTH BJ, SHORT P, BURNS P, NAIR A. Effects of intranasal salmeterol and fluticasone given alone and in combination in persistent allergic rhinitis. Ann Allergy Asthma Immunol 2012:108;54-59

Date of last completed
14.09.2010

Objectives
To evaluate the effects of intranasal salmeterol and fluticasone propionate alone and in combination on the response to nasal adenosine monophosphate (AMP) challenge to assess mast cell activation.

Methodology
Twenty-three patients with persistent allergic rhinitis completed a randomized, double-blind, placebo-controlled, 4-way crossover trial. They received once daily treatment with placebo, salmeterol, 50 µg, fluticasone propionate, 500 µg, or fluticasone propionate and salmeterol combination, 500/50 µg, delivered via an antistatic spacer with nasal adapter for 1 week each, with trough measurements being made 12 hours after the first and last dose.

Number of patients planned
30 patients recruited to ensure 20 patients complete the study per protocol

Number of patients analysed
23

Diagnosis and main criteria for inclusion
Non-asthmatic patients, 18-65 years of age, ≥1positive skin prick test result, history of persistent allergic rhinitis to perennial or seasonal allergens, ≥ 20% decrease in peak nasal inspiratory flow after nasal AMP challenge.

Test product dose
Arm A
Fluticasone Propionate 250 µg 2 puffs nocte delivered by a customized nasal adaptor connected to a spacer device
Arm B
Salmeterol 25 µg 2 puffs nocte delivered by a customized nasal adaptor connected to a spacer device
Arm C
Salmeterol + Fluticasone Propionate 2 puffs nocte delivered by a customized nasal adaptor connected to a spacer device
Arm D
Placebo 2 puffs nocte delivered by a customized nasal adaptor connected to a spacer device

Duration of treatment
4 weeks (4 treatment periods of 1 week)

Reference therapy
None

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Primary Endpoint
The maximum percentage decrease in peak nasal inspiratory flow after nasal AMP challenge.

Secondary Endpoints
TNS4 score, nasal nitric oxide, serum eosinophilic cationic protein level, or nasal airway resistance, Mini-RQLQ Score

Statistical methods
Data analysis was performed using SPSS statistical software for Windows, version 17 (SPSS Inc, Chicago, Illinois). The study was powered (>80%) on a sample size of 20 patients completing per protocol to show a 20% difference in maximum PNIF response (the primary outcome) to nasal AMP challenge for active treatments vs placebo. An overall, multifactorial, repeated-measures analysis of variance was performed, and where significant, this was followed by Bonferroni-corrected, multiple, pairwise testing with an α error of .05 (2 tailed).

Results
For the primary outcome there was significant protection after single and long-term dosing with fluticasone alone and fluticasone-salmeterol combination, whereas salmeterol alone only afforded protection after the first dose. Fluticasone-salmeterol combination and fluticasone but not salmeterol conferred significant chronic dosing effects on secondary outcomes of nasal symptoms and disease-specific quality of life. There was no potentiation of the response to fluticasone by salmeterol on any outcomes when given in combination.

Conclusion
Chronic dosing with fluticasone but not salmeterol confers anti-inflammatory activity against nasal AMP challenge, but there was no potentiation of fluticasone when given in combination with salmeterol. Thus, salmeterol may not be an effective treatment for use in allergic rhinitis.

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