

*Short Communication*

## Effects of a Topical Microemulsion in House Dust Mite Allergic Rhinitis

Morgan Andersson<sup>1</sup>, Lennart Greiff<sup>1</sup> and Per Wollmer<sup>2</sup>

<sup>1</sup>Department of ORL, Head and Neck Surgery, Skåne University Hospital, Lund, Sweden, and <sup>2</sup>Department of Clinical Physiology, Skåne University Hospital, Malmö, Sweden

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**Abstract:** We have previously demonstrated that a topical microemulsion can attenuate symptoms and signs of seasonal allergic rhinitis. This likely reflects that the microemulsion interferes with the interaction between the allergen and the mucosa. Whether or not the finding translates to conditions caused by other inhaled agents such as house dust mite allergen is unknown. Patients with perennial allergic rhinitis caused by house dust mite were subjected to topical microemulsion treatment in a randomized, double-blinded and crossover design with isotonic saline as control. Morning symptoms were monitored, change from baseline was assessed and the treatments were compared. On the first days of the isotonic saline and microemulsion runs, before any treatment was given, total nasal symptoms were scored to 2.8 and 3.1 (range 0–9), respectively. Nasal symptoms were reduced by intervention with the microemulsion: the change from baseline was consistent for the microemulsion and the difference between the microemulsion and isotonic saline reached statistical significance in favour of the former. We conclude that intervention with a microemulsion may reduce symptoms of house dust mite allergic rhinitis at natural allergen exposure. Our findings suggest the possibility that topical microemulsions can be a useful option to reduce nasal mucosal exposure to allergen in perennial allergic rhinitis.

### Introduction and Background

The nasal mucosa constitutes a barrier protecting the body from potentially noxious factors such as inhaled particles. We recently demonstrated that this barrier could be enforced in seasonal allergic rhinitis by experimental administration of a microemulsion to its surface [1]. Accordingly, a single administration of a specific mixture of lipids, surface-active agents and water reduced symptoms induced by acute allergen exposure as well as the associated inflammatory plasma exudation that characterized the condition. We hypothesized that the mechanism of action was that the microemulsion reduced the interaction between the allergen and the mucosa.

Perennial allergic rhinitis caused by house dust mite features symptoms that often are of a lesser intensity than at seasonal allergic rhinitis, but the characteristic nasal morning symptoms often require treatment with topical corticosteroids for extended periods of time [2]. While this treatment is usually well tolerated, side effects including crusting and nosebleed may occur [3]. Our observation that a topical microemulsion may be beneficial in allergic rhinitis caused by pollen allergen, and the likely mechanism of action, suggests

that microemulsion treatment may be efficacious also against other inhaled allergens. In this study, we therefore examined patients with perennial allergic rhinitis caused by house dust mite. The patients were subjected to topical microemulsion treatment in a randomized and cross-over design where isotonic saline was used as control. The patients were monitored by assessment of morning symptoms at natural allergen exposure.

### Material and Methods

The study was of a randomized, double-blinded and cross-over design using isotonic saline (nasal spray) as control treatment. Patients with house dust mite allergic rhinitis were subjected to withdrawal of on-going anti-allergy medication for 2 weeks. Thereafter, they received treatment for two periods of 6 days separated by 1 week. Nasal symptoms were recorded in the morning of treatment days 2 through 6. Symptoms were also scored on treatment day 1 prior to treatment and used as baseline.

Twenty patients (aged 19–48 years, five women) were recruited. Inclusion criteria: History of perennial allergic rhinitis for at least 2 years and positive skin prick test to house dust mite allergen. (Seventeen patients also had seasonal allergies but were not exposed to these allergens because the study was performed outside the pollen season). Exclusion criteria: History or signs of chronic rhinosinusitis or polyposis, upper respiratory tract infection within 7 days of the study start, use of nasal drugs and oral antihistamines/corticosteroids <2 weeks before the start of the study. The study was approved by the regional ethics committee and informed consent was obtained.

Author for correspondence: Lennart Greiff, Department of Otorhinolaryngology, Head and Neck Surgery, Skåne University Hospital, SE-221 85 Lund, Sweden (fax +46 46 2110968, e-mail lennart.greiff@skane.se).

In randomized order, treatments with a microemulsion and isotonic saline were carried out for 6 days each. The treatments were given using spray devices delivering 50  $\mu$ L per actuation. One puff per nasal cavity was given twice daily, i.e., in the morning and in the evening. The interventions were carried out with a 1-week washout period. The microemulsion was a mixture of glycerol-monooleate, propylene-glycol, polyethylene-glycol 400, sesame oil, polysorbate-80 and isotonic saline.

The patients scored nasal symptoms every morning. Accordingly, secretion, blockage and sneezes were scored on a four-point scale where 0 = no, 1 = mild, 2 = moderate and 3 = severe symptoms, and a total nasal symptom score was calculated (range 0–9). Differences from baseline (assessment on treatment day 1 prior to the treatment) to post-challenge scores (recorded on treatment days 2 through 6) were calculated, and differences between the interventions with isotonic saline (control treatment) and microemulsion were compared using the ANOVA/Student's *t*-test. Data were normally distributed.

### Results and Discussion

On-going treatment for allergic rhinitis was withdrawn in the present study, and 2 weeks later the patients experienced mild to moderate symptoms dominated by nasal blockage. On the first days of the isotonic saline and microemulsion runs, before any treatment was given, total nasal symptoms were scored to  $2.8 \pm 0.3$  and  $3.1 \pm 0.3$  (mean  $\pm$  S.E.M.), respectively. This observation confirmed the history of perennial allergic rhinitis and the positive result of the house dust mite skin prick test and indicated that the symptoms were of the same magnitude when patients underwent active and placebo treatment.

Nasal symptoms were reduced by intervention with the microemulsion: the change from baseline was consistent for the microemulsion and the difference between the microemulsion and isotonic saline reached statistical significance on treatment days 3, 4 and 6 (Fig. 1). Similarly, taken the whole treatment period into account, a statistically significant

difference was observed in favour of the microemulsion ( $p < 0.01$ ). The finding is in agreement with our previous observation on symptom-relieving effects of a microemulsion in seasonal allergic rhinitis, and it supports the hypothesis that the microemulsion reduces the interaction between the allergen and the mucosa in a non-specific fashion [1]. Accordingly, we suggest that microemulsions may be efficacious for allergic rhinitis independent on the type of allergen that produces nasal symptoms.

In contrast to our previous study in which a pool device was used for experimental administration of a large volume of microemulsion [1], the present study involved administration of small volumes (50  $\mu$ L) using a spray device. Symptoms were recorded at a time-point 12 hr after dosing (i.e., morning symptoms following dosing on the previous evening), and the results therefore indicate that the microemulsion, administered using a spray device, was effective for several hours. Microemulsions containing glycerol monooleate are known to be bioadhesive and are probably not cleared by mucociliary activity as rapidly as, e.g. suspensions [4]. Preliminary data have also shown prolonged nasal retention of topical microemulsions (Wollmer *et al.* unpublished results). The present volume and nasal spray administration twice daily (this study) is a feasible mode of administration for patients with allergic rhinitis.

Isotonic saline was used as control treatment in the present study. This measure was not a true placebo because isotonic (and hypertonic) saline might be effective in allergic rhinitis [5–7]. For example, Garavento *et al.* [7] demonstrated that nasal administration of isotonic saline was efficacious in children with seasonal allergic rhinitis. The possibility that saline may exert such effects (even if this is not suggested from the present study: Fig. 1), in combination with the significant differences between the microemulsion and isotonic saline in the present study, strengthens our conclusion that the microemulsion is effective in perennial allergic rhinitis.

Interventions aiming at avoiding allergen exposure have recently received attention. A gel-forming cellulose powder was introduced after observations in an open study involving patients with allergic rhinitis [8]. Emberlin & Lewis [9] later showed, in a placebo-controlled study, that cellulose powder reduced rescue medication at seasonal allergen exposure, while nasal symptoms were only marginally reduced. Furthermore, symptoms were reduced by cellulose powder in an experimental challenge model involving dust mite allergens (Der p1 and Der f1) [10]. Accordingly, cellulose powder shows emerging promise as a treatment for allergic rhinitis. A thixotropic fluid (nasal spray) is now also available as a treatment for allergic rhinitis. It is claimed to relieve symptoms in allergic rhinitis, but this is as yet not substantiated by published controlled studies. However, taken together the above concepts and our observations performed with topical microemulsions highlight the possibility that devices aiming at physically protecting the nasal mucosa against allergen may be valid treatment options in allergic rhinitis. This may be viewed as being in line with current recommendations of allergen avoidance in allergic rhinitis [2].

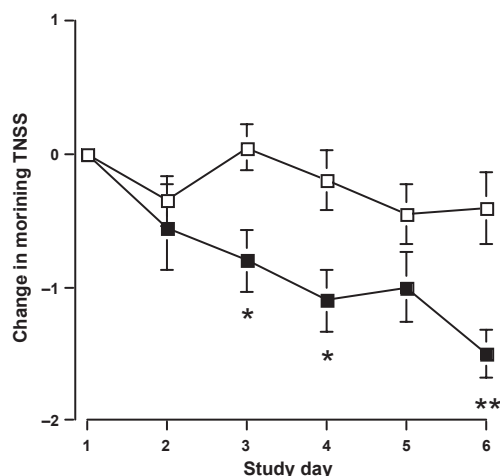


Fig. 1. Change (mean  $\pm$  S.E.M.) from baseline symptoms after the start of treatment with isotonic saline (open symbols) and microemulsion (filled symbols) in a cross-over design. Symptoms were reduced by microemulsion treatment *c.f.* isotonic saline: \* and \*\* denote  $p < 0.05$  and  $0.01$ , respectively. TNSS: total nasal symptom score.

While the microemulsion reduced symptoms of allergic rhinitis in this study, other facets of its use need to be addressed. These include comparisons with established treatments for allergic rhinitis including antihistamines and topical corticosteroids. Furthermore, effects of prolonged treatment periods need to be evaluated in terms of whether the efficacy of the microemulsion is maintained and if side effects will develop. (No side effects were recorded in this study). In addition, it should be examined whether administration of the microemulsion interferes with other topical drugs, e.g. topical antihistamines and corticosteroids.

Based on this preliminary study, we conclude that intervention with a microemulsion reduces symptoms of house dust mite allergic rhinitis at natural allergen exposure. Our findings suggest the possibility that topical microemulsions may be a useful option to avoid mucosal exposure to allergen in perennial allergic rhinitis. We suggest microemulsions be viewed as a means by which mucosal exposure to harmful inhaled factors in general may be reduced.

### References

- 1 Andersson M, Greiff L, Wollmer P. Nasal treatment with a microemulsion reduces allergen challenge-induced symptoms and signs of allergic rhinitis. *Acta Otolaryngol* 2008;**128**:666–9.
- 2 Bousquet J, Van Cauwenberge P, Bachert C, Canonica GW, Demoly P, Durham SR *et al.* Requirements for medication commonly used in the treatment of allergic rhinitis. *European Academy of Allergy and Clinical Immunology (EAACI), Allergic Rhinitis and its Impact on Asthma (ARIA)*. *Allergy* 2003;**58**:192–7.
- 3 Cervin A, Andersson M. Intranasal steroids and septum perforation – an overlooked complication? A description of the course of events and a discussion of the causes. *Rhinology* 1998;**36**:128–32.
- 4 Nielsen LS, Schubert L, Hansen J. Bioadhesive drug delivery systems I. Characterisation of mucoadhesive properties of systems based on glyceryl mono-oleate and glyceryl monolinoleate. *Eur J Pharm Sci* 1998;**6**:231–9.
- 5 Gerogitis JW. Nasal hyperthermia and simple irrigation for perennial allergic rhinitis. Changes in inflammatory mediators. *Chest* 1994;**106**:1487–92.
- 6 Subiza JL, Subiza J, Barjau MC, Rodríguez R, Gavilán MJ. Inhibition of the seasonal IgE increase to *Dactylis glomerata* by daily sodium chloride nasal-sinus irrigation during the grass pollen season. *J Allergy Clin Immunol* 1999;**104**:711–2.
- 7 Garavento W, Di Berardino F, Romagnoli M, Sambataro G, Gaini RM. Nasal rinsing with hypertonic solution: an adjunctive treatment for pediatric seasonal allergic rhinoconjunctivitis. *Int Arch Allergy Immunol* 2005;**137**:310–4.
- 8 Josling P, Steadman S. Use of cellulose powder for the treatment of seasonal allergic rhinitis. *Adv Ther* 2003;**20**:213–9.
- 9 Emberlin JC, Lewis RA. A double blind, placebo controlled trial of inert cellulose powder for the relief of symptoms of hay fever in adults. *Curr Med Res Opin* 2006;**22**:275–85.
- 10 Emberlin JC, Lewis RA. A double blind, placebo-controlled crossover trial cellulose powder by nasal provocation with Der p1 and Der f1. *Curr Med Res Opin* 2007;**23**:2423–31.