

Novel approach to assessing the effects of sulphurous thermal waters on an in vitro 3D nasal integrity model from allergic rhinitis patients

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Background Chronic allergic rhinitis is associated with inflammation of the nasal mucosa, changes in nasal epithelial integrity and subsequent clinical symptoms. Sulphurous (natural mineral) thermal waters (STWs) have been used as complementary therapeutic approach to chronic rhinitis / rhinosinusitis, with studies demonstrating clinical efficacy, namely in terms of improvement in mucociliary clearance time, nasal resistance and nasal flow. However, very few data exist regarding the effects of STW-based treatment on nasal epithelial integrity parameters. We have hypothesized that STWs treatment will modulate an amelioration of general integrity of allergic rhinitis nasal mucosa.

Purpose In this preliminary study, we aimed to develop a method to assess the effects of STWs and control isotonic sodium chloride solution (ISCS) in an in vitro allergic rhinitis model.

Methods 3D nasal inserts from a non-smoking patient with chronic allergic rhinitis (MucilAir-HFAllergic Rhinitis) were placed in culture and exposed to STWs or ISCS using a specially designed bioaerosol nebulizing generator for 1, 2, 4, and 8 minutes for 7 days (n = 3). Trans-epithelial electric resistance (TEER) was measured before and 24 h after each exposure, as a measure of epithelial integrity. TEER values between 200 – 600 Ω .cm² were regarded as being representative of undamaged epithelia, in accordance with international criteria.

Results Initial TEER values of all nasal inserts were higher than 600 Ω .cm², indicating values above normal. ISCS exposure maintained TEER levels above 600 Ω .cm², although, on day 5 of aerosol exposure there was a drastic reduction of

TEER values. In contrast, on the 2nd day of STWs exposure, there was a trend for TEER values to become lower than $600 \Omega \cdot \text{cm}^2$, at all time points. However, this reduction was only maintained up to the 4th nebulization when cells were exposed to STWs only for 4 minutes. From then on, TEER values rose to levels observed before aerosol exposure.

Conclusions Dose-response results suggest that, unlike exposure to ISCS, exposure of nasal mucosa of a patient with allergic rhinitis to STWs for 4 minutes per day may improve and preserve epithelial integrity. Thus, this may be a suitable in vitro set up to mimic in vivo treatments of chronic rhinitis with STWs. Nevertheless, further studies are warranted to understand the effects of STWs on MucilAir-HF-Allergic rhinitis epithelial integrity as well as function.