

Cystic Fibrosis Research News

Title:

Sino-nasal Inhalation of Isotonic versus Hypertonic Saline (6.0 %) in CF Patients with Chronic Rhinosinusitis – Results of a Multicentre, Prospective, Randomized, Double-blind, Controlled Trial

Authors:

Jochen G Mainz¹, Ulrike Schumacher², Katja Schädlich¹, Julia Hentschel^{1,17}, Christiane Koitschev³, Assen Koitschev³, Joachim Riethmüller⁴, Freerk Prenzel⁵, Olaf Sommerburg⁶, Bärbel Wiedemann⁷, Doris Staab⁸, Wolfgang Gleiber⁹, Rainald Fischer¹⁰, James F Beck¹ and Christin Arnold¹

Cooperators: Claudia Schien¹, Anika Nader¹, Constance Henn⁵, Christina Smaczny⁹, Claudius Werner¹¹, Helge Hebestreit¹², Hans Eberhard Heuer¹³, Sebastian Schmidt¹⁴, Corinna Eichhorn¹⁵, Isabella Schiller¹⁵, Andrea Roessler¹⁵, Ingo Baumann¹⁶

Affiliations:

¹Jena University Hospital, CF Centre, Jena, Germany

²Jena University Hospital, Institute of Medical Statistics and Documentation, Jena, Germany

³Klinikum Stuttgart, Pediatric Otorhinolaryngology, Stuttgart, Germany

⁴Tübingen University Hospital, Pediatric CF Centre, Tübingen, Germany

⁵Leipzig University Hospital, Pediatric Pneumology/Allergy, Leipzig, Germany

⁶Heidelberg University Hospital, Pediatric CF Centre, Heidelberg, Germany

⁷Institute for Medical Informatics and Biometry, Technical University of Dresden, Germany

⁸Charité' University Hospital Berlin, CF Centre, Berlin, Germany

⁹Frankfurt University Hospital, Pneumology/Allergology, Frankfurt, Germany

¹⁰München University Hospital, CF Centre, München, Germany

¹¹Münster University Hospital, Pediatric Pneumology, Münster, Germany

¹²Würzburg University Hospital, Pediatric Pneumology, Würzburg, Germany

¹³CF Center Hamburg, Hamburg, Germany

¹⁴Greifswald University Hospital, Pneumology/Allergology, Greifswald, Germany

¹⁵Jena University Hospital, Centre for Clinical Studies, Jena, Germany

¹⁶Heidelberg University Hospital, Ear-Nose-Throat Department, Heidelberg, Germany

¹⁷Institute of Human Genetics, University of Leipzig Hospitals and Clinics, Leipzig, Germany

Cystic Fibrosis Research News

What was your research question?

Previously, we found that dornase alfa inhaled as a vibrating aerosol into the nose and the paranasal sinuses (hollow rooms at the inner sides of the nose) reduced sinonasal symptoms that include congestion or secretions. This study assesses, whether hypertonic saline (NaCl 6.0%) compared to isotonic saline (NaCl 0.9%) has similar effects.

Why is this important?

The nasal airways and paranasal sinuses are affected by defective cystic fibrosis transmembrane conductance regulator (CFTR)-channels in cystic fibrosis (CF) and computed tomography (a procedure used to obtain images of an area inside the body) reveals abnormalities in almost all people with CF. Consequently, many people with CF suffer from chronic rhinosinusitis with nasal obstruction, secretions and crusts, pain and loss of smell. Since the CFTR-defect cannot be corrected by surgery, it is important to assess non-invasive methods to reduce these chronic sinonasal problems. Additionally, the sinonasal space was found to be a site of first and persistent colonisation with pathogens including *Pseudomonas aeruginosa*. Therefore, improvement of clearance and ventilation of the sinonasal space is important for overall health in CF.

What did you do?

In a double-blind, controlled cross-over study 69 people with CF suffering from chronic sinonasal symptoms nasally inhaled Hypertonic saline or Isotonic saline over 4 weeks as a vibrating aerosol with the PariSinus™ nebulizer. After 4 weeks without using the device ('wash-out'), each person then switched to the other nasally inhaled medication. The trial outcome was measured with a specially designed questionnaire (Sinonasal-Outcome Test 20 = 'SNOT-20') that asks about 20 symptoms (e.g. sneezing, secretions from the upper airways or nasal obstruction) or issues (e.g. embarrassment), which are influenced by sinonasal symptoms, to obtain a 'symptom score'. Additionally nasal lavages (rinsing 10 mL of NaCl 0.9% through each nostril) were collected to measure inflammation, nasal airflow and resistance (similar to a lung function test but for the nose) and lung function.

What did you find?

Both treatments were well tolerated by the participating people with CF. Sinonasal vibrating inhalation with both concentrations of saline led to a slight reduction of symptoms (Hypertonic saline : reduction of -3.1 points, Isotonic saline : reduction of -5.1 points). The most specific sinonasal symptoms including nasal obstruction, sneezing, runny nose, thick nasal discharge, and reduced smell improved to a similar degree using either concentration



Cystic Fibrosis Research News

of saline (Hypertonic saline : 4.2 points; Isotonic saline : 7.0 points). We did not measure relevant changes of inflammatory mediators in nasal lavage or in nasal and lung function testing.

What does this mean and reasons for caution?

This study shows that Hypertonic saline is not better than Isotonic saline to treat sinonasal symptoms. A limitation is that a side effect of hypertonic saline is irritation or coughing after bronchial inhalation. Furthermore, the use of symptom-scores, like the SNOT-20 does not adequately reflect that hypertonic saline is a relatively cheap therapeutic option for, reducing sinonasal secretions and crusts. However, measuring the amount of sinonasal secretions that are removed is almost impossible in a clinical trial.

What's next?

Previous case reports and pilot studies with the device used here are promising and sinonasal vibrating inhalation with antibiotics (tobramycin/colistin or aztreonam) could allow eradication of disease-causing bacteria, such as *P. aeruginosa*, from the sinonasal space. Large and multi-centre clinical trials are required to assess this therapeutic option.

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Cystic Fibrosis Research News



Figure 1: Sinonasal inhalation with vibrating aerosols is performed during periods of breath holding with elevated soft palate (almost saying 'k') and with semi occluded contralateral nostril. The additional tube superposes the vibration which is required to bring the medication into the paranasal sinuses.