Efficacy of peripheral deposition of inhaled rhDNase in CF patients during a respiratory tract exacerbation

E.M. Bakker1, S. Volpi1, E. Saladini2, B. Müllinger3, P. Kroneberg3, W.C.J. Hop4, B.M. Assael1, H.A.W.M. Tiddens1,5, 1Erasmus MC – Sophia Children’s Hospital, Pediatric Pulmonology, Rotterdam, Netherlands; 2Azienda Ospedaliera di Verona, Cystic Fibrosis Centre, Verona, Italy; 3Actiaco mour GmbH, Gemenaden, Germany; 4Erasmus MC – Sophia Children’s Hospital, Epidemiology and Biostatistics, Rotterdam, Netherlands; 5Erasmus MC, Radiology, Rotterdam, Netherlands

Introduction: Increased sputum production during a respiratory tract exacerbation (RTE) can result in preferential deposition of nebulized rhDNase in central airways. More efficient deposition of rhDNase in peripheral airways might improve mobilization of sputum from these airways.

Aim: To compare efficacy of rhDNase nebulization targeted to the peripheral airways with that of rhDNase targeted to central airways in CF patients with a RTE.

Methods: Inclusion criteria: CF, admitted for RTE, FVC > 40%. Randomized controlled, double blind, clinical trial in 2 CF centres. Primary endpoint FEFF75. Day 1–5 run-in: rhDNase inhalation with conventional nebulizer. Day 6 switch to Akita® nebulizer and randomization to:

- peripheral setting: MMAD 3.0 μm, slow inhalation, aerosol bolus at start of breath; or
- central setting: MMAD 6.0 μm, normal inhalation, aerosol bolus in middle of breath. Minimal treatment duration with Akita®: 7 days. ANOVA analysis was performed.

Results: 39 CF patients included, 17 male. Mean age 21 yrs. Spirometry at start of study: FVC 74%; FEV1 58%; FEFF75 21% pred. 37 patients completed the study. Treatment effect for peripheral versus central was a factor 1.15, 95% CI 0.9−1.5, p = 0.3 (posters figs. 1−3). For FEV1 similar results were found. Treatment effect for peripheral versus central was a factor 1.15, 95% CI 0.9−1.5, p = 0.3 (posters figs. 1−3). For FEV1 similar results were found.

Conclusion: In this pilot study there was no significant difference in treatment effect between peripheral and central deposition of inhaled rhDNase in CF patients during a RTE. However, lung function and responses varied widely between patients. It is well possible that this study was underpowered to observe a significant difference. A similar study is stable CF patients is ongoing.

Hyaluronic acid in the prevention of bronchial obstruction induced by hypertonic saline

U. Pradai1, A. Borruso1, E. Saladini1, E. Fedrigo1, L. Menin1, C. Tartali1, B.M. Assael1, 1Cystic Fibrosis Center, Verona, Italy

Bronchial obstruction is a possible complication of inhaled hypertonic saline (HS), such that a premedication with bronchodilators is suggested. Adding hyaluronic acid (HA) to HS (HAHS) has been recently shown to partially protect patients from intolerance symptoms induced by HS [1]. However, the protective effect of HAHS on bronchial hyper-reactivity is not documented yet.

The aim of the present study was to evaluate the presence of induced bronchoconstriction after a single inhaled dose of HS and HAHS. 36 CF patients (12 M, 24 F) aged 11−45 yrs entered the study. On two separate occasions, patients inhaled HS (0.7 bar) or HAHS (0.7 bar) using a normal volume metering nebulizer. Lung function testing was performed at baseline, after the inhalation of salbutamol 200 mcg and after HS/HAHS. The change (A) in lung function parameters before salbutamol and after HS/HAHS was considered. A significant bronchoconstriction was defined as a drop in FEV1 of at least 12% (or 200 ml) after HS/HAHS when compared to baseline.

Overall, no difference was found between HS and HAHS for AFEV1/FVC (1.6±4.0 vs 3.0±2.40 respectively), AFEFV1(–3.2±4.0 vs −6.6±6.5%pr.) and ΔFEFV1 (−0.4±4.0 vs 0.2±3.6%pr.), whereas ΔMEF20% was significantly increased after HAHS (0.7±24.2 vs 5.5±10.2%pr., p = 0.02). Five patients (14%) experienced significant bronchial obstruction after HS. In two of them (6%) airway narrowing was induced by HAHS as well. No patient showed bronchial obstruction after HS alone.

The present study shows that HS induced bronchial obstruction more frequently than HAHS, suggesting a possible protective role of HA on bronchial hyper-reactivity.

Reference(s)

Particle size determination of a generic nebulized tobramycin

C.D. Kofman1, J.E. Balinotti1, A.M. Tepel1, 1Hospital de Niños Ricardo Gutierrez, Centro Respiratorio, Buenos Aires, Argentina

Rationale: Use of nebulized tobramycin is a relevant treatment for controlling chronic infection of Pseudomonas aeruginosa in cystic fibrosis patients. Many commercial brands of tobramycin are available in the market. To characterize in vitro properties of a generic tobramycin is necessary to evaluate not only the suspension but also the ability to generate acceptable particles to deeply achieve the smaller airways when the suspension is nebulized.

Objective: To compare the dispersion of size of particles obtained with a generic tobramycin (Tobradosa™) with the original (Tobi™).

Methods: Particle size was determined through a laser diffractor analyzer (Malvern Sizer) during the nebulization of Tobradosa or Tobi with a Pari Jet nebulizer and a Devilbiss compressor. Three determinations were done for each medication.

Results: Average median diameter (± geometric standard deviation) was 4.83±2.2 μm and 5.29±1.8 μm (NS) for Tobradosa and Tobi respectively. Percentage of particles smaller than 4.8 μm was 54.3% and 56.9% (NS), and smaller than 3.1 μm was 34.8% and 38.4% (NS) for Tobradosa and Tobi respectively.

Conclusion: Particle size obtained during nebulization of a generic tobramycin (Tobradosa™) was similar to that of the original tobramycin (Tobi™).

Optimization of inhalation treatment – assessment of the influence of type of nebulizer and value of compressed air pressure on aerosol particle size of rhDNase

Z. Podolec1, J. Siekaniec1, 1Dept. of Aerosology and Aerosol Bioengineering Research and Development Centre MEDiNET, Cracow, Poland

Introduction: The subject of study was to examine the influence of Sidestream® [Respironics, UK] nebulizer equipment and the value of compressed air pressure from the NEBSTEER® pneumos dosimeter [abcMED, PL] on the distribution of aerosol particle size of rhDNase [Pulmozyme®, Roche CH]. Sidestream® nebulizer with T-connector or BCTS-head is ventilated but with T-connector is non-ventilated nebulizer. NEBSTEER® is used to monitor the constant value of air pressure during the study.

Methods: Aerosol’s dose and particle size were measured by laser diffraction method.

Results: The study demonstrated statistically significant influence of air pressure on aerosol particle size. For Sidestream® nebulizer with T-connector (non ventilated), MMAD value was 0.54, 0.89 and 0.93 μm for air pressure 0.6, 0.8 and 1.0 bar respectively. For Sidestream® nebulizer with BCTS-head, MMAD value was 0.41 μm for air pressure 1.0 bar, whereas for Sidestream® nebulizer with TV-connector (ventilated) the change of air pressure for 0.6, 0.8 and 1 bar causes the change of MMAD value for 2.24, 3.69 and 4.27 μm respectively. This change differs statistically significant in comparison to the influence of the air pressure on aerosol particle diameter for non-ventilated set and ventilated set with BCTS-head.

Conclusion: The individual adaptation of the aerosol particle diameter and air flow during inspiration enables optimization of inhalation treatment. Supported by: abcMED Poland.