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

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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 FEF75. 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%; FEF75 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 (poster figs. 1–3). For FEV1 similar results were found. Treatment effect might be age dependent (poster fig. 4).
Conclusions: 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.

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

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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 days patients inhaled HS (5.8% NaCl, 4 ml) and HAHS (7% NaCl + 0.1% HA, 5 ml) in random order. Lung function testing was performed at baseline, after the inhalation of salbutamol 200 mcg and after HS/HAHS. The change (Δ) in lung function parameters before salbutamol and after HS/HAHS was considered. A significant bronchoconstriction was defined as a drop in FEV_1 of at least 12% (or 200 ml) after HS/HAHS when compared to baseline.
Overall, no difference was found between HS and HAHS for ΔFEV_1/FVC (1.6±4.0 vs 3.0±4.0 respectively), ΔFVC (−3.2±4.0 vs −3.6±6.5 %pr.) and ΔFEV_1 (−0.4±4.0 vs 0.2±3.6 %pr.), whereas ΔMEF_{50} 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 HAHS 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)

[1] Pediatr Pulmonol 2009; 44 (S32): 243.

241 Particle size determination of a generic nebulized tobramycin

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Rationale: Use of nebulized tobramycin is a relevant treatment for controlling chronic infection of Pseudomona 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 orginal (Tobi ™).
Methods: Particles size was determined through a lasser difractor 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: Particles size obtained during nebulization of a generic tobramycin (Tobradosa ™) was similar to that of the original tobramycin (Tobi ™).

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

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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® pneumodosimeter [abcMED, PL] on the distribution of aerosol particle size of rhDNase [Pulmozyme®, Roche CH]. Sidestream® nebulizer with TV-connector or BCTS-head® is ventilated but with T-connector is non ventilated nebulizer. NEBSTEER® is PC spirometer with dosimeter using to administer aerosol by pneumatic or pneumodosimetric method. The device has the possibility to programme the dose and the time of administration of aerosol basing on the constant analysis of breathing.
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.
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