Re: Effectiveness of hypertonic saline nebulization in airway clearance in children with non-cystic fibrosis bronchiectasis: a randomized control trial

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Abstract

This first RCT of hypertonic saline use in pediatric non-CF bronchiectasis patients uses a cross over design and demonstrates an improvement in predicted FEV1 and FVC. Limitations include lack of blinding and risk of information bias, as well as reduced precision due to absence of within subject comparisons.

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Short title : Re: RCT of 3% saline in pediatric non-CF bronchiectasis

Conflict of Interest Disclosures:

Dr. Valji does not have any conflicts of interest relevant to this article to disclose.

Dr. Mehta does not have any conflicts of interest relevant to this article to disclose.

Dr. Hicks is a site co-investigator for the Vertex-CF disease modifying drugs and AstraZeneca-RSV prophylaxis trials. She is a site primary investigator for the Sanofi-asthma biologics trial.

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Abstract

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Dear Editor,

I congratulate the authors of "Effectiveness of hypertonic saline nebulization in airway clearance in children with non-cystic fibrosis (non-CF) bronchiectasis: a randomized control trial" on performing the first randomized control trial of its kind in the pediatric population. Through a crossover design, the authors demonstrate that nebulized 3% saline significantly improved mean predicted forced expiratory volume in 1 second and predicted forced vital capacity.

Unfortunately, the absence of a placebo introduces significant bias to the authors' intended comparison of conventional airway clearance therapy (ACT) to conventional ACT with hypertonic saline. Isotonic saline (+/- amiloride to mask taste) has been used as a placebo in cystic fibrosis studies with no significant therapeutic effect[1]. Although a bronchiolitis and chronic obstructive pulmonary disease study suggest that isotonic saline may not be benign, consideration of a placebo would still be reasonable in this context[2],[3]. With this non-blinded design in a population of patients who demonstrated adherence prior to participation, knowledge of the intervention status may have influenced participant behaviour. Differential adherence to conventional ACT would lead to information bias.

Furthermore, the 2010 British Thoracic Society bronchiectasis definition includes subjective elements: perception of increased cough, sputum, and fatigue. Non-blinded participants and investigators were at risk for differential misclassification of exacerbations.

The method of analysing the intervention and control arms for each phase of the study allows the two phases to be easily compared by the reader but does not take advantage of the cross over design. Performing within subject comparisons would have decreased variability within the data and enabled a more precise treatment effect.

The European Respiratory Society regards non-CF bronchiectasis as "one of the most neglected diseases in respiratory medicine"[4]. There is disproportionately even less research in children than adults. This article is much appreciated, and will hopefully result in larger, potentially multisite studies that incorporate blinding and are powered to enable stratification by bronchiectasis type.

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