Reviewer’s report

Title: Acute Inhalation of Hypertonic Saline does not Improve Mucociliary Clearance in all Children with Cystic Fibrosis

Version: 3 Date: 15 March 2011

Reviewer: Mark Elkins

Reviewer’s report:

1. "baseline MCC was normal in these children"
This is not necessarily true. A control group of healthy adults differs by two factors - age and disease status. Therefore the fact that the groups had similar baseline MCC is no guarantee that baseline MCC is normal in these CF children. It may be that healthy children should have faster clearance than healthy adults, but we have no data to confirm this.

2. "not all children with minimal CF lung disease will benefit from acute HS therapy"

HS has other mechanisms of benefit besides accelerating MCC at 60 to 90min. For example, immediate increases in clearance during the inhalation of the HS (which is when most of the effect was seen in the Robinson studies), disruption of existing biofilms, inhibition of new biofilms, etc. Therefore this study has by no means proven that not all children with minimal CF lung disease will benefit from acute HS therapy.

3. "more studies are needed to clarify the clinical significance of the observed gender difference in basal MCC"

There are only 5 subjects in the male subgroup, which is insufficient to determine whether the assumptions required for conducting the statistical analysis (eg, that the data can be characterised by a mean and SD) are valid. The effect itself seems largely due to artefact from baseline imbalances in the two gender subgroup. This alleged gender difference is precisely the sort of non-intuitive random finding that one expects from post-hoc analyses chosen after observing the data (even if the other contrasts are only observed and not calculated). It deserves one sentence in this paper at most.

4. The sample size calculation is wrong - it dictates 14 not 12. Furthermore, the SDs obtained are larger than those anticipated. Therefore this study appears to be substantially underpowered. It is not possible to further demonstrate this because the authors do not report mean differences with 95% confidence intervals for any of their non-significant results. However, I am fairly certain they would find that these 95%CIs do not exclude their nominated clinically important difference of 5%.

5. "double blind"
What a joke. The authors have made no attempt to blind the taste of the trial solutions.

6. "it is unknown if a single dose study ... can predict the efficacy of long-term treatment with HS in healthy CF patients"
This was not investigated in the study, so what is the relevance of stating this as a conclusion?

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests