Heliox treatment and Bronchiolitis: Trial marred by conclusions


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We congratulate Chowdhury et al on their RCT comparing Heliox to Airox in infants with bronchiolitis(1). Previous studies investigating the use of Heliox in bronchiolitis have had limitations precluding any definitive conclusions regarding efficacy. The authors should be commended on their attention to study protocol and standardisation of interventions across sites. However, we have concerns regarding the methodology and analysis that question the recommendations made by the authors. We urge caution in interpretation of study findings.

It is unclear what stratification was used during randomisation. In addition, the labelling of intervention gases as cylinder A and B means that the study was only semi-blinded potentially exposing the study to assessment bias. It was pleasing to see the primary outcome as LoT that is less easily confounded than length of stay. However, the frequency of assessment throughout treatment was not specified.

Although the authors state that data was analysed by intention to treat, Figure 2 suggests that results were in fact based on a per protocol analysis. Patients discontinuing the intervention were excluded from final analysis, a significant oversight.

Though the study was powered to detect a reduction in LoT of 0.75 days between groups the author’s main finding of a significant reduction in LoT in the Heliox arm (0.55 days) was only in the subgroup of FM tolerant children (30% of participants) for which the study was underpowered. In terms of statistical methods, there are inconsistencies between the statistics used to calculate the sample size and analysis for primary outcome (the former based on a comparison of means, and the latter a non-parametric test). The additional reduction in LoT in the RSV+ FM tolerant Heliox group is based on an even smaller sample (n=61). RSV testing is not routine in many institutions and results would not be available early enough to dictate management as proposed.

The data presented by the authors in Table 3 is confusing. The origin of all values is not immediately clear, and the total number of patients in subgroups do not match the overall numbers in each treatment arm. We also question the use of means and confidence intervals for summarising LoT given the skewed nature of this outcome.

The discussion is thorough and well balanced and the authors place their findings in the context of available literature. Given there was no evidence of an overall difference in LoT between Heliox and Airox groups it could be argued that their clinical recommendation regarding the use of Heliox in infants with bronchiolitis is overstated.
Despite the shortcomings to the study by Chowdhury and colleagues that preclude definitive recommendations at this stage, it is a valuable addition to the literature. The study provides encouraging preliminary results regarding the use of Heliox in certain subgroups of infants with bronchiolitis. We eagerly await the results of future adequately powered prospective randomised controlled studies as outlined by the authors to provide the definitive evidence needed that will lead to a change in current clinical management.