Reviewer's report

Title: Validation of a portable nitric oxide analyser for screening in primary ciliary dyskinesia

Version: 1 Date: 3 October 2013

Reviewer: Sharon Dell

Reviewer's report:

Introduction:
1. NIOX mino uses an electrochemical sensoring technique as opposed to the gold standard chemiluminescence. This difference should be described somewhere in the intro or methods.

2. The aim could be reworded for better clarity: you are evaluating ability of nNO measurement by the NIOX MINO to discriminate between PCD, other respiratory disease and healthy controls.

3. Throughout the manuscript you describe the older desktop NIOX chemiluminescent analyzer as “static” which is a misnomer, since of course it is measuring and outputting readings of NNO concentrations in a dynamic way. The word “stationary” would be a better descriptor.

Methods:
1. It would be useful to describe the nasal NO measurement in terms of NO production in L/min (NO production nl/min = concentration in ppb x aspiration flow rate in L/min). This adjusts for the effect of flow rate and makes the measurements more comparable within studies (when using different flow rates) and across studies where different flow rates may be used (see 2005 ERS/ATS recommendations on this). It would also explain the differences seen between the NIOX mino 2ml/sec and 5 ml/sec protocol.

2. Were patients selected to be stable and free of upper respiratory tract infection for at least two weeks before the study?

3. What diagnoses did the CSLD participants have? Did they have bronchiectasis? Was immunodeficiency ruled out?

4. Did you measure and account for the possible affect of ambient NO?

5. Chemiluminescent technique: How often did you calibrate the machine and how did you make sure that it was calibrated with each test? How long of a measurement plateau did you require? Did you require the 3 maneuvers to be reproducible within 10% to make sure that you had a proper “gold standard” technique for comparison? Why did you choose the maximum of the three values rather than the average?

6. NIOX Mino electrochemical sensor technique: Please clarify timing for the 2ml/sec and 5ml/sec tidal breathing maneuvers. Was it 45 seconds and 90 seconds as mentioned in the previous sentence for the breath hold technique?
As a quality control criteria, did you require reproducibility between the 3 measurements in each patient in order to report it? Why did you choose the highest measurement instead of the average of the three?

7. Statistical analyses: Paired t-tests should only be used for the comparisons between analysers (same patients) but not between groups (different patients). Please clarify this.

Results:
1. Fig 1 ROC curves are not helpful. Suggest replacing these with a table that suggests cut-off values with sensitivity and specificity for PCD using the various measurement devices.
2. Bar graphs or scatter plot to show the distribution of the data would be more descriptive of nNO values than table one.
3. When comparing nNO values of NIOX mino at 5ml/sec versus 2 ml/sec, assuming the measurements are done correctly, one would expect the 2ml/sec procedure to have systematically higher values due to the lower flow rate (see ATS/ERS statement). This would be the reason to use NO output instead of concentration. If the measurements are similar using NO output, one would have more confidence in the device.

Discussion:
1. The discussion should include obvious reasons for differences between the various measurements that are accounted for by factors other than the device such as flow rate and velum closure (non velum closure techniques result in systematically lower NNO values due to contamination with lower airway NO).
2. Did the two patients with CSLD and low NO have alternate diagnoses to PCD? Did they have in vivo studies of mucociliary clearance (nuclear medicine clearance scans)?
3. Please compare your results to the recently published article by June Marthin and Nielson in PLOS ONE feb 2013, vol8, e57262

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

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