Reviewer’s report

Title: Randomised controlled trial of weaning strategies for preterm infants on nasal continuous positive airway pressure

Version: 0 Date: 18 Aug 2015

Reviewer: Brigitte Lemyre

Reviewer's report:

The authors report a pilot study whereby 4 different methods of weaning infants born <30 weeks gestation from their nCPAP are compared. It is a single center, factorial design RCT. 60 infants were enrolled, with 15 in each group, where abrupt or progressive wean off CPAP and use of high-flow nasal cannula (HFNC) were used.

Background:

I think the primary aim of the study should be restated, as what is currently stated appears to be the goal of a very large RCT, and not a pilot study. I would suggest stating as the objective of the trial the first sentence of the discussion: "pilot designed to determine the optimal comparisons for a larger trial".

Methods:

Well written, reasonably easy to follow. 3 inclusion criteria are listed: the last inclusion criteria (stable on CPAP and tolerating 6 hours off nCPAP) reflects a much lower illness severity than the other 2 criteria to me. Yet, no information is provided in the results regarding the breakdown of patients, per inclusion criteria, per assigned group. Is it possible that one group had a lower illness severity than another? Some measure of illness severity at trial entry appears to be missing.

Intervention groups where HFNC was part of the intervention received 6 LPM of HFNC. Methods do not state how this might have been weaned over time.

There are too many outcomes stated, given the size of the trial and the fact it is a pilot, in my opinion. Authors should focus on a few (3-4 in total), which are most important to meet the objectives of the trial. They do adjust the p-value accordingly though.

No sample size calculation or mention of justification for the sample size chosen. This would be required, even for a pilot, if only to state convenience.

Results:

Figure 1: numbers excluded do not add up to 29, unless deaths are included. Figure needs some tweaking.
Given the wide range of age at trial start (2 to 76 days) and the fact that some infants tolerated up to 15h off CPAP at the start of the trial, some measure of illness severity will need to be included in the larger trial. It will be difficult to interpret results otherwise.

The four-group comparison paragraph is fairly lengthy, with many information already in the table. There is a significant risk of type 2 error, which the authors acknowledge in the discussion. It is to be expected that the days on CPAP will be shorter with an abrupt strategy and HFNC, since both essentially provide some degree of distending pressure. The clinically relevant outcome, number of days on pressure support is unchanged. It is the mode of delivering such pressure that is different. One stated reason in the literature is patient comfort and nasal breakdown: this study was not powered to look at this.

Discussion:

Line 54, "lower level of respiratory support"; I think there is a typo and should read "higher level"
Discussion should emphasize more the pilot nature of the study (as in first paragraph) and discuss findings of relevance for future design consideration, or give suggestion of which 2 arms of intervention to compare, or 4 arms. Authors do commit to say that HFNC appears to be best strategy, but seem uncertain about gradual weaning off CPAP (line 38, last paragraph of discussion).

Given the pilot nature of the trial and sample size, authors should be careful about wording and strength of any conclusion regarding safety. 3rd paragraph of discussion, to state that previous trials and this study suggest HFNC has similar efficacy to nCPAP for infants and is associated with a reduced risk of nasal trauma is overstated and should be corrected.

Authors gleaned important information regarding acceptability for parents of the abrupt weaning approach. It would be nice to hear reasons for withdrawals. In our unit, it would be from influence of allied health who prefer nasal prongs over CPAP as opposed to true parent withdrawal. Authors may wish to discuss that.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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