Reviewer's report

Title: Pressure- versus volume-limited sustained inflations: recruiting the preterm lung.

Version: 1 Date: 3 October 2013

Reviewer: Vasanth Kumar

Reviewer's report:

The study by Polgase et al is an important study that needs to be addressed. The authors have put in effort to address an important question and the reviewer is very appreciative of that. The study adds to the literature, however the authors need to address the following suggestions by the reviewer -

Minor Revisions –

Introduction –

Para 2. Line 1: A sustained inflation is used by some neonatologists …… (5,6). Wording change – Sustained lung inflation at birth is practiced at some centers for early establishment of infant’s FRC at birth ().

Methods –

Sustained inflation and Ventilation Strategies –

What was the FiO2 0.3 at birth in both the groups?
Similarly what was the FiO2 at 20 secs at the end of sustained inflation? (again was it 0.3) – needs clarification

Results –

It would have been interesting to see the blood gases at the end of 20 secs in the two groups. Do we have a gas at the end of intervention?

PVR changes with FRC and pH. The pH was lower in the Pressure SI group before birth. However PVR is lowest at FRC. Both of them could influence FiO2 requirement depending on pulmonary hemodynamics.

Figure 5 can be deleted as it has not been discussed much in the discussion section.

Discussion –

Para 3 – Physiologic changes seen in pressure / volume curves are not reflected in lung injury markers. The authors cannot make a conclusion of “slow rather than rapid delivery of the targeted initial inflating volume may identify a strategy that affords protection from both barotrauma and volutrauma”. The authors have
to be careful about this.

Page 15. Line 21/22 – Our failure to observe differences…………similarly injurious. The reviewer feels that the authors have to say it straight that the initial sustained inflation with either pressure ventilation or volume ventilation does not make a difference as we did not find any differences at 15 minutes.

Limitations –

The reviewer is curious to know why the pressure was not adjusted based on end tidal volume to match that of volume SI. This would have enabled both groups to be somewhat similar.

Abstract –

Methods - Delete “significance was determined using……ANOVA” (details of statistics in methods; also 1-way not mentioned in methods)

Major Revisions –

Introduction –

P2, L2: recommended for the initial……in the recent European resuscitation guidelines (7). The reviewer thinks that the authors have to be careful with this statement. I do not think, the European RC guidelines do not make any recommendations regarding sustained inflation due to paucity of data on inflation time (may be wrong – please check this). If there are no concrete recommendations, then say it as it is and compare them to AAP resuscitation guidelines (2010). This will make the study more interesting.

Para 3, Line 1: Needs reworking – AAP does not recommend sustained inflation. Also you have to discuss the three clinical studies somewhere (either in the introduction or in the discussion - Vyas et al 1981; Linder et al 2005; Harling et al 2005) and then go on to tell why sustained inflation delivered by pressure method is not favorable. The later part of the Para 3 in good.

Methods –

Postmortem analyses –

Why was the lungs ventilated with 100% oxygen for 2 minutes? 100% oxygen is toxic / inflammatory. This could have altered the results of gene expression analysis. Lambs were exposed to $2 + 3 = 5$ minutes of 100% oxygen in an experimental duration of 20 minutes $(15 + 5) = 25\%$ of the time; for a sustained inflation of 20 secs $(< 1\%$ of the experiment). Why was oxygen reabsorption done? Lungs can be flash frozen without causing additional injury. Just curious? You just add additional variables that could influence the results. I am wondering whether you masked important results.

Was oxygen absorption done for Pressure volume studies?
Discussion –

Para 1 – The authors have to simplify the wordings a little bit. They use FRC in one sentence (Line 5) and end expiratory volume in their data (Line 7). Do they mean they are the same? If they are the same then volume inflation was no more beneficial than pressure inflation to establish FRC. This has to be made clear.

The baseline pH were not similar between the groups and this has to be mentioned in the discussion.

Page 14; Para 1 – Even though there was variability, it was not big enough for it to be statistically significant. Moreover, this was not accompanied by any differences in lung injury markers in their study. Even though the authors hypothesized that tidal volume inflation is better, their data does not suggest it. This has to be brought out and the factors discussed.

Page 14; Para 2: Thus the critical question.......................The authors have not answered this critical question as all the injury markers were similar in both the groups. So they have to modify this statement that in our experiments we did not find either pressure or volume ventilation sustained inflation make any difference in terms of lung injury at 15 minutes.......something like that.

The authors need to explain why FiO2 went up in the volume ventilation group in the absence of inflammation? This happened despite the volumes being similar at 15 minutes (figure 6) in both the groups

Summary –

First sentence – In conclusion.............the efficacy of volume-limited sustained inflation for lung recruitment......... The reviewer finds this statement surprising despite the volume group having high FiO2 requirement and no other differences between the groups. The authors have to rewrite that one is not better than the other based on this study.

Title –

It should reflect the results of the study. Also it does not tell whether this is in lambs or in infants. The title feels that it is a review article. Something like – Pressure versus Volume limited sustained inflation at Resuscitation in Premature newborn Lambs

Abstract –

Conclusions – Also a sentence such as – “Pressure or volume ventilation sustained inflation at resuscitation did not make a significant difference in terms of physiologic variables or early markers of lung inflammation measured in preterm newborn lambs in our study.

**Level of interest:** An article of importance in its field
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'