Reviewer's report

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

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Reviewer: Gianluca Lista

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Lung recruitment at birth is crucial for lung volume optimization and to try to limit lung injury.

Sustained Inflation (SI) is one of the modalities to reach the lung recruitment at birth. Anyway the best way to deliver a sustained inflation is still unknown. The Authors have planned the animal study to understand whether a SI inflation that targets a preset delivered volume/kg birth weight will provide a more consistent FRC and more homogeneous aeration than is achieved using a pressure-limited SI, potentially with a reduced lung inflammatory response. The results demonstrated the efficacy of volume-limited SI for lung recruitment in preterm lambs without substantial differences in physiological variables or early markers of lung inflammation and injury between the two strategies. Nevertheless the data need to be verified in human setting, where the possibility to set the Vt in course of SI is till now not available in delivery room and because the worse oxygenation in volume-limited SI registered during transition (15 minutes after birth), could suggest a possible scenario of high oxidative stress with this modality used to deliver SI.

SPECIFIC COMMENTS

Methods:
At page 7: Sustained inflation and ventilation strategies (first paragraph) The Authors could explain why the lambs were maintained in prone position. The human setting is different (preterm infants are supine in the “infant warmer” in the delivery room) and we wish to have some information to share in clinical practice. Can the Authors confirm that the results of the experiment could be the same changing the position (e.g. supine) of the lambs during respiratory assistance?

At page 7: Sustained inflation and ventilation strategies (second paragraph) we know from the literature that the effect of SI is “maximum” when is immediately followed by a PEEP. Were the animals managed with a PEEP after the SI (both volume-limited and pressure-limited) before to receive a volume targeted ventilation (vt at 7 ml/Kg, plus PEEP)? Did the Authors evaluate the EEL with or without PEEP, after SI?

At page 9: Post-mortem analysis (third paragraph) : can the Authors present
some pictures showing the lung tissue after the two different SI approach? Even if the lung inflammation response analyzed by BAL was similar, may be interesting to evaluate the lung architecture

Results

At page 10: Arterial blood-gas and ventilation variables (second paragraph) in the volume-limited SI group the Authors have registered significantly higher FiO2 level at 15 min. The Authors in the discussion have suggested that was due to rapid delivery of the targeted initial inflating volume. Which was the flow used to deliver SI? In case of absence of PEEP immediately after SI, can we hypothesize that this event has amplified the negative effect on oxygenation by volume-limited SI?

In the method (at page 7) the Authors have reported that the SI “was maintained for a further 15 s”. Which was the exact duration of the maneuver? In fact all the results (arterial blood-gas values and ventilator variables) are reported at 20 seconds of SI.

At page 10, hemodynamic measurements (first paragraph): The Authors are requested to explain the sentence: in both groups, heart rate and carotid arterial pressure decreased with time (p<0.001 for both). We know that SI acts not only on lung function but also on circulation (e.g. Klingerberg C, Arch Dis Child Fetal Neon ed 2013 “.....SI after birth improved speed of circulatory recovery…”). Can we speculate that the results reported by the Authors are considered as the recovery phase after SI? Is a positive or negative effect? Or they have other suggestions?

At page 11, regional aeration, (second paragraph): Why global end-expiratory lung volume significantly decreased after the sustained inflation in the VolSI group but not in the PressSI group? Can we hypothesize a better lung recruitment? Moreover tissue resistance and tissue elastance were lower in SI pressure group: why? Can we hypothesize a different effect of volume-limited SI on lung recruitment?

Discussion

The Authors could underline better that the data need to be verified in human setting, where the possibility to set the Vt in course of SI is till now not available in delivery room; moreover the worst oxygenation in volume-limited SI registered during transition (15 minutes after birth), could suggest a possible scenario of high oxidative stress with this modality used to deliver SI.

Moreover the Authors reported: “The 131 d lamb is approximately similar to 34-36 w GA in the human infant – a group that is still prone to respiratory distress due to surfactant deficiency”. Can we hypothesize that the two modalities to deliver SI could give the same results if the Authors will study lambs with lower GA and with higher surfactant deficiency?
Can a different ventilator strategy amplify or reduce the inflammatory response after volume-limited and pressure-limited SI?