Peer Review File

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Review comments

Comment 1. Whether or not LISA should be carried out with or without analgesia has been discussed. Do the authors mean sucrose is sufficient or is an opioid needed? Please discuss this.

Reply: We thank the reviewer for this thoughtful comment. We have significantly amended the manuscript according to this recommendation, esp., Page 13, line 373, which now reads "The use of medication for procedures requiring direct laryngoscopy is a matter of ongoing debate. The location for such interventions in the setting of preterm stabilisation, whether laryngoscopy is performed on delivery suite or NICU, adds another level of complexity. In preparation for the LISA procedure on the NICU, a dose of caffeine citrate (20mg/kg, intravenously or orally) should be given to preterm infants < 30 weeks' gestation and birth weights < 1250 gram, to enhance respiratory drive (13). Equally, Atropine may be given to decrease the incidence or bradycardia during LISA (13, 44). Whether or not LISA should be carried out with or without analgesia / sedation is the topic of heated discussion, as the current state of evidence remains inadequate to make firm recommendations. As an alternative to pharmacological agents, oral sucrose might be considered as a form of non-pharmacological analgesia. Whilst sucrose clearly is not a true analgesic, its administration has been described to enhance the tolerability of the LISA procedure (44). In summary, the choice of premedication should be based on the difference of GA and also include a balance between the perceived benefits and risks. (13)".

Comment 2. The application of caffeine and atropine in the delivery room is as far as I understand not evidence-based. Atropine has been removed a long time ago for newborn resuscitation. By preventing bradycardia this drug may just mask the problem leading to bradycardia. However, if the bradycardia is reflex induced, it may have a role. Still, personally, I would hesitate to recommend it routinely. Please comment.
Reply: We thank the reviewer for this thoughtful comment. Please see above for our explanation. Thank you.

I have a similar position regarding routine caffeine in the delivery room. It is, as far as I know not evidence-based.

Reply: We thank the reviewer for this thoughtful comment. Please see above.

Comment 3. Gestational age limit. LISA seems to be most efficient from week 26. Could the authors discuss whether or not there is a lower Gestational age limit for applying LISA?

Reply: We thank the reviewer for this very sensible comment. We agree that whilst LISA has been described as successful by experienced operators in infants as immature as 22 weeks gestation, the safety and success of LISA is highly reliant on the local expertise and proficiency. Thus, we have clarified our view on LISA by extending our recommendations significantly. On page 12, line 295, this now reads “Whilst it is noted that centres experienced in providing LISA report its successful application to preterm infants of all gestational ages, starting from 22 weeks to term infants, it is strongly recommend that a) centres should have bespoke local guidelines, which take the local level of experience into account and b) to define different gestational age thresholds at which to perform LISA (13).”.

Comment 4. Perhaps the authors should give a summary in for instance a table, with their own recommendations regarding practical details as I mentioned above?

Reply: We thank the reviewer. We have given an instructive, consensus based recommendation in form of a recently published, freely available at no charge which discusses the current knowns and unknowns and particularly outlines the LISA procedure as best know at present: Vento M, Bohlin K, Herting E, Roehr CC, et al. Surfactant Administration via Thin Catheter: A Practical Guide. Neonatology 2019; 116: 211-26.

Comment 5. Page 7 line 13. This sentence needs to be corrected. Perhaps there is a "the" which needs to be removed?

Reply: We thank the reviewer and have amended the error.