Reviewer's report

**Title:** Exogenous surfactant therapy in 2013: what is next? Who, when and how should we treat newborn infants in the future?

**Version:** 1  **Date:** 24 June 2013

**Reviewer:** Gautham Suresh

**Reviewer's report:**

Overall I found this review to be comprehensive and well written. My comments are provided below. I see these as major compulsory revisions.

The search strategy used to identify all relevant articles and the method of appraisal of these articles should be described (see review articles in the Lancet as examples).

Organization of the review.
The authors focus on three main questions, but in reality there are more than three questions that practicing clinicians face:
1. Whom to treat (which includes broad categories of patients e.g. preterm infants and also how to identify those that are surfactant deficient within those categories),
2. When to treat (which includes sub-questions about prophylactic surfactant and also about early vs late surfactant),
3. Which surfactant product to use,
4. How to administer the surfactant, and
5. When and to whom to administer repeat doses.

The topic of surfactant therapy is vast and is hard to cover in a single review. Perhaps the authors could restrict the review to some controversial or confusing topics being faced by clinicians at present, or they could restrict it to emerging or innovative concepts and techniques. This is implicit in their approach, but could be stated and framed more explicitly, and used to guide the language and the content of the review.

Much of the evidence on how to administer surfactant and what surfactant product is superior comes from studies on preterm infants. For example, there are no studies on surfactant administration by LMA on term infants with meconium aspiration. Therefore it would make sense to describe surfactant for treatment of RDS in preterms as an entire section first (including methods of administration) and then talk about other conditions where surfactant may have a role.

Suggest including the click test described by several authors (most recently by Osborn et al) as a potential method of selection.
Prophylactic surfactant.
In this section I suggest the authors distinguish two categories of studies (with rescue surfactant administered selectively in both categories) - those that compared prophylactic surfactant to infants not receiving supplemental oxygen only as needed and those that compared it to infants receiving CPAP or intubation only.

Suggest that the authors use the increasing use of antenatal betamethasone in the current era as an explanation for why prophylactic surfactant might not have a big impact (as opposed to the trials in which prophylaxis was found effective, in which the antenatal steroid usage rate was not high).

Mention that in the SUPPORT study, a high proportion of infants randomized to initial CPAP still ended up getting intubated and surfactant.

The current question faced by most clinicians is - whom to administer prophylactic surfactant to? In this era of increasing use of CPAP as a stabilization method in the delivery room is there still a role for prophylactic surfactant? If so, how should eligible infants be identified?

Early vs late surfactant
There needs to be a section on benefits of early treatment vs delayed (> 2 hours) treatment, based on the OSIRIS and similar trials (see the relevant Cochrane review).

How should surfactant be administered?
In this section the effects of surfactant itself are confounded by the method of administration.

Many of the newer methods of surfactant administration including MIST are innovative and experimental and deserve more testing before they can be recommended. Therefore they should all be described under a heading such as ‘Emerging techniques of administration’. I think administration by ET tube is still the gold standard and we should not be abandoning it until further evidence accumulates. The situation in Europe is different from that in the US, where MIST is rarely used.

Adverse effects of surfactant therapy, and safety
Suggest including a small section on this.

Level of interest: An article of limited interest

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