Author's response to reviews

Title: Morphine for elective endotracheal intubation in neonates: a randomized trial

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Author's response to reviews: see over
To: Editorial team at BioMed Central

RE: Point by point description of changes made to manuscript #116646073381010

July 27, 2004

Thank you for considering publishing our manuscript. The peer review process was quick, and fair. Please find enclosed our response, point by point to the reviewer’s comments.

Minor/editorial changes

1. Capital letters to be changed on page 1: page 1 was reformatted to comply with the formatting checklist
2. Change thus to they on page 4: done
3. Move information relating to blood pressure and bradycardia on page 9 to paragraph 1, page 9: done

Discretionary revisions

1. a) Clarify who were approached for consent

Two sentences were added in paragraph 1, page 4, to clarify who was approached for consent and when. All infants, for whom the likelihood of an elective intubation was high during their stay, were approached (their parents) for consent shortly after birth. Others were approached when an elective intubation was required.

b) Is it a policy to change endotracheal tubes after 10 days, if the infant is stable on ventilation?

No. As stated on page 4, paragraph 1, such change is considered only if the infant is unstable from a respiratory standpoint.

c) Justify the dose of morphine used

The usual loading dose of morphine is 100 mcg/kg. Because of the perceived acuity of pain produced by an endotracheal intubation, the study group felt that a larger dose may be more effective, to decrease pain the therefore fighting/struggling by infants during the procedure. A sentence has been added on page 5, paragraph 1, to clarify.

Was information on the ventilatory parameters for the next 12-24h collected?

Yes, in infants already ventilated, who had a tube change, investigators noted if ventilator parameters had to be increased after the change, as compared to before, for the following 24h. 4/10 infants in the morphine group, compared to 1/10 infants
in the placebo group required either an increase in their rate, peak inspiratory pressure or fiO2 (p=0.3). These numbers are too small to draw any conclusion. A sentence was added on page 9, paragraph 3 at the end of the results section to highlight this.

2. a) Can we quantify the outcome “#of infants who experienced some degree of severe hypoxemia”?

This was the primary outcome of the trial. Information on rate of event and median duration of this outcome is given in table 2 and in the results section. No action was taken following that comment.

b) How do we explain why the Tx group did worse than the placebo?

In paragraph 1, page 12, we discuss the possibility of a decreased FRC, by the morphine, compounded by the inability to provide a PEEP with a self-inflating bag. A sentence has been added, to discuss the possibility that the dose of morphine chosen contributes to the problem, on page 12, paragraph 1.

c) Was physiological stability maintained in infants who did not have an ETT in situ, after the study Rx was given?

Yes, it was, for all infants. A sentence was added to clarify this on page 8, paragraph 1.

d) The sample size was based on experience, rather than hard data on outcome.

As specified by the reviewer, this was acknowledged in the discussion. No action was taken on that comment.

3. The manuscript has no abstract

The abstract was submitted electronically, in the box where it was requested, therefore not attached to the manuscript per se.

4. The authors did not postulate why morphine alone was not effective.

In paragraph 2, page 11, we speculate that, although the onset of action of morphine is about 5 minutes, the peak action is at 15-30 minutes. Thus the 5 minutes that we waited before proceeding with the intubation, could have been too short, therefore contributing to the lack of effectiveness of morphine in such circumstances. Insufficiently relaxed infants will struggle and not permit adequate airway visualisation, thus leading to more attempts, longer attempts and hypoxemia. A sentence has been added to that effect on page 11, paragraph 2.
Should yourselves or the reviewer have any concerns or further comments, please do not hesitate to contact me. Please note that I am currently on maternity leave, thus my response time to emails is a few days.

Sincerely,

Brigitte Lemyre, MD  FRCPC