Author's response to reviews

**Title:** Continuous positive airway pressure for bronchiolitis in a general paediatric ward

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**Author's response to reviews:** see over
We hereby submit a revision of the manuscript “Continuous positive airway pressure for bronchiolitis in a general paediatric ward”. We appreciate the comprehensive and highly valuable comments from reviewers and have revised the manuscript accordingly. We consider the manuscript to be significantly improved, especially regarding Methods; description of the ward including staffing.

Comments to reviewers

Reviewer no 1

Reviewer's report
Title: Continuous positive airway pressure in bronchiolitis; a safe and effective treatment in ordinary paediatric wards
Version: 2
Date: 14 November 2013
Reviewer: Etienne Javouhey

Reviewer's report:
Review of the paper entitled “Continuous positive airway pressure in bronchiolitis; a safe and effective treatment in ordinary paediatric wards” from Knut Oymar and Kjersti Bardsen.

This paper provides interesting data on experience of CPAP in children with bronchiolitis in ordinary wards. The subject of CPAP in bronchiolitis is not original but the idea of performing CPAP in ordinary wards is subject to debate. This study concerns a small population so it is difficult to conclude that CPAP is feasible and safe in ordinary wards. That is the major concern of this paper. It is not because the authors did not observe complications in 53 patients (33 in ordinary wards) that mean that CPAP can be performed safely in ordinary wards.

The statement regarding efficacy and safety is also commented on by reviewer no 2 and 3. We agree, and have modified the title, abstract and text accordingly. Our conclusion is that CPAP may possibly be given to infants with bronchiolitis in ordinary wards, given that sufficient training, staffing and monitoring is available.

Moreover, details on the patients/nurses and patients/physicians ratios in the wards are not provided. We have to know how was performed the monitoring of the patients, how was organized the continuous monitoring and assessment of the children in the wards, during the day and the night. How were the nurses trained? To deliver CPAP in small infants specific training of the care providers are necessary. If the care providers are well trained and if the monitoring is continuous, with centralization return, CPAP is probably feasible and safe but the authors should provide these precisions in their manuscript and in their conclusion. The risk is not negligible because some of these infants can develop severe apneas, respiratory arrests, cyanosis, seizure due to hyponatremia, bacterial superinfection that require immediate intervention. If the monitoring is
intermittent and if the patients/nurse ratio is high, the risk of a delayed intervention is high with a risk of cardiopulmonary arrest and severe hypoxemia. The monitoring by capillary PCO2 requires specific training as well. In pediatric hospitals, it is not sure that all the nurses are well trained to this technic.

We appreciate these comments, and acknowledge that these points may differ substantially between countries and hospitals, and that our experiences must be seen in the light of these details. More details regarding training, staffing and routines are now given in the methods. Samples for capillary PCO2 is taken and analyzed by laboratorial staff, which is now also written in the manuscript.

Concerning the results of this study, it is interesting to note that the level of cPCO2 was higher in patients who required hospitalization in PICU compared to patients treated in ordinary wards. That would mean that this criteria may help to decide what patients can be managed in ordinary wards. Similarly experiences have been reported in other countries.

We agree and have included this issue further in the discussion.

One of the main factor to consider when performing CPAP in infants with bronchiolitis, is the presence of not of apneas and the response to CPAP during the first hours. The authors should discuss these criteria in their discussion. Apnea and not improvement with CPAP are factors associated with intubation, prolonged hospital stay and complications. We are surprised by the fact that the authors did not report any apnea in their patients.

We agree, and have extended the discussion on this. One infant failed on CPAP due to severe apnoe, we did not consider this as a side effect of the CPAP but have rewritten to clarify.

We don’t know if the patients who failed to CPAP were placed on NIPPV before being intubated. In our experience some of them can be safely managed by NIPPV avoiding intubation.

In figure 1 and in the text it is shown that one child was given MV without initial CPAP due to the severe clinical situation, and two were given CPAP first but failed. We have rewritten to clarify.

The authors could better describe the 9 patients who failed to CPAP and were transferred to PICU to those who succeeded. It would be interesting to do so in order to better understand why some patients fail.

As described elsewhere, we regret that mor detail on these children are not available, e.g clinical score. They were referred to the ICU due to respiratory distress in spite of CPAP according to the given in-house guidelines and by the decision of the attending physician.

The conclusion and the title of the paper are excessive. The authors should temper their opinion because the sample is too small to conclude of a complete
safety, the conditions to perform CPAP in ordinary wards are not mentioned, and because in some countries the care organization is different (patients nurse ratios...).

We agree, and as stated above, we have modified the title, abstract, text and conclusion. Our conclusion is that CPAP may be feasible for bronchiolitis in general wards, given that sufficient training, staffing and observation and the possible referral to an ICU is available.

Reviewer no 2:

Reviewer’s report
Title: Continuous positive airway pressure in bronchiolitis; a safe and effective treatment in ordinary paediatric wards
Version: 2 Date: 12 March 2014
Reviewer: Fabrice Michel

Reviewer’s report:
The authors report a 4 years experience in CPAP treatment in bronchiolitis. 46 were treated with CPAP during this period. Among them 33 were treated in an ordinary pediatric unit while 13 required ICU admission. The main message of the study is that CPAP treatment can be safely performed in a ordinary unit. CPAP is became the first line treatment of severe acute bronchiolitis despite lack of solid study proving that it decreases intubation rate. During epidemic periods, PICUs are full of children with CPAP for severe bronchiolitis. Therefore, CPAP use outside PICU may be a solution to limit PICU admission and the described clinical experience is therefore interesting. Nevertheless, such a organization can be dangerous for children because the level of care in standard units is not as high as in PICU.

Comments
Major Compulsory revisions
1. CPAP efficiency to decrease PCO2 has already be showed and is a secondary objective in this study.

We agree that this is a secondary objective, but in order to demonstrate that CPAP may be feasible also in general wards it is of value to show that levels of pCO2 was reduced. However, the text has been modified to emphasize that the main topic of this manuscript is the possible treatment with CPAP at paediatric wards.

2. The main objective of the study is to present a clinical experience in a paediatric ward. The conclusion of the study can be “CPAP in this ordinary paediatric ward is possible” but the authors cannot affirm it is safe.

We agree, and also as according to reviewer no1 we have modified the title and text, suggesting the CPAP may be feasible at an general pediatric ward given sufficient staffing, training and monitoring.

3. It is no clear if the authors want to treat severe bronchiolitis in an ordinary
We agree. We emphasize that the main topic of the paper is to evaluate the use of CPAP at a general ward. However, this may facilitate that CPAP may be used at an earlier stage, as discussed. Further, more information about staffing etc are given, and we have expanded the discussion regarding safety aspects.

4. The methodology should precise if it is a prospective or retrospective evaluation. If it is prospective, why clinical score or oxygenation parameters were not recorded? This data are really lacking. Severity of patient is unknow. PCO2 is the only parameter available and not sufficient for severity evaluation.

The registration was prospective with a specific scheme for registration as written, but unfortunately a clinical scoring was not included. Moreover, the oxygen parameters were not of sufficient quality to be included. We agree that including these parameters could have improved the severity evaluation of the patients, which is discussed.

5. Regarding data, it seems that patients have low severity. Gestational age, and age at admission are high compared with patients included in other studies. Similarly, duration of CPAP was very short. Length of stay in table 2 must be precised: is it hospital stay? These points must be discussed because probably that in other countries, or other town the management of such patients is different.

Our hospital treats all patients with bronchiolitis in this area, so there is no selection of patients. The length of stay is hospital stay, which is now emphasized.

6. Criteria for CPAP instauration or PICU admission are very fuzzy.

We may agree, but are not aware of more specific criteria in the literature. The most important is a good description of the status of the infants who were actually treated with CPAP or admitted to ICU, as the correct indication for giving CPAP is not known.

7. In the methods, details about care organization must be provided: number of children for one nurse by day and night, number of children in the pediatric ward… Were the children continuously monitored (SpO2, HR, respiratory rate etc…)? Was a physician promptly available in case of problem? Did the parents slept with their child? If no, was the protocol the same?

We agree that these issues are important information, and have substantially expanded the information in this part of methods.
8. Because of high fresh gas flow used in CPAP, there is a risk of nasal obstruction with secretions. How was managed this problem? How were the gas humidified? How many nasal cares were provided?

Careful nasal suctioning was given to infants with copious secretion. Except for inhalations, the gas was not humidified. We have now included this information in the methods.

9. Statistics: it seems that PCO2 would be compared using ANOVA for repeated measures?

We appreciate the comment. It is correct that a test for variance must be used, but with non-parametric data the Kruskall-Wallis and Friedmans test are the appropriate. The statistics are rewritten and recalculated, but without changing the results and the conclusion of analyses.

10. In the discussion the authors are considering their study as a “before-after” study but only one period was considered in this study. However, it would have been interesting to compare patients admitted in PICU before and after the new practices instauration. In the same manner to compare patients treated in the pediatric ward before and after the new practices. Differences between the two periods could support the interest of CPAP use outside PICU.

We agree that this would have been interesting, but no data exist on patient characteristics before CPAP was introduced at the ordinary ward. That would be a new study, fully retrospective for the “before” period with all the limitations. We are sorry that this will be beyond the scope of this prospective study. We have omitted the description of our study as “before-after”, and this is appropriate as our aim was not to study the effect of CPAP, but the use of CPAP in a general ward.

The authors consider that PICU hospitalization is frightening for the parents. I don’t think that parent’s fear should be an argument to not admit a child in PICU. In contrary, with good information, a high level of care is probably more secure for the parents than a unit with overwhelmed nurses as it can be seen in some standard care unit.

We fully agree that parent’s possible fears should not be an argument for keeping a child in the ward. However, if the same level of symptoms can be treated at a regular ward instead of at the ICU, and with the same effect and safety, this may be a better experience for the parents. We have rewritten.

Minor essential revisions
1. The sentence “When extra oxygen was needed…” is not clear. Is this situation is during nebulisation?
Oxygen was given into the circuit both during and outside nebulization to keep a satisfactory SpO2. We have rewritten to clarify.

2. An important limit of the study is the low number of patients. It must be
discussed.

This has now been further discussed. We suggest that our results are
evaluated in larger studies, including more observational parameters.

3. Finally, at the end of discussion the authors suggest that early introduction of
CPAP may improve outcome. An article (Essouri et al intensive care medicine)
has recently tested this hypothesis and should be cited.

We appreciate, this was a new important study published after our submission.
It has now been cited and discussed.

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published
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

Reviewer no 3:

Reviewer’s report
Title: Continuous positive airway pressure in bronchiolitis; a safe and effective
treatment in ordinary paediatric wards
Version: 2 Date: 12 March 2014
Reviewer: Sandrine ESSOURI

Reviewer’s report:

Management of severe bronchiolitis with early CPAP is an emerging therapy that
has proven its efficacy. Mostly, CPAP is performed in intensive care unit because
it is a life support therapy.
The authors address in this study the feasibility of such therapy outside the
pediatric ICU, in paediatric general ward.

Major compulsory revisions
- the main objective of this study is to demonstrate the feasibility of CPAP in
paediatric general ward. Most of the manuscript detaille the efficacy of CPAP,
which has been already demonstrated in numerous previous studies, but the
authors failed to describe the features of performing CPAP in general ward.

We have rewritten to clarify that the main objective of the study was the
feasibility of giving CPAP in a general ward. However, it is of value to show that
the treatment was effective on levels of cCO$_2$, which supports the benefit of
CPAP at this level of care.

- Do the physicians of this unit have the experience of non invasive ventilation?
Even for chronic respiratory failure? Does the nurse team was trained before
implementation of CPAP?
All these crucial elements are missing in the manuscript. It has been describe that
training program are relevant to insure high level of care and to improve
efficacy of a new therapy.
As also suggested by the other reviewers, the level of staffing, training and monitoring of the infants are now thoroughly described in the methods.

-In the method section we have no idea of the number of beds, the ratio nurse/patient, the global management and monitoring of such patients.

This information has now been included.

- The table 1: It does not look like a table and could be added in the manuscript. What is the definition of severe respiratory distress? When do you consider high or increasing capillary CO2? ......You must describe precisely these parameters.

It could be an option to include in the manuscript which we have considered, but we conclude that the readability is better in this set-up. The parameters mentioned are now better described.

- The mean weight of your patients is lacking but probably around 3.5-4 kgs as previously in most studies on bronchiolitis with CPAP. The ventilator used in this work is a ventilator designed for home ventilation of patients weighting over 30 kilos. Is it reasonable to use it in these small patients and not in intensive care? Why do you use this system instead of system available and designed for CPAP in infants such as the bubble CPAP (used with your ICU but with a ventilator).

We agree that this could have been better described. The CPAP for home ventilation was chosen because it does not need pressured air, permitting the use in wards/rooms without such. In addition, this CPAP is easy to use, was familiar to the staff (from children with home ventilation) and with the option of oxygen supply. We have added information to the manuscript.

- You must describe what is the monitoring of such patients, it is a major point because the reader knew that CPAP in severe bronchiolitis is effective but they want to know if they can do it in safe condition in general ward or not. You have to prove that all safety conditions are present.

We agree. More information about the monitoring of patients has been included. Infants were continuously monitored with SpO2, a nurse was continuously with that single patient during the initial phase, and later continuously or frequently seen. Parents were always with the child, and a child was never left alone.

- You described 42 infants managed with CPAP in your unit during 4 years thus just 10 patients per year. Do you think it's enough to ensure a high quality of level of care?

We agree that this may be at the border regarding staff quality and experience. On the other hand, the study is from one of the largest hospitals in Norway, many units caring for children with bronchiolitis will be of this size, and our study may suggest that CPAP may be feasible at such units.

- In the table 2, the length of stay for patients in ICU is 8 days in ICU? or total
hospital length of stay? because it is upper than length of stay previously described.

**It is the total length of stay at hospital, has now been changed in the table**

- In the discussion section you say that it may have economic benefits and the treatment and procedures may be less frightening for the parents. It would have been interesting to have the feeling of parents.

**We agree that this would have been interesting, but this was unfortunately not monitored.**

- You clearly explain that "almost one third of the children were need in referral to an ICU, the possibility of such referral must be easily available". You could further discuss on the ratio benefice/risk of such management.

**The need of an ICU available has been emphasized in the discussion.**

- Data on NIV in emergency are available for adult only but it will be relevant to discuss about the adult experience

**We are sorry that we do not quite understand what the reviewer means here.**

Minor essentials revisions:
- Introduction: "patients at risk of severe bronchiolitis", age < to 3 months is lacking and it is the most common case.
**We agree and have included.**

- "CPAP works by keeping .....and reducing work of breathing" The reference for reduction of work of breathing in bronchiolitis are not Greenough and Donlan but the physiological works of Cambonie ICM 2008 and Essouri ICM 2011.
**We appreciate the comment and have changed accordingly.**

- Some descriptive studies on CPAP and bronchiolitis are missing Campion Arch of Ped 2006, Larrar Arch of ped 2006.

**The studies are now included**

- You must precise that masks used are nasal masks with leaks.

**This information has been included**

- Results:"four children were excluded ... figure 2". It seems to be rather the figure 1 such as in the following paragraph.
There is no figure 3, the evolution of level of PCO2 is the figure 2.

**We appreciate, and the number on the figures are now correct.**

- discussion: "This may have economic benefits" One recent large descriptive study on CPAP in bronchiolitis has described the impact of CPAP on the
economic burden of severe bronchiolitis, Essouri et al ICM 2014. The main cause was the reduction of ICU and total hospitalisation length of stay. Does CPAP reduces your LOS?

The design does not allow for studying if CPAP reduces the length of stay as there is no control group. The reduction in the use of ICU will be economical beneficial, and the reference from Essouri et al has been included to support this.

- Table 2: weight is lacking

We agree that weight could have been included but were not registered systematically. We consider that age and gestational age are the most relevant variables.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.