Peer Review File

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To the reviewers

General comments

This is a clinically relevant randomized controlled study (RCT) that investigates the effect of vibrating expiratory pressure (PEP) on airway clearance following remission from refractory Mycoplasma pneumoniae (M. pneumoniae) pneumonia (RMPP) in children.

The overall impression of the study validity is relatively good with a careful selection of children eligible for inclusion. The observational period contains no data on adherence and no objectively measured data on disease development (e.g. sputum, blood, radiology, hospital visits, readmissions) which is complete opposite to the stringent inclusion and selection validity. The primary outcome (radiologic infiltration) was measured only once two months following discharge. The literature on the potential restorative effect of PEP (and similar) on lung infiltrates and derived from RCT's is superficial and should be stronger inbuild in background and discussion.

Reply: Thank you for this suggestion very much. According to this comments, we add adherence data in the results. "All 60 participants completed this study, and there was no lost to follow-up. All participants completed the daily log, and all reported that they adhered the corresponding treatment." All participants were in the stage of pulmonary rehabilitation when they entered into this study, their lab indicators (sputum, blood) were normal. So we choose pulmonary images as an objective data. In control group, one patients had another visit to the outpatient for a common cold; two patients in PEP group had another visits to the outpatient, one for common cold, another for allergic rhinitis. All the authors discussed this, and we think that there was no strong association between these revisits and the study, so we didn't add these results in the manuscript. We revised "discussion" of the manuscript in red fond. We have chosen the recent literatures about PEP therapy.

Changes in the text: page 8 Line 3 "and there was no lost to follow-up (Figure 3)."

Page 10 Line 5 "In these studies, forced expiratory volume in one second was the most frequently measured primary outcome, and sputum volume or

weight was the secondary outcome. In this study, resolution of lung images was used as primary outcome as it is a relatively objective measurement. In addition, spirometry measurements is difficult to young children. We use sputum period as the secondary outcome because it isn't easy for children to spit out the sputum, which they often swallow. A systematic review showed that PEP device appeared to be effective for children with stable bronchiectasis, however, the effectiveness in people with an acute exacerbation of bronchiectasis is unknown (17). Another review showed that PEP was also effective in exacerbations of cystic fibrosis (26). Our findings were consistent with these reports, suggesting that PEP was effective for children with stable RMPP.".

Some questions:

Comment 1: How was the attendance for the study?

Reply 1: Thank you very much. To describe this detailed, we added "and there was no lost to follow-up" and an attendance figure 3.

Changes in the text: Page 8 Line 3 "and there was no lost to follow-up (Figure 3)"

Comment 2: Why were children classified as suffering from refractory MPP, while they all were evaluated to be in state of remission at time of inclusion?

Reply 2: Thanks. Children with RMPP have two stages of course. The first stage is the acute stage which means patients need antibiotics to treat Mp and other integrated treatment. The second stage is the remission stage or pulmonary rehabilitation stage, which means patients don't need antibiotics to treat Mp, what they need is the pulmonary rehabilitation treatment. We enrolled patients of RMPP in remission stage is to study effect of the PEP treatment on pulmonary rehabilitation, excluding the biases especially antibiotics treatment.

Changes in the text: No.

Comment 3: Adherence to PEP was based on self-report. However, no adherence rate and variance are stated?

Reply 3: Thank you for this detailed comments. In this study, every patient completed the daily log. Based on their self-report, they all adhered the treatment as required.

Changes in the text: Page 8 Line 10-11 "All participants completed the daily log, and all reported that they adhered the corresponding treatment."

Comment 4: How was sample size determined?

Reply 4: Thank you for this comment. At the design stage of this study, we indeed can't determine the suitable sample size because the references were few. Reference 21 reported "No suitable data was available to carry out a sample size calculation", so we just estimated the sample size as 60 subjects according to this reference. As the study progresses, we retrospectly sampled the study based on the resolution of chest image in this study. In control group, resolution of chest image was 10% in control group, while resolution of chest image was 60% in acapella group, power was set at 0.8, alpha was set as 0.05, N1:N2 was set as 1:1. We use PASS 11.0 software to calculate the sample size as 13 in each group. Which suggests that the 60 subjects is enough for this study.

Two Independent Proportions (Null Case) Power Analysis
Numeric Results of Tests Based on the Difference: P1 - P2
H0: P1-P2=0. H1: P1-P2=D1<>0. Test Statistic: Z test with pooled variance

Power	Sample Size Grp 1 N1	Sample Size Grp 2 N2	Prop|H1 Grp 1 or Trtmnt P1	Prop Grp 2 or Control P2	Diff if H0 D0	Diff if H1 D1	Target Alpha	Actual Alpha	Beta
0.8403	13	13	0.6000	0.1000	0.0000	0.5000	0.0500	0.0181	0.1597

Note: exact results based on the binomial were only calculated when both N1 and N2 were less than 100.

Changes in the text: No.

Comment 5: What is the authors judgement on the validity of using a daily log? Why are no results at all presented from the log?

Reply 5: Thank you very much. In this clinical study, we use daily log to record whether patients had a cough, had produced sputum, or had chest tightness or difficulty breathing; whether their usual activity or sleepwas affected; frequency of treatment, whether use of Acapella or chest percussion; and side effects of their treatment. To encourage them to fill the daily log timely, participants were followed up weekly by phone or visits. Daily log has some merits such as that participants can remember events clearly and freshly during the single day and it is very convenient and less costly. Daily log is widely used in clinical study. Indeed, the limits of daily log is that there may be disagreement between diaries and true practice. In this manuscript, we didn't use another "gold standard"methods compared with the daily log to validate the log. To present the daily log and the results clearly. We add the figure of daily log. We also add "All participants completed the daily log, and all reported that they adhered the

corresponding treatment.”In the paragraph of demographic data.
Changes in the text: Page 8 Line 10-11 “All participants completed the daily log, and all reported that they adhered the corresponding treatment.”

Comment 6: Since the effect of PEP is convincing on lung exudate with 63% of children having a full resolution in the intervention group compared to controls (10%), it seems unlikely that control children did not have any additional health check following discharge?
Reply 6: Thanks. Children in both groups were in the stage of pulmonary sequela stage, which suggest that they need pulmonary rehabilitation treatment. Both groups indeed received pulmonary rehabilitation treatment in this study. Although full resolution in control group covered just 10%, some resolution covers 76.7%, which suggested that control group was getting better too. In addition, participants in both groups were followed up weekly by phone or visits.
Changes in the text: No.

Comment 7: How was exacerbations and relapse of disease treated and/or advised?
Reply 7: Thanks. Children in this study were in the stage of a clinical remission, which suggested that they were in the stage of pulmonary sequel stage and their situations were stable. The possibility of exacerbations and relapse is very low. If there is a new infection, antibiotics and supportive treatments are advised to treat.
Changes in the text: No.

Comment 8: It is somewhat unclear whether the intervention was performed within the hospital or solely following discharge. I assume the later, but this should be clearly stated.
Reply 8: Thank you very much. Thank you for this thoughtful reminder, we clearly expressed this as “These treatments were carried out after patients were discharged, meaning that they perform the therapy at home.”
Changes in the text: Page 6Line 13-14 “These treatments were carried out after patients were discharged, meaning that they perform the therapy at home.”