

LETTER TO THE EDITOR

Open Access



# High flow nasal therapy during early pulmonary rehabilitation in patients with acute severe exacerbation of COPD: beneficial or illusory?

Guillaume Prieur<sup>1,2,3\*</sup>, Yann Combret<sup>1,3</sup> and Clement Medrinal<sup>2,3</sup>

## Abstract

In study “Effect of high-flow nasal therapy during early pulmonary rehabilitation in patients with severe AECOPD: a randomized controlled study” by Tung et al., authors concluded HFNT utilization led to enhanced exercise tolerance and a reduction of systemic inflammation. Nevertheless, some points requires additional discussion, the conclusion of the trial seems overstated. The baseline differences between groups induces substantial modifications in the conclusions of this trial. HFNT does not seem to add any benefit on exercise tolerance or systemic inflammation, nor on pulmonary function. The only difference that remained significant in homogenous statistical significance is dyspnea on the mMRC scale but clinical significance is highly questionable.

**Keywords:** COPD, Exacerbation, High flow nasal, Pulmonary rehabilitation

To the Editor,

We read with great interest the study by Tung et al. entitled “Effect of high-flow nasal therapy during early pulmonary rehabilitation in patients with severe AECOPD: a randomized controlled study” [1].

In this randomized controlled trial, the authors aimed to evaluate the feasibility and efficacy of high flow nasal therapy (HFNT) during early pulmonary rehabilitation (48 h after hospitalization due to acute exacerbation) in patients with COPD. The authors concluded HFNT utilization led to enhanced exercise tolerance and a reduction of systemic inflammation (C-reactive protein: CRP). Moreover, the authors underlined the hypothesis that HFNT may decrease lung hyperinflation and increase pulmonary function.

\* Correspondence: [gprieur.kine@gmail.com](mailto:gprieur.kine@gmail.com)

<sup>1</sup>Institut de Recherche Expérimentale et Clinique (IREC), Pôle de Pneumologie, ORL & Dermatologie, Groupe de Recherche en Kinésithérapie Respiratoire, Université Catholique de Louvain, 1200 Brussels, Belgium

<sup>2</sup>Institute for Research and Innovation in Biomedicine (IRIB), Normandie Univ, UNIROUEN, EA3830-GRHV, 76000 Rouen, France

Full list of author information is available at the end of the article

Nevertheless, some points requires additional discussion. First, the sample size is small (22 patients per group) and patient allocation resulted in differences in several parameters at baseline (mMRC, CAT and BODE indexes). Patients in the control group presented more severe respiratory symptoms that patients allocated to the HFNT intervention. Rightly, findings were reported as changes from baseline and follow-up at 4 and 12 weeks for these parameters to compare both groups. However, the same strategy was not applied to report the findings of all the outcomes measured in this study.

The study findings reported an increase in exercise tolerance associated with the use of HFNT during early pulmonary rehabilitation. For the analysis of exercise tolerance, baseline comparisons revealed a questioning trend ( $p = 0.052$ ) that favored the exercise capacity in the HFNT group with a mean difference of 48.5 m. Considering this large difference, the same strategy that the one applied for mMRC, CAT and BODE indexes (e.g. comparisons of delta rather that absolute values) should have



© The Author(s). 2020 **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

been applied as well. The within-group change indicate that the 6-min walking distance increased similarly in the HFNT and in the control group (mean increase 125.7 m and 117.0 m, respectively). In the present case, the mean difference between groups would have finally been an increase of 8.7 m in favor of the HFNT group that would not have reached statistical significance.

A significant decrease in dyspnea (measured by the mMRC score) was also reported for the HFNT group at 12 weeks of follow-up by comparing the mean changes from baseline in both groups (mean difference 0.27 points (CI 95% 0.061 to 0.48)). Although the statistical analysis of this outcome reached significance, the difference and CI reported was lower than the MCID of 0.6 points chosen by the authors (the reference cited by authors is not correct). The clinical significance of this result could therefore deserve further discussion.

Furthermore, the authors stated that “*Serum CRP may provide prognostic information about morbidity and mortality in COPD [ ...]. Our study proved that an HFNT PR program reduced CRP levels better than a non-HFNT PR program*”. It is important to note that CRP levels at 12 weeks were very low for both HFNT and control groups leading to very limited clinical relevance ( $0.07 \pm 0.12$  mg/dl and  $0.30 \pm 0.39$  mg/dl, respectively). The previously reported statement that HFNT reduces systemic inflammation therefore seems confusing. Patients in the control group presented higher CRP levels at baseline that nearly reached statistical significance ( $p = 0.086$ ). Alike analysis of exercise tolerance, delta CRP levels (baseline - 12 weeks) should have been compared between groups. Besides, between groups differences in change from baseline seemed to highlight a significant higher diminution in the control group compared to the HFNT group (mean decrease  $-8.1$  mg/dl and  $-5.04$  mg/dl, respectively).

To conclude, after a careful examination of the results presented in this study, the conclusion of the trial seems overstated. We believe that the authors should have undertaken homogenous statistical analysis for all the variables evaluated in the present study (as inspiratory capacity, mMRC scale, CAT and BODE index). The baseline differences between groups induces substantial modifications in the conclusions of this trial. Given the points mentioned above, HFNT does not seem to add any benefit on exercise tolerance or systemic inflammation, nor on pulmonary function. The only difference that remained significant in homogenous statistical significance is dyspnea on the mMRC scale but clinical significance is highly questionable. These points raise some concerns that should be further discussed for transparency, especially since the addition of HFNT during exercise seems to induce substantial patient discomfort [2].

#### Abbreviations

AECOPD: Acute exacerbation of COPD; BODE: health index: Body-mass index, degree of airway obstruction and dyspnea, and exercise capacity; CAT: COPD assessment test; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; CRP: C-reactive protein; HFNT: High flow nasal therapy; MCID: Minimal clinically important difference; mMRC: Modified medical research council scale

#### Acknowledgements

None.

#### Authors' contributions

Drafting the article: GP, CM, YC. The author(s) read and approved the final manuscript.

#### Funding

Not applicable.

#### Availability of data and materials

Not applicable.

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

Not applicable.

#### Competing interests

None of the authors have any conflict of interest.

#### Author details

<sup>1</sup>Institut de Recherche Expérimentale et Clinique (IREC), Pôle de Pneumologie, ORL & Dermatologie, Groupe de Recherche en Kinésithérapie Respiratoire, Université Catholique de Louvain, 1200 Brussels, Belgium.

<sup>2</sup>Institute for Research and Innovation in Biomedicine (IRIB), Normandie Univ, UNIROUEN, EA3830-GRHV, 76000 Rouen, France. <sup>3</sup>Groupe Hospitalier du Havre, Pulmonology department and pulmonary rehabilitation department, avenue Pierre Mendès France, 76290 Montivilliers, France.

Received: 25 May 2020 Accepted: 7 June 2020

Published online: 12 June 2020

#### References

1. Tung L-F, Shen S-Y, Shih H-H, Chen Y-T, Yen C, Ho S-C. Effect of high-flow nasal therapy during early pulmonary rehabilitation in patients with severe AECOPD: a randomized controlled study. *Respir Res*. 2020. <https://doi.org/10.1186/s12931-020-1328-z>.
2. Prieur G, Medrinal C, Combret Y, Dupuis Lozeron E, Bonnevie T, Gravier F, et al. Nasal high flow does not improve exercise tolerance in COPD patients recovering from acute exacerbation: A randomized crossover study. *Respirology*. 2019. <https://doi.org/10.1111/resp.13664>.

#### Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more [biomedcentral.com/submissions](https://biomedcentral.com/submissions)

