Archivos de Bronconeumología 59 (2023) 71–72

Sociedad Española de Neumología y Cirugía Torácica SEPAR

ARCHIVOS DE Bronconeumología

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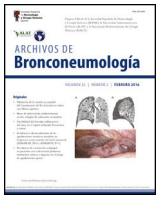

Editorial

Home High-Flow Nasal Cannula Oxygen Therapy for Stable Hypercapnic COPD: So Far, So Good

During the last decades, the use of ventilatory support and long-term oxygen therapy (LTOT) in patients with chronic obstructive pulmonary disease (COPD) has given rise to a certain amount of controversy.[1,2] In this context, high-flow nasal cannula (HFNC) oxygen therapy has emerged as a new way of administering oxygen for patients with severe hypoxemia, producing remarkable results in various clinical settings. This therapy delivers high flows of oxygen while maintaining control of the fraction of inspired oxygen and the temperature of the air delivered. The main physiological effects of HFNC are well described and can be summarized as achieving effective oxygenation, mobilization of secretions, reduction in effort required to breathe, increase in end-expiratory lung pressure and volume, reduction of inspiratory resistance and the clearance of anatomical dead space in the upper airways.[3,4] Consequently, its effects in the treatment of acute hypoxemic respiratory failure have been documented frequently.[5,6]

With these effects in mind, several authors have hypothesized whether HFNC could play a role in patients with COPD and hypercapnic respiratory failure.[7] In particular, a recent meta-analysis showed that HFNC not only improved gas exchange, but also reduced the number of exacerbations and improved quality of life.[8] However, to date, there have been no clinical trials evaluating the efficacy and safety of using high oxygen flows in COPD patients with chronic hypercapnia. Recently, Nagata K, et al. published the first clinical trial evaluating the use of HFNC in this clinical setting compared to conventional LTOT.[9] By designing a randomized clinical trial in patients with moderate to severe COPD with chronic hypercapnic respiratory failure receiving LTOT, the authors evaluated the effect of a combination of HFNC/LTOT versus LTOT, using the number of exacerbations during a 52-week follow-up as the primary endpoint. The authors affirm that HFNC is a valid therapeutic option in this clinical setting, since it reduces the number of exacerbations and the time to first exacerbation, as well as some parameters of lung function and quality of life, without any notable adverse effects being observed. These results constitute encouraging data for the use of HFNC in COPD patients with chronic hypercapnia.

However, a number of methodological considerations should be taken into account in order to correctly interpret the results of this clinical trial. Firstly, the main results of the study are based on a sample size that barely reaches the estimated size. Secondly, the authors did not perform an intention-to-treat analysis. In fact, 12 patients dropped out of the study in the intervention arm, compared to 9 in the control arm. These dropouts were due to either the patient's or physician's decision or to adverse effects, which further limited the sample size, and may have led to a selection bias in the sample, as well as affecting the evaluation of the efficacy and safety of the treatment. Thirdly, the evaluation of the primary endpoint (number of moderate/severe exacerbations) was carried out by adjusting for age, sex and GOLD stage. However, there are other variables associated with the clinical outcome under study, the main one being the number of previous exacerbations. Not only do the authors not take this variable into account, but they do not even describe the baseline situation in their population. Consequently, the multivariate adjusted study could have been different if other variables had been considered in the model. Similarly, the analysis of time to first exacerbation was performed without adjusting for covariates.

Regarding the assessment of secondary outcomes, the authors evaluate functional changes and the impact on quality of life. However, in relation to the symptomatic impact and impact on quality of life, the authors again fail to describe the baseline situation, making it difficult to form a clear idea of the real clinical impact or the clinical relevance of the differences found. Interestingly, the functional benefits are not maintained at one year, which, together with the small sample size, could indicate a spurious association. Finally, these secondary outcomes again do not appear to be adjusted for covariates in a multivariate model, nor are they adjusted for multiplicity.

From the point of view of safety, an analysis of the gasometrical findings produces interesting outcome results. The patients did not present hypoxemia from the baseline visit, suggesting that they were well adapted to oxygen therapy without this leading to an increase in $PaCO_2$ during the year of treatment with the established protocol. However, there was an increase in the other adverse effects in the HFNC arm, especially in the cardiovascular sphere, although the numbers are low, which does not permit a reliable calculation of the statistical significance. Interestingly, the HFNC group had fewer cases of community pneumonia and COPD exacerbations, which are considered as adverse effects.

In short, the clinical trial by Nagata K, et al.[9] evaluates the role of HFNC in patients with stable COPD in hypercapnic respiratory failure. Their results suggest that HFNC may have a role in preventing exacerbations in COPD patients, although several methodological limitations and a possible association of adverse effects suggest that we should interpret the results with caution. One important note for the clinician to keep in mind is the potential technical difficulty

https://doi.org/10.1016/j.arbres.2022.10.001

of home use of this device, which is intended for use in intermediate respiratory care units or intensive care units for particularly frail patients, to ensure that the correct quantity of oxygen, obtained from an oxygen cylinder, is delivered over the required number of days. Finally, a cost study would need to be carried out to evaluate the budgetary impact of this widespread measure in the community in relation to the effectiveness achieved.

Recalling the title of the 1993 album by the Canadian artist Brian Adams, we can say, "So far, so good". In extremely fragile patients with previous exacerbations who are dependent on an oxygen therapy program, we must clearly evaluate the efficacy and safety of the interventions to be implemented, collecting sufficient evidence to ensure that we are providing these frail patients with the best possible medicine.

Funding

This research was supported byCIBER – Consorcio Centro de Investigación Biomédica en Red – (CIBERES), Instituto de Salud Carlos III, Ministerio de Ciencia e Innovación.

Conflict of interests

JLLC has received honoraria during the last 3 years for lecturing, scientific advice, participation in clinical studies or writing for publications for (alphabetical order): AstraZeneca, Bial, Boehringer, Chiesi, CSL Behring, Faes, Ferrer, Gebro, Grifols, GSK, Megalabs, Menarini, and Novartis.

Acknowledgments

The authors would like to thank Simon Armour (Academia Britanica) for his support in the English adaptation of the present manuscript

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