Reply to: F_{IO_2}, P_{aO_2}, or Else – What Matters in Noninvasive Ventilation in Stable COPD?

To the Editor:

We read with interest the comments from Sarc et al[1] about our previous study on F_{IO_2} delivered by noninvasive ventilation (NIV) compared with long-term oxygen therapy at the same flow.[2] We want to give some precision in response to their comments. Sarc et al[1] state that our result of a decrease in F_{IO_2} delivered by NIV at the same oxygen flow delivered by nasal cannula is not surprising. Indeed, it is an expected result related to the dilution of oxygen by the NIV flow. To our knowledge, this had not yet been clearly demonstrated in real-life home conditions.

Their main remark concerns the lack of data on P_{aO_2}, stating that F_{IO_2} cannot be directly translated into P_{aO_2} and suggests that the decrease in F_{IO_2} would be compensated by the increase in alveolar ventilation; in other words, the decrease in P_{aCO_2}. We are not totally agreed with this point. F_{IO_2} is the main determinant of alveolar oxygen pressure (P_{AO_2}): $P_{AO_2} = P_{iO_2} - P_{aCO_2} / R = (PB - PH_2O) F_{IO_2} - (P_{aCO_2} / R)$. In the the studies by Murphy et al[3] and Köhnlein et al,[4] the change in P_{aCO_2} associated with NIV use was 5 mm Hg and 6.75 mm Hg, respectively. With a commonly accepted respiratory coefficient of 0.82, P_{AO_2} variation would be from 6.1 to 8.2 points. In our study, the P_{AO_2} change related to the decrease in F_{IO_2} (from ~31% with daytime oxygen therapy to 25% on average with NIV) would be ~42.8 points. Therefore, the drop in P_{aCO_2} cannot compensate for the drop in P_{iO_2} (linked to the drop in F_{IO_2} related to compensation for leaks). This results in a drop in P_{AO_2} and, therefore, in P_{aO_2}. In addition, a study by Storre et al[5] demonstrated that significant leaks influence both F_{IO_2} and P_{aO_2}. In our study[2], monitoring S_{pO_2} was usable in 5 subjects; in all the subjects, we noticed a drop in S_{pO_2} when the leaks increased and the F_{IO_2} decreased (Fig. 1).

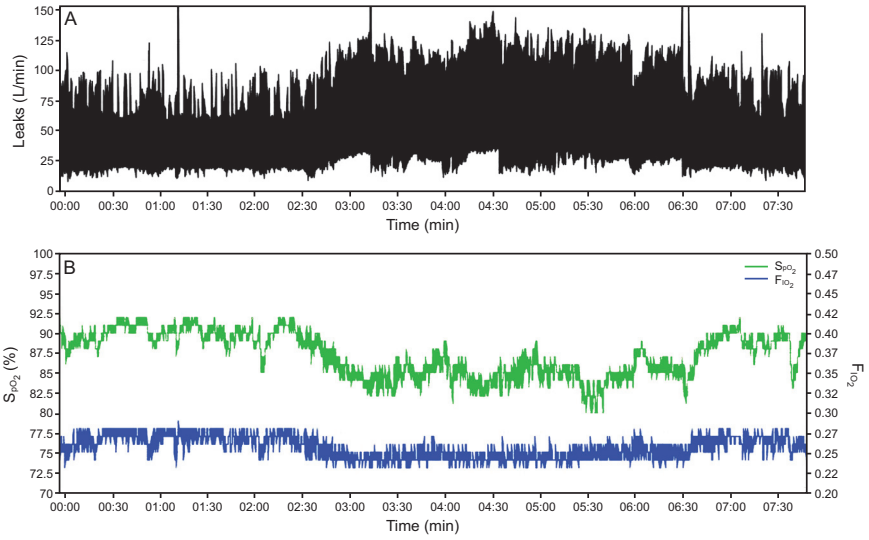

Fig. 1. Leaks, S_{pO_2} and F_{IO_2} variations during nocturnal noninvasive ventilation.

The consequences of nocturnal hypoxemia are multiple, and nocturnal oxygen supplementation can improve arrhythmias and reduce blood pressure surges.[6,7] The benefits for sleep quality are not well established.[8,9] The association between nocturnal oxygen desaturation and the development of chronic pulmonary hypertension remains unclear. Data on mortality and its association with nocturnal oxygen desaturation in COPD are scarce and have not demonstrated a survival benefit when corrected by oxygen supplementation. However, the 2 studies that looked at this topic were carried out on small cohorts and concerned subjects with low hypoxemia (mean P_{aO_2} of 76 mm Hg and 62.7 mm Hg).[10,11]

Finally, Sarc et al[1] state that oxygen flow should be titrated to P_{aO_2}. However, this is difficult to achieve in the daily practice at the patient's home. We believe that it is simpler in daily practice to determine the oxygen flow according to the F_{IO_2} delivered. Like the servo flow regulator that titrates oxygen flow based on pulse oximetry feedback,[12] technologic innovation would be the introduction of an oxygen flow regulator based on the flow of the home ventilator turbine and, therefore, of the leaks, so that the increase in the oxygen flow would limit the drop in F_{IO_2} linked to leaks.

Michael Cardinale
Pierre-Julien Cungi
Pierre Esnault
Eric Meaudre
Philippe Goutorbe
Department of Anesthesiology and Intensive Care
Military Hospital
Hôpital d'Instruction des Armées
Sainte-Anne
Toulon, France

REFERENCES

1. Sarc I, Ziherl K, Esquinas A. F_{IO2}, P_{aO2} or else - what matters in noninvasive ventilation in stable COPD? Respir Care 2021;66(8):1368-1369.
2. Cardinale M, Cungi P-J, Esnault P, Castagna O, Nguyen C, Daranda E, et al. In COPD, nocturnal noninvasive ventilation reduces the F_{IO2} delivered compared with long-term oxygen therapy at the same flow. Respir Care 2020;65(12):1897-1903.
3. Murphy PB, Rehal S, Arbane G, Bourke S, Calverley PMA, Crook AM, et al. Effect of home noninvasive ventilation with oxygen therapy vs oxygen therapy alone on hospital readmission or death after an acute COPD exacerbation: a randomized clinical trial. JAMA 2017;317(21):2177-2186.
4. Köhnlein T, Windisch W, Köhler D, Drabik A, Geiseler J, Hartl S, et al. Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre,

Correspondence: Michael Cardinale MD, Fédération d'Anesthésie – Réanimation, Hôpital d'Instruction des Armées Sainte-Anne, Boulevard Sainte-Anne, BP 20545 - 83041, Toulon Cedex 9, France. E-mail: mickaelcardinale@hotmail.fr.

Dr Goutorbe discloses a relationship with Breas Medical, in addition, Dr Goutorbe has patent systems and methods for automatically adjusting a determined supply of F_{IO_2} generated from a CPAP, noninvasive ventilation, or other ventilator systems issued. Drs Cardinale, Esnault, Cungi, and Meaudre declare no conflict of interest.

DOI: 10.4187/respcare.09172

randomised, controlled clinical trial. Lancet Respir Med 2014;2(9):698-705.
5. Storre JH, Huttmann SE, Ekkernkamp E, Walterspacher S, Schmoor C, Dreher M, Windisch W. Oxygen supplementation in noninvasive home mechanical ventilation: the crucial roles of CO_2 exhalation systems and leakages. Respir Care 2014;59(1):113-120.
6. Flick MR, Block AJ. Nocturnal vs diurnal cardiac arrhythmias in patients with chronic obstructive pulmonary disease. Chest 1979;75 (1):8-11.
7. Fletcher EC, Levin DC. Cardiopulmonary hemodynamics during sleep in subjects with chronic obstructive pulmonary disease. The effect of short- and long-term oxygen. Chest 1984;85(1):6-14.
8. Calverley PM, Brezinova V, Douglas NJ, Catterall JR, Flenley DC. The effect of oxygenation on sleep quality in chronic bronchitis and emphysema. Am Rev Respir Dis 1982;126(2):206-210.
9. Fleetham J, West P, Mezon B, Conway W, Roth T, Kryger M. Sleep, arousals, and oxygen desaturation in chronic obstructive pulmonary disease. The effect of oxygen therapy. Am Rev Respir Dis 1982;126(3):429-433.
10. Fletcher EC, Luckett RA, Goodnight-White S, Miller CC, Qian W, Costarangos-Galarza C. A double-blind trial of nocturnal supplemental oxygen for sleep desaturation in patients with chronic obstructive pulmonary disease and a daytime P_{aO2} above 60 mm Hg. Am Rev Respir Dis 1992;145 (5):1070-1076.
11. Chaouat A, Weitzenblum E, Kessler R, Charpentier C, Ehrhart M, Schott R, et al. A randomized trial of nocturnal oxygen therapy in chronic obstructive pulmonary disease patients. Eur Respir J 1999;14(5):1002-1008.
12. Cirio S, Nava S. Pilot study of a new device to titrate oxygen flow in hypoxic patients on long-term oxygen therapy. Respir Care 2011;56(4):429-434.