Automated versus manual oxygen titration in COPD exacerbation: machine or hands, this is the question

Gulsah Karaoren1
Senay Goksu Tomruk1
Antonio M Esquinas2

1Department of Anesthesiology and Reanimation, Istanbul Umranıye Research Hospital, Istanbul, Turkey;
2Intensive Care Unit, Hospital Morales Meseguer, Murcia, Spain

Dear editor

We have read the article titled “Automated oxygen titration and weaning with FreeO2 in patients with acute exacerbation of COPD: a pilot randomized trial” by Lellouche et al with great interest; however, there are some key aspects to take into account for proper practical implications.1

First, regarding ethical aspects, there seem to be some confusing points about disclosure and researchers. Of the researchers, one is a co-inventor of company that developed the device and two are owners of free oxygen generator. We could not clarify whether any of the authors are medical doctors.

With regard to other aspects in the manuscript, the study included COPD patients (aged >40 years) with exacerbation and resting saturation <90% at room environment in whom SpO2 increased to <92% by 8 L/min oxygen supplementation. It was mentioned that it was impossible to obtain informed consent from patients who stayed in the hospital for >24 h, those with antibiotic-resistant infection, those who underwent intermittent nonintensive ventilation, and those with cognitive dysfunction. Also, the authors did not mention comorbid conditions, body mass index, exercise capacity, duration of COPD, current therapies received, and, most importantly, whether there is comorbid heart failure in the patients.2 The authors performed pulmonary function tests by post-bronchodilator spirometry; however, they did not take COPD grade (mild/moderate/severe) into account during standardization.3 In addition, there were no data regarding concurrent therapies given at emergency department and during admission. Did all patients undergo a standard treatment protocol? Moreover, patients of a broad range of age were included in the study. Thus, it is impossible to have no variations in exercise capacity, cognitive functions, and treatment response in this wide range of age from 40 to 80 years.

The finding that use of free oxygen device was only an effective factor in improved saturation and shortened length of hospital stay by neglecting many parameters arises some questions about the results obtained in this study. In the limitations, the authors mentioned that sample size per group was small. However, no power analysis was performed.

It was reported that the principal investigators were not involved in the care and disposition of study patients and that emergency room clinicians and nurses performed works related to the study; however, it was impossible that clinicians and nurses...
involved in the study were blind to study. Thus, the bias in the patient selection and management is controversial.

In conclusion, the study should have to be performed on selected patients by independent clinicians without funding.

Disclosure
The authors report no conflicts of interest in this communication.

References
1. Lellouche F, Bouchard PA, Roberge M, et al. Automated oxygen titration and weaning with FreeO\textsubscript{2} in patients with acute exacerbation of COPD: a pilot randomized trial. \textit{Int J Chron Obstruct Pulmon Dis}. 2016;11:1983–1990.
2. Richardson A, Tolley E, Hartmann J, et al. Evaluation of chronic obstructive pulmonary disease (COPD) and reduced ejection fraction heart failure (HFrEF) discharge medication prescribing: is drug therapy concordant with national guidelines associated with a reduction in 30-day readmissions? \textit{Respir Med}. 2016;119:135–140.
3. Wells JM, Estepar RS, McDonald MN, et al. Clinical, physiologic, and radiographic factors contributing to development of hypoxemia in moderate to severe COPD: a cohort study. \textit{BMC Pulm Med}. 2016;16(1):169.
Dear editor

The letter from Karaoren et al referring to our recently published paper on the evaluation of FreeO2 during acute exacerbation of COPD1 raises questions regarding the possibility for researchers to evaluate their own innovations. Indeed, the FreeO2 system that automatically adjusts the oxygen flow rate in spontaneously breathing patients to stabilize SpO2 within a predetermined range was developed in our laboratory,2 with the input of local researchers, pulmonologists, respiratory therapists, nurses, and biomedical engineers. This collaboration led to the development of a prototype that we naturally evaluated in our institution.

The authors of the letter imply that there are ethical issues in the evaluation of our own invention. We certainly do not share this position and would argue that we could not have done differently. We have already published the results obtained from other preliminary evaluations conducted in several clinical conditions and various clinical settings in >500 patients.1–6 On every occasion, we did disclose our conflicts of interest. In addition, the results of other independent evaluations are yet to be published.

The patients who participated in our trial were managed by using a standardized clinical pathway that has been applied in our institution for years, except for oxygen administration. The body mass index and cardiac comorbidities did not differ between the groups. Exercise capacity before hospitalization was unknown for most of the patients. We would not consider this information as critical to the proper interpretation of our findings. The issue of blinding is certainly relevant. However, as in most respiratory support studies, it was not possible to incorporate blinding in the study design. A power analysis was not conducted in this pilot study. Based on the current results, power analysis will be feasible for further studies.

Oxygen manual titration with flowmeters is used in hospitals for more than one century, and certainly, there is room for improvement.7 As shown in several studies, compared to manual/hand titration, automated oxygen titration with the FreeO2 system or similar devices might reduce the hypoxemia and hyperoxia rates and has the potential to reduce oxygen therapy duration as well as hospital length-of-stay.1,4,5 We thus see innovation with this new device.

Disclosure

The Fond de Recherche en Santé du Québec contributes to FL’s salary for research activities (clinical research scholar) and to the research assistant’s salary (clinical research grant). FL and ELH are the co-inventors of the FreeO2 system and made the first prototypes with the engineering department of Laval University. FL and ELH are the cofounders of a Laval University spin-off research and development company (OxyNov) to develop automated systems for respiratory support. FM holds a GlaxoSmithKline/Canadian Institutes of Health Research chair on COPD at Laval University. FM and YL participate in Innovair, a company that owns shares in OxyNov, the owner of the FreeO2 device. The authors report no other conflicts of interest in this communication.

References

1. Lellouche F, Bouchard PA, Roberge M, et al. Automated oxygen titration and weaning with FreeO2 in patients with acute exacerbation of COPD: a pilot randomized trial. Int J Chron Obstruct Pulmon Dis. 2016;11:1983–1990.
2. Lellouche F, L’Her E. Automated oxygen flow titration to maintain constant oxygenation. Respir Care. 2012;57:1254–1262.
3. Lellouche F, L’Her E, Bouchard PA, Brouillard C, Maltais F. Automatic oxygen titration during walking in subjects with COPD: a randomized crossover controlled study. Respir Care. 2016;61:1456–1464.
4. L’Her E, Dias F, Gouillou M, et al. Automation of oxygen titration in patients with acute respiratory distress at the emergency department. A multicentric international randomized controlled study. Am J Respir Crit Care Med. 2015;191:A6329.
5. Vivodtzev I, L’Her E, Yankoff C, et al. Automatically adjusted oxygen flow rates to stabilize oxygen saturation during exercise in O2-dependent and hypercapnic COPD. Eur Respir J. 2016;48:1567.
6. Huyah-Ky MT, Bouchard PA, L’Her E, Sarrazin JF, Lellouche F. Closed-loop adjustment of oxygen flowrate with FreeO2 in patients with acute coronary syndrome: comparison of two SpO2 target and manual adjustment. A randomized controlled study. In: Program and abstracts of the Société de Réanimation de Langue Française, Réanimation 2017; January 11–13, 2017; Paris. Abstract 5676.
7. Foregger R. The rotameter and the waterwheel. Anaesthesist. 2001;50:701–708.
8. Claure N, Bancalari E. Automated closed loop control of inspired oxygen concentration. Respir Care. 2013;58:151–161.
Dove Medical Press encourages responsible, free and frank academic debate. The content of the International Journal of Chronic Obstructive Pulmonary Disease 'letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the International Journal of Chronic Obstructive Pulmonary Disease editors. While all reasonable steps have been taken to confirm the content of each letter, Dove Medical Press accepts no liability in respect of the content of any letter, nor is it responsible for the content and accuracy of any letter to the editor.