F_{IO_2}: An Inspired Solution for a Universal Problem

Early recognition of pulmonary dysfunction is critical in accurately and rapidly diagnosing respiratory illnesses such as acute hypoxic respiratory failure, ARDS, and community-acquired pneumonia because the prognosis is largely dependent on how soon the treatment is initiated after the diagnosis. Unfortunately, few easily accessible (noninvasive) techniques exist for measuring oxygenation needs. We congratulate Chalmers et al[1] for the study in this issue of RESPIRATORY CARE in which they identified changes in F_{IO_2} as an early prognostic marker in patients with ARDS and community-acquired pneumonia. Specifically, the investigators examined a cohort of ~3,000 subjects with ARDS or community-acquired pneumonia who were admitted to the ICU. The study identified F_{IO_2} to be easily accessible in electronic health records and, through careful monitoring, F_{IO_2} trajectory was a predictor of ventilator-free days.[1]

P_{aO_2}/F_{IO_2} is the primary classification index and the accepted standard for determining the severity of respiratory illness. However, measurements are noncontinuous, require invasive regular arterial blood gas measurements, and are costly and time intensive for respiratory therapists and other clinicians. Alternatively, S_{pO_2}/F_{IO_2} has been used to stratify ARDS by using the relationship of the oxygen-hemoglobin dissociation curve and P_{aO_2}.[2] Although there are limitations with using S_{pO_2} to estimate arterial oxygen saturation (S_{aO_2}) because some inaccuracies occur in hypoxic ranges,[3] S_{pO_2} is a strong surrogate for S_{aO_2} and has practicality for treating patients with ARDS over a conservative range (P_{aO_2} of 55–80 mm Hg).[4] The sigmoidal shape of the oxygen-hemoglobin dissociation curve (Fig. 1) represents the binding affinity between hemoglobin and oxygen, and highlights a direct curvilinear relationship of P_{aO_2} and S_{aO_2} from a P_{aO_2} of 25–80 mm Hg; however, after the genu (somewhere between 70–80 mm Hg), the relationship between P_{aO_2} and S_{aO_2} becomes less predictable, and increases in P_{aO_2} do not reliably improve oxygen saturation. By using this information, P_{aO_2} levels of 70–80 mm Hg are sufficient and do not justify an increase in F_{IO_2}. Chalmers et al[1] concluded that F_{IO_2} can be used as an indicator of illness trajectory with similar accuracy to P_{aO_2}/F_{IO_2}. A more novel finding was that decreased F_{IO_2} correlated with an increase in ventilator-free days in subjects with acute hypoxic respiratory failure who were in the ICU. A strength of their cohort was that F_{IO_2} was tightly maintained (ICU protocol driven) to achieve an oxygen saturation in the low 90%.

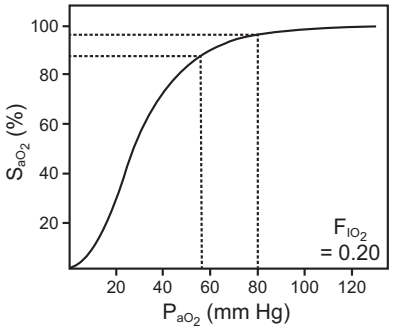

Figure 1. The oxyhemoglobin dissociation curve showing the relationship between the arterial oxygen saturation (S_{aO_2}) and the partial pressure of arterial oxygen (P_{aO_2}).

SEE THE ORIGINAL STUDY ON PAGE 1521

Interestingly, many ICUs err on the side of high normal oxygen levels. This practice base is hypoxia averse. Clinical indices set by the American-European Con-sensus Committee target a P_{aO_2} between 80 and 115 mm Hg to obtain "normoxemia."[5] Although it is crucial to keep the organs adequately oxygenated, little benefit in oxygenation occurs after an oxygen saturation of 93% (Fig. 1). More importantly, there is a risk of hyperoxygenation, which has been shown to increase barotrauma[6] and is associated with decreased ventilator-free days and increased mortality.[7] Furthermore, hyperoxia worsens outcomes after myocardial infarction and strokes. Therefore, for F_{IO_2} to be a useful metric, it has to be tailored to an S_{aO_2}/S_{pO_2} of 90%–95%. This requires more frequent monitoring and adjustment of F_{IO_2} at the patient's bedside. F_{IO_2} adjustments are the single most common intervention performed in the ICU. However, these interventions require expertise, equipment, and personnel to adjust and monitor F_{IO_2} levels. There is a clear need for an efficient, conservative, and proactive technology for recognizing and treating pulmonary injuries.

The authors have disclosed no conflicts of interest.

Correspondence: Catherine M Sampson PhD, Department of Anesthesiology, University of Texas Medical Branch, 301 University Blvd, Galveston, TX 77555-5302. E-mail: casampso@utmb.edu.

DOI: 10.4187/respcare.09552

Closed loop control of F_{IO_2} in patients on mechanical ventilation grew out of an unmet need for providing oxygen in remote environments. For purposes of this editorial, closed loop control of PEEP will not be discussed. Specifically, closed loop control of F_{IO_2} was developed to provide the standard of care oxygenation in the absence of bedside personnel. In addition, remote or austere environments require the need to transport and carry oxygen. Thus, closed loop control of F_{IO_2} was also developed to conserve oxygen as a resource. A key study by Johannigman et al,[8] demonstrated that closed loop control of F_{IO_2} improves efficacy (better target oxygen saturation leading to less incidence of hypoxia and hyperoxia) and efficiency (less oxygen usage – upto 50% reduction). Another unique aspect of closed loop control of F_{IO_2} is that the closed loop control algorithm possesses diagnostic utility. Specifically, the activity of the closed loop control of the F_{IO_2} algorithm identifies pulmonary (dys) function, a novel signature of the S_{pO_2} to closed loop control of F_{IO_2} ratio. In a preclinical ARDS model, the embedded closed loop control of the F_{IO_2} algorithm was incorporated into an alert decision support technology, called the smart oxygenation system, which provided earlier recognition of pulmonary dysfunction.[9] In addition, by implementing a more-rapid initiation of lifesaving interventions via the smart oxygenation system, the ARDS severity changed from severe to mild.[10]

In the context of the severe acute respiratory syndrome-coronavirus-2 pandemic, there has been an increased need for clinical expertise, ventilators, oxygen, and supplies associated with treating ARDS. Rapid, noninvasive diagnostic and therapeutic systems that efficiently and effectively provide goal-directed oxygen therapy are needed. Automated tasks or remote monitoring controls for oxygenation and ventilation would confer protection for respiratory therapists and other bedside clinicians who take care of patients who are highly contagious. Although there are commercially available ventilators that perform closed loop control of F_{IO_2}, currently none are approved by the FDA in the United States. The FDA has provided an emergency use authorization for closed loop control of F_{IO_2} for ventilators during this pandemic. Indices, such as changes in F_{IO_2} or S_{pO_2}/F_{IO_2} that maintain oxygen saturation between 90% and 95% can be strong tools to assess lung function. Perhaps, when coupled to closed loop control of F_{IO_2} and/or smart oxygenation systems, these tools can lead to a quicker therapeutic response, thereby improving outcomes for acute lung injury.

Catherine M Sampson
Department of Anesthesiology
University of Texas Medical Branch
Galveston, Texas

Muzna N Khan
Department of Respiratory Care
School of Health Professions
University of Texas Medical Branch
Galveston, Texas

Michael P Kinsky
Clinical Research Center
Department of Anesthesiology
University of Texas Medical Branch
Galveston, Texas

REFERENCES

1. Chalmers SJ, Odeyemi YE, Lal A, Li H, Frank RD, Gajic O, et al. FIO2 trajectory as a pragmatic intermediate marker in acute hypoxic respiratory failure. Respir Care 2021;66(10):1521-1530.
2. Rice TW, Wheeler AP, Bernard GR, Hayden DL, Schoenfeld DA, Ware LB. Comparison of the SpO2/FIO2 ratio and the PaO2/FIO2 ratio in patients with acute lung injury or ARDS. Chest 2007;132 (2):410-417.
3. Jubran A, Tobin MJ. Reliability of pulse oximetry in titrating supplemental oxygen therapy in ventilator-dependent patients. Chest 1990;97(6):1420-1425.
4. Brower RG, Ware LB, Berthiaume Y, Matthay MA. Treatment of ARDS. Chest 2001;120(4):1347-1367.
5. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. Report of the American-European consensus conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial coordination. The Consensus Committee. Intensive Care Med 1994;20 (3):225-232.
6. Aggarwal NR, Brower RG. Targeting normoxemia in acute respiratory distress syndrome may cause worse short-term outcomes because of oxygen toxicity. Ann Am Thorac Soc 2014;11(9):1449-1453.
7. Smallwood N, Holland AE. Over-oxygenation in the acute hospital setting: an implementation failure in need of an implementation science solution. Intern Med J 2021;51(5):633-635.
8. Johannigman JA, Branson RD, Beck G, Lacroy D. Oxygen Conservation with autonomous control of inspired oxygen concentration in ventilated trauma patients. J Trauma 2009;66:386-392.
9. Soejima K, Schmalstieg FC, Sakurai H, Traber LD, Traber DL. Pathophysiological analysis of combined burn and smoke inhalation injuries in sheep. Am J Physiol Lung Cell Mol Physiol 2001;280(6): L1233-L1241.
10. Liu NT, Salter MG, Khan MN, Branson RD, Enkhbaatar P, Kramer GC, et al. Closed-loop control of FiO2 rapidly identifies need for rescue ventilation and reduces ARDS severity in a conscious sheep model of burn and smoke inhalation injury. Shock 2017;47(2):200-207.