Optimal oxygen titration in patients with chronic obstructive pulmonary disease: A role for automated oxygen delivery?

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Oxygen therapy can be life-saving for patients with chronic obstructive pulmonary disease (COPD) and is the backbone of any acute COPD treatment strategy. Although largely considered to be a benign drug, many publications have highlighted the need to accurately adjust oxygen delivery to avoid both hypoxemia and the problem of hyperoxia-induced hypercapnia. Recent clinical data have shown that the deleterious effects of excess oxygen treatment can not only alter carbon dioxide levels (which has been known for more than 60 years) but can also lead to an increase in mortality. Nevertheless, despite the extensive literature, the risks associated with hyperoxia are often overlooked and published clinical recommendations are largely ignored. This failure in knowledge translation has become increasingly important not only because of the desire to reduce medical error, but in a society with limited health care resources, the economic burden of COPD is such that it cannot afford to make preventable medical mistakes. Recently, novel devices have been developed to automatically adjust oxygen flow rates to maintain stable oxygen saturations. These closed-loop oxygen delivery systems have the potential to reduce medical error, improve morbidity and mortality, and reduce health care costs. Preliminary data in this field are promising and will require a significant amount of research in the coming years to determine the precise indications for these systems. The importance of appropriate oxygen dosing and the current literature regarding novel oxygen delivery systems are reviewed.

Key Words: Closed-loop systems; Complications; COPD; Hypercapnia-induced hyperoxia; Hyperoxia; Knowledge transfer; Oxygen therapy

Deleterious effects of hyperoxia in patients with chronic obstructive pulmonary disease (COPD) are often overlooked despite abundant literature regarding the subject (1). Recently, novel closed-loop oxygen delivery systems have been developed with the potential to optimize oxygen titration and reduce complications associated with oxygen therapy (2).

METHODOLODY
A literature search and review for the most significant articles regarding hyperoxia-induced hypercapnia were conducted (3-8). Past and present evidence are discussed, including a recent randomized controlled trial demonstrating the impact of hyperoxia in patients with acute respiratory failure on mortality in the prehospital setting (9). Preliminary data regarding new devices that automatically titrate oxygen flow to maintain constant oxygen saturation (2,10-12) are also reviewed.

OXYGEN THERAPY IN COPD: A FAILURE IN KNOWLEDGE TRANSFER
Risks associated with both hypoxemia and hyperoxia have been well described and, consequently, accurate adjustment of oxygen flow rates in COPD patients is of particular importance. However, to date, due to limited advancements in technology as well as slow knowledge transfer, this goal remains elusive. The risks of hyperoxia, especially induced hypercapnia, although known since 1949 (6), are often overlooked; Beasley et al (1), however, have recently sounded the alarm bell. The first recommendations to adjust oxygen supply were published in 1967 by Campbell (4). Several medical societies have issued similar recommendations (5,7); however, these recommendations are often not followed (13,14). Reasons are likely multifactorial and are due, at least in part, to an underappreciation of the problem, especially in emergent situations and during prehospital transport. The recent demonstration in a large randomized controlled trial of excess mortality due to oxygenation during prehospital transport (9) has revived the discussion regarding the potential harm of oxygen therapy (1).

CLINICAL IMPACT OF EXCESSIVE OXYGENATION DURING EXACERBATIONS OF COPD
Oxygen therapy is the most frequently administered emergency treatment in hospital and during prehospital care (7). The adverse effects of hyperoxia are well known in patients with COPD and are particularly marked during exacerbations (3,8) (Figure 1). Plant et al (8) assessed the frequency and impact of respiratory acidosis in 983 COPD patients admitted to the emergency department. Respiratory acidosis...
the incidence of noncompliance with current guidelines and proportional to the prevalence of the disease. Recent statistical data regarding hospitalizations in Canada from the Canadian Institute for Health Information show that COPD is now associated with the highest rate of hospitalization among the major chronic diseases in Canada (16) (Figure 2). The total cost of COPD exacerbations is expected to exceed $1 billion dollars annually by 2015 (17). Considering the economic burden of COPD, the strict control of oxygen flow rates should not be considered a minor problem. Thus, treatments that can be easily modified to limit morbidity and mortality have the potential for significant cost savings.

**FACILITATED KNOWLEDGE TRANSLATION VIA AUTOMATED OXYGEN THERAPY**

With regard to oxygen therapy, despite more than 50 years of research, transfer of knowledge to clinical practice to adequately adjust oxygen levels and minimize oxygen toxicity has been a failure (1). Current practice requires manual adjustments of oxygen flow rates via ‘oxygen flowmeters’. The first report describing the use of an oxygen flowmeter was published in 1910 (18) and, since then, few innovations have occurred in the field of oxygen therapy. However, technological improvements have now allowed the use of more sophisticated devices to titrate oxygen therapy. One possible modern solution to facilitate knowledge transfer is to automate repetitive and relatively simple medical tasks. The adjustment of oxygen via a closed-loop system is promising. In such systems, the main parameter taken into account is \( \text{SpO}_2 \), which continuously feeds the algorithm. A proportional integral controller adjusts the oxygen flow within a range (that differs from one device to another), with the aim of maintaining the \( \text{SpO}_2 \) within a predefined target that can be set by the clinician. Three systems that attempt to achieve this goal have recently been developed (2,10-12) (Figures 3 and 4); however, only preliminary data are available.

In one study, the authors evaluated a closed-loop system (O2 Flow Regulator, Dima, Italy), adjusting oxygen during exercise in COPD patients while receiving long-term oxygen therapy (10). The mean (± SD) \( \text{SpO}_2 \) was 95±2% with automated adjustment and 93±3% with manual adjustment (P=0.04). A reduction in the respiratory therapists’ workload was documented with automated adjustment compared with manual adjustment (2±0.1 min versus 5±3.7 min; P=0.005). In another study with a similar device (AccuO2, Optisat Medical, USA) set to target a \( \text{SpO}_2 \) of 90%, the mean \( \text{SpO}_2 \) was significantly different (90.7±1.9% versus 92.4±3.6% versus 92.2±4.4%) compared with traditional systems of oxygen delivery (12). In
addition, this system allowed for a reduction in oxygen consumption. The FreeO2 device (Oxynov, Canada) was validated in a preliminary study involving healthy volunteers under conditions of moderate hypoxemia (11) and in COPD patients during exercise.

These systems have the potential to decrease health care costs by minimizing the risks of hyperoxia and associated complications caused by the inadvertent administration of high-flow oxygen. In addition, these systems allow for automated oxygen weaning and remote monitoring, which may facilitate early hospital discharge following exacerbations of COPD. Such strategies have the potential to substantially decrease the related health care costs given that hospitalizations represent the main cost associated with severe exacerbations of COPD (17).

RECOMMENDATIONS FOR CLINICAL PRACTICE AND FUTURE RESEARCH

Oxygen therapy can be life-saving; however, too much of a good thing can be harmful. Given the accumulation of recent data, clinicians should titrate oxygen therapy to avoid both hypoxia and hyperoxia. Modern oxygen delivery systems may help achieve accurate oxygen delivery in the future. The potential benefits of automated oxygen titration may exist for both patients (better control of oxygenation, better monitoring) and for the health care system (reduced workload, improved monitoring with fewer adverse events, better compliance with recommendations, reduced oxygen use and early hospital discharge following exacerbations of COPD). However, additional data are required to demonstrate the safety of these systems in different settings (prehospital transportation, emergency, hospital and home care) and cost/benefits of such systems should be adequately demonstrated.

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