Supplemental oxygen: More isn’t always better

A recent study says that in certain populations, supplemental oxygen above certain levels can increase mortality.

**PRACTICE CHANGER**

Do not use liberal oxygen therapy (SpO₂ > 96%) in acutely ill adults, as it is associated with increased all-cause mortality.¹

**STRENGTH OF RECOMMENDATION**

A: Based on a systematic review and meta-analysis of 25 randomized controlled trials.


**ILLUSTRATIVE CASE**

A 60-year-old woman who is generally healthy except for a history of recurrent urinary tract infections presents to the emergency department with fever, hypotension, and altered mental status, meeting criteria for septic shock. During her resuscitation, supplemental oxygen is administered. Standard treatment calls for a minimum SpO₂ (saturation of peripheral oxygen) > 90%. What should your SpO₂ goal be?

Use of supplemental oxygen in the acute care of the critically ill adult is a common practice in pre-hospital, emergency department (ED), and hospitalized settings.²⁻³ Despite their prevalence, guidelines about appropriate oxygen concentration and target SpO₂ levels are often conflicting or vague.³⁻⁵

Excessive oxygen supplementation in acute illness may be harmful and cause increased risk of hypercapnic respiratory failure, delayed recognition of clinical deterioration, and oxygen toxicity.²⁻⁶ The perception of oxygen safety persists despite these findings, and it likely contributes to the ongoing practice of liberal oxygen supplementation in the acutely ill adult.²⁻⁷⁻⁸

**STUDY SUMMARY**

Liberal supplemental O₂ linked to increased mortality

The Improving Oxygen Therapy in Acute illness (IOTA) study was a systematic review and meta-analysis of 25 randomized controlled trials (RCTs) that compared liberal vs conservative oxygen strategies for acutely ill adults (N = 16,037; median age = 64 years; range = 28-76 years). Patients with sepsis, critical illness, stroke, trauma, myocardial infarction, or cardiac arrest, and patients who had emergency surgery were included. Studies were excluded if they involved patients who had chronic respiratory illness or psychiatric diseases, were receiving extracorporeal membrane oxygenation, were undergoing elective surgeries, were being treated with hyperbaric oxygen therapy, or were pregnant.

The outcomes studied were mortality (in-hospital, at 30 days, and at the longest follow-up) and morbidity (disability measured by the modified Rankin Scale at longest follow-up, risk of hospital-acquired pneumonia, risk of any hospital-acquired infection, and hospital length of stay).

Liberal supplemental oxygen, above an
SpO\textsubscript{2} range of 94% to 96%, increased mortality during inpatient stays (relative risk [RR] = 1.21; 95% confidence interval [CI], 1.03-1.43; N = 15,071), at 30 days (RR = 1.14; 95% CI, 1.01-1.29; N = 15,053), and at longest follow-up (RR = 1.10; 95% CI, 1.00-1.20; N = 15,754; median = 90 days; range = 14,365 days). There was no difference in morbidity outcomes between groups.

While it’s difficult to define a specific target SpO\textsubscript{2} range, the number needed to harm when using a liberal oxygen approach (SpO\textsubscript{2} > 96%) resulting in 1 death was 71 (95% CI, 37-1000).

**CHALLENGES TO IMPLEMENTATION**

Reversing the tide

Liberal oxygen administration continues to be practiced in many health care settings. The main challenges to implementing the conclusions of this study are these pervasive practices.

**WHAT’S NEW**

High-quality evidence points to the dangers of liberal O\textsubscript{2} therapy

This comprehensive meta-analysis is the first high-quality evidence to suggest that liberal use of oxygen in acutely ill adults above a specific SpO\textsubscript{2} level increases all-cause mortality. Previous small RCTs and observational studies have examined the effect of liberal oxygen only on specific presenting conditions, thus making more generalizable conclusions challenging.9-12

**CAVEATS**

Varied definitions of “liberal” and “conservative”

This review included studies with variable ranges of SpO\textsubscript{2} defined as liberal vs conservative supplementation. However, in all of these, SpO\textsubscript{2} above 96% was correlated with unfavorable outcomes.

The study excluded 2 potentially important patient groups: patients with chronic respiratory diseases and pregnant patients. Increased oxygen supplementation in patients with chronic respiratory diseases in noncritical settings has been shown to be deleterious.13-15 While this study does not address the issue of oxygen supplementation in acutely ill patients with chronic respiratory disease, use should be considered with caution. The results from this study may not be generalizable to women who are pregnant.

**ACKNOWLEDGMENT**

The PURLS Surveillance System was supported in part by Grant Number UL1RR024999 from the National Center for Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Research Resources or the National Institutes of Health.

Copyright © 2019. The Family Physicians Inquiries Network. All rights reserved.