

**Ventilation**

# Current oxygen management in mechanically ventilated patients: A prospective observational cohort study<sup>☆</sup>

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**Abstract**

**Purpose:** Oxygen (O<sub>2</sub>) is the most common therapy in mechanically ventilated patients, but targets and dose are poorly understood. We aimed to describe current O<sub>2</sub> administration and titration in such patients in an academic intensive care unit.

**Materials and Methods:** In consecutive ventilated (>48 hours) patients we prospectively obtained fraction of inspired O<sub>2</sub> (F<sub>IO<sub>2</sub></sub>), pulse oximetry O<sub>2</sub> saturation (SpO<sub>2</sub>) and arterial O<sub>2</sub> tension (PaO<sub>2</sub>) every 6 hours. We calculated the amount of excess O<sub>2</sub> delivery and the intensivists' response to hyperoxemia (SpO<sub>2</sub> >98%).

**Results:** During 358 mechanical ventilation days in 51 critically ill patients, median calculated excess O<sub>2</sub> delivery was 3472 L per patient. Patients spent most of their time with their SpO<sub>2</sub> >98% (59% [29–83]) and PaO<sub>2</sub> between 80 and 120 mm Hg (59% [38–72]). In addition, 50% of all observations showed hyperoxemia and 4% severe hyperoxemia (PaO<sub>2</sub> >202.5 mm Hg). Moreover, 71% of the calculated total excess 263,841 L of O<sub>2</sub> was delivered when the F<sub>IO<sub>2</sub></sub> was 0.3 to 0.5. When hyperoxemia occurred with an F<sub>IO<sub>2</sub></sub> between 0.3 and 0.4, for 88% of episodes, no F<sub>IO<sub>2</sub></sub> adjustments were made.

**Conclusions:** Excess O<sub>2</sub> delivery and liberal O<sub>2</sub> therapy were common in mechanically ventilated patients. Current O<sub>2</sub> therapy practice may be suboptimal and further investigations are warranted.

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**1. Introduction**

The administration of oxygen (O<sub>2</sub>) is the most widely prescribed therapy in mechanically ventilated intensive care units (ICU) patients and can be life saving. However,

excessive supplemental O<sub>2</sub> may also be injurious [1,2]. For example, a high fraction of inspired O<sub>2</sub> (F<sub>IO<sub>2</sub></sub>) may cause lung injury, induce interstitial fibrosis, atelectasis, tracheo-bronchitis, alveolar protein leakage and infiltration by neutrophils [3–5]. Systemically, O<sub>2</sub> can decrease cardiac output [5–8] and generate free radicals in various organs [9]. Clinical adverse outcomes of hyperoxemia have been also reported in patients with acute exacerbations of chronic obstructive pulmonary disease [10], after cardiac arrest [11] and in critical illness [12].

Despite the above concerns, many ICU clinicians believe that levels of F<sub>IO<sub>2</sub></sub> up to 0.4 are not harmful [13]. When

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surveyed about O<sub>2</sub> administration practice, most Australian and New Zealand intensivists were less concerned about high FIO<sub>2</sub>-induced lung injury than barotrauma [14]. However, beyond such self-reported impressions, there is little knowledge, let alone understanding, of current practice in the field of O<sub>2</sub> therapy in mechanically ventilated ICU patients. In particular, no prospective studies have yet investigated this issue. Accordingly, we conducted a prospective observational study to assess the administration of O<sub>2</sub> therapy to a cohort of mechanically ventilated patients admitted to our tertiary intensive care unit. We hypothesized that hyperoxemia would be common (>50% of time) and that adjustments to correct it would be uncommon (<20% of observations).

## 2. Methods

We prospectively screened all patients admitted to our tertiary ICU between March and June 2012. Patients were eligible if they were adult (aged 18 years or greater) and required mechanical ventilation (MV) for more than 48 hours. Patients were ineligible if they were either considered at risk for imminent death by the treating medical team or required extracorporeal membrane oxygenation. All patients received MV with an Evita 4, Evita XL (Drägerwerk AG, Lübeck, Germany) or an AVEA ventilator (CareFusion, Yorba Linda, CA). The Human Research Ethics Committee of the Austin Hospital approved this study protocol (approval no. H2011/04252) and waived the need for informed consent.

### 2.1. Data collection

Using a standardized case report form, we collected information on age, sex, reason for ICU admission (surgical and non-surgical) and Acute Physiology and Chronic Health Evaluation (APACHE) III score. We recorded MV mode, positive end-expiratory pressure (PEEP) level, ventilator-derived minute ventilation, FIO<sub>2</sub>, pulse oximetry derived O<sub>2</sub> saturation (SpO<sub>2</sub>) (Philips Healthcare, Eindhoven, The Netherlands), arterial oxygen saturation (SaO<sub>2</sub>) and PaO<sub>2</sub> as oxygenation-related variables. Simultaneously, we also collected arterial blood pH and arterial carbon dioxide tension (PaCO<sub>2</sub>). Arterial blood gas analysis was performed with ABL800 FLEX (Radiometer, Copenhagen, Denmark). We collected these data following the commencement of MV until the patient was free of MV for greater than 24 consecutive hours. We obtained these data at 4 time points — 06:00, 12:00, 18:00, and 24:00, using the measurement closest to that time point. For patients who were readmitted to ICU and required MV ≥48 hours, only the index admission was considered. Oxygenation goals for each patient were prescribed at the discretion of bedside clinicians. To avoid a Hawthorne effect, clinicians were kept strictly unaware of the study.

### 2.2. Statistical analysis

Continuous data are reported as means (SD) or medians [interquartile range], depending on the underlying data distribution. Categorical data are reported as proportions. All analysis was performed by using JMP version 8.0.2 (SAS Institute, Cary, NC). A 2-sided *P* value of .05 was considered to be statistically significant. Throughout this study, hyperoxemia was defined as SpO<sub>2</sub> >98% according to the British Thoracic Society guideline [15] and a recent review [16] that recommend target SpO<sub>2</sub> of 94% to 98% for most acutely ill patients.

We calculated the time spent in predefined bands of the variables of interest (FIO<sub>2</sub>, SpO<sub>2</sub>, and PaO<sub>2</sub>) assuming a linear trend between individual measurements, and expressing the result as a proportion of the whole duration of MV. The band was defined as follows: FIO<sub>2</sub> was divided into 8 bands of 0.1: SpO<sub>2</sub> above 92% was divided into 8 bands of 1%: PaO<sub>2</sub> was divided into 4 bands (≤60, 60-80, 80-120, <120 mm Hg).

To avoid surveillance bias, we calculated the time-weighted averages of the oxygenation-related variables. The time-weighted value was determined by calculating the mean value between consecutive time points and multiplying it by the period of time between such points [18]. The sum of such time-weighted values is then divided by the total time to obtain the time-weighted average. We calculated the time-weighted average of all data for each patient as the time-weighted average during MV (TWA<sub>MV</sub>). Similarly, we assumed the time-weighted average of 4 consecutive data sets of each day to be the time-weighted average for each 24-hour period (TWA<sub>24</sub>). We excluded days when fewer than 12 hours of data were available for the day, for example, if patient was extubated, had a brief spontaneous breathing with a T-piece circuit, did not have arterial blood gas data, had surgery, or died.

When O<sub>2</sub> was delivered to a patient at an SpO<sub>2</sub> >98% (hyperoxemia) and continued without a decrease in FIO<sub>2</sub> despite an SpO<sub>2</sub> >98% at the following set of observations, we defined such therapy as “excess O<sub>2</sub> delivery” and calculated the amount. Excess O<sub>2</sub> delivery rate for each observation was determined as minute ventilation × (FIO<sub>2</sub> – 0.21) (L/min). Their time-weighted values provided calculated amount of excess O<sub>2</sub> delivery between consecutive time points.

We performed unadjusted univariate analysis with oxygenation-related variables for comparison between groups according to hospital survival status using the  $\chi^2$  test for proportions, Student *t* test for normally distributed outcomes, and Wilcoxon rank sum test for nonparametric data. In the same way, to investigate the clinical ramifications according to hyperoxemic status, patients were classified as having “hyperoxemia” and “non-hyperoxemia” using their TWA<sub>MV</sub>-SpO<sub>2</sub> (TWA<sub>MV</sub>-related hyperoxemia and TWA<sub>MV</sub>-related non-hyperoxemia, respectively). Moreover, patients who spent >50% of their mechanical ventilation time with hyperoxemia were classified as having “persistent hyperoxemia” and those who spent ≤50% of the time with hyperoxemia as “transient hyperoxemia.” Additionally, we assessed trends over time in the variables of

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