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SELF-REPORTED ATTITUDES VERSUS ACTUAL PRACTICE OF OXYGEN THERAPY BY ICU PHYSICIANS AND NURSES

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ABSTRACT

Background
High inspiratory oxygen concentrations are frequently administered in ventilated patients in the intensive care unit (ICU) but may induce lung injury and systemic toxicity. We compared beliefs and actual clinical practice regarding oxygen therapy in critically ill patients.

Methods
In three large teaching hospitals in the Netherlands, ICU physicians and nurses were invited to complete a questionnaire about oxygen therapy. Furthermore, arterial blood gas (ABG) analysis data and ventilator settings were retrieved to assess actual oxygen practice in the same hospitals 1 year prior to the survey.

Results
In total, 59% of the 215 respondents believed that oxygen-induced lung injury is a concern. The majority of physicians and nurses stated that minimal acceptable oxygen saturation and partial arterial oxygen pressure (PaO₂) ranges were 85% to 95% and 7 to 10 kPa (52.5 to 75 mmHg), respectively. Analysis of 107,888 ABG results with concurrent ventilator settings, derived from 5,565 patient admissions, showed a median (interquartile range (IQR)) PaO₂ of 11.7 kPa (9.9 to 14.3) [87.8 mmHg], median fractions of inspired oxygen (FiO₂) of 0.4 (0.4 to 0.5), and median positive end-expiratory pressure (PEEP) of 5 (5 to 8) cm H₂O. Of all PaO₂ values, 73% were higher than the upper limit of the commonly self-reported acceptable range, and in 58% of these cases, neither FiO₂ nor PEEP levels were lowered until the next ABG sample was taken.

Conclusions
Most ICU clinicians acknowledge the potential adverse effects of prolonged exposure to hyperoxia and report a low tolerance for high oxygen levels. However, in actual clinical practice, a large proportion of their ICU patients was exposed to higher arterial oxygen levels than self-reported target ranges.
BACKGROUND

Oxygen supply during mechanical ventilation is a highly effective and uniformly used intervention to support oxygenation of mechanically ventilated patients in the intensive care unit (ICU). Although oxygen administration is a lifesaving strategy in the management of patients with respiratory insufficiency, the clinical implications of hyperoxia remain an important subject of debate (1). The controversies are triggered by a considerable number of studies showing both beneficial, harmful and/or insignificant effects of oxygen therapy on outcome in different subgroups (2-15). However, morbidity and mortality may be substantially impacted by the used threshold and depend on degree, duration, and susceptibility for hyperoxia.

The emerging laboratory evidence for the double-edged nature of oxygen (lifesaving but also potentially harmful) is compelling (16-22), but robust clinical studies and evidence-based guidelines in critically ill patients are still limited (23-26). Consequently, the attitudes and beliefs in the management of oxygen administration vary considerably in clinical practice (27, 28). In general, physicians are inclined to treat hypoxemia aggressively in order to achieve satisfactory tissue oxygenation (23, 29, 30). However, hyperoxemia is often considered acceptable, especially when applied fractions of inspired oxygen (FiO₂) are relatively low (31-33).

Given the lack of established guidelines on oxygen therapy in ICU patients, our study was designed to investigate the common beliefs and self-reported attitudes of ICU physicians and nurses on oxygenation targets and to compare this with actual treatment of ICU patients in the same hospitals. We hypothesized that the potential harmful effects of oxygen are well known and generally acknowledged, but that in real clinical practice, hyperoxia is not a major concern for ICU professionals.

METHODS

Questionnaire

An anonymous online survey was performed between June and August 2012 to elicit the self-reported behavior of ICU personnel with respect to oxygen therapy. The questionnaire was a modified and comprehensive version of previously used questionnaires from Canada and Australia/New Zealand (27, 28) and comprised multiple choice questions (see Additional file 1). The target population consisted of physicians and nurses, working in closed format, mixed medical and surgical, tertiary care ICUs of three participating hospitals, including two academic and one large teaching hospital in the Netherlands. Participants were invited by email to complete the online questionnaire. A reminder was sent once to all participants.

Patient data

Analyses were performed on data recorded between 1 April 2011 and 31 March 2012 for all patients admitted to the ICU departments of the same hospitals that participated in the questionnaire study. Anonymous encrypted data were collected from the patient data management system (PDMS) database (MetaVision, iMDsoft, Leiden, The Netherlands). According to the Dutch Medical Research Involving Human Subjects Act, there was no need for informed patient consent or approval by ethical committees, as only registries without patient identifying information were used.
Arterial blood gas (ABG) analyses and concurrent ventilator settings were extracted to retrospectively assess actual practices regarding oxygen therapy. Data from ICU admission to dismissal or death were included for analysis. Data with a partial arterial oxygen pressure (PaO$_2$) of ≤4.5 kPa or 33.8 mmHg (n=209) were excluded to prevent confounding by venous blood gas samples. Further exclusion of samples with PaO$_2$ of 4.5 to 5.0 kPa (n=146) or PaO$_2$ of 5.0 to 6.0 kPa (n=356) did not materially change our observations (data not shown). Every set of ABG data and ventilator settings was compared with the following set, as described previously (32). Prone positioning, recruitment maneuvers, and other efforts that may improve oxygenation could not be explored in this database. Clinicians’ responses to ABG results were explored by analyzing the FiO$_2$ and positive end-expiratory pressure (PEEP) adjustments in a subsample of mechanically ventilated patients when more than two ABG samples and ventilator settings were recorded. PaO$_2$ values were categorized according to the commonly self-reported acceptable range (7 to 10 kPa or 52.5 to 75 mmHg) extracted from the survey results (Fig. 1). This range is roughly consistent with oxygenation goals (7.3 to 10.7 kPa or 55 to 80 mmHg) previously suggested by the Acute Respiratory Distress Syndrome (ARDS) network (30, 34).

**Mechanical ventilation protocol**

Local guidelines, applicable during the survey and collection of ABG and ventilation data, instructed for lowest acceptable FiO$_2$ levels. FiO$_2$ levels higher than 60% should be avoided by increasing PEEP levels, instituting inverse-ratio ventilation or prone positioning. No explicit target ranges for PaO$_2$, FiO$_2$, or saturation were specified in the participating hospitals during this period.

**Statistical analysis**

All data are expressed as percentages of the total number of respondents for the particular questions, unless otherwise specified. Data are presented as means (±SD) or medians (interquartile range, IQR) depending on data distributions, unless stated otherwise. For assessing differences between physicians and nurses, ICU personnel were grouped according to their respective profession and data were analyzed using Fisher’s exact tests. ICU physicians, fellows, and residents were classified as physicians; ICU nurses and ICU nurses in training were classified as nurses.

Statistical analyses were conducted using STATA/SE 10.1 (StataCorp LP, College Station, TX, USA).

**RESULTS**

**Data derived from questionnaire**

**Respondent characteristics**

Approximately 500 potential participants were invited to complete the online questionnaire. Full or partial responses were received from 215 ICU physicians and nurses with a mean age of 40.4±10.0 years (range 24 to 62). In total, 171 (80%) respondents fully completed all questions. The group of respondents consisted of 28 (13%) critical care physicians, 15 (7%) fellows, 15 (7%) residents, 141 (66%) ICU nurses, 11 (5%) ICU nurses in training, and 5 (2%) ICU clinicians with another type of practice.
Opinions towards oxygen toxicity

The responses are listed in Table 1. Overall, 126 (59%) respondents considered oxygen induced lung injury in mechanically ventilated patients a major concern. However, the vast majority of respondents (81%) considered high tidal volumes and high inspiratory pressures as the greatest risk for lung injury in mechanically ventilated patients. No differences between physicians and nurses were detected.

Self-reported acceptance of hyperoxemia and hypoxemia

The percentages of respondents accepting various oxygenation ranges in a young to middle-aged mechanically ventilated patient with ARDS are shown in Figure 1.

For both short and longer lasting periods, the vast majority of respondents choose 7 to 10 kPa (52.5 to 75 mmHg) as the lowest acceptable PaO$_2$ range. Physicians were more tolerant towards lower PaO$_2$ limits for short duration than nurses (P<0.001).

Table 1. Questionnaire responses regarding risks assessment and management in oxygen therapy

<table>
<thead>
<tr>
<th>Question</th>
<th>Responses (% of total)</th>
<th>Physicians vs. nurses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is oxygen induced lung injury a concern when placing a patient on mechanical ventilation?</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>YES, a major concern</td>
<td>126 (59%)</td>
<td></td>
</tr>
<tr>
<td>due to the <em>high incidence</em> of injury</td>
<td>13 (6%)</td>
<td></td>
</tr>
<tr>
<td>due to the <em>severity</em> of injury</td>
<td>63 (29%)</td>
<td></td>
</tr>
<tr>
<td>due to the <em>high incidence and severity</em> of injury</td>
<td>50 (23%)</td>
<td></td>
</tr>
<tr>
<td>YES, but not a major concern</td>
<td>80 (37%)</td>
<td></td>
</tr>
<tr>
<td>NO, it is not a concern</td>
<td>9 (4%)</td>
<td></td>
</tr>
<tr>
<td>In your opinion, which one of the following two situations poses a greater threat of lung injury for mechanically ventilated patients?</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>High FiO$_2$</td>
<td>35 (16%)</td>
<td></td>
</tr>
<tr>
<td>High tidal volumes and high ventilator pressures</td>
<td>173 (81%)</td>
<td></td>
</tr>
<tr>
<td>Don’t know</td>
<td>7 (3%)</td>
<td></td>
</tr>
<tr>
<td>In situations when maximal SaO$_2$ achievable is low (±85%) or when FiO$_2$ requirements are high, do you assess indices of tissue oxygenation?</td>
<td></td>
<td>P=0.05</td>
</tr>
<tr>
<td>NO</td>
<td>91 (43%)</td>
<td></td>
</tr>
<tr>
<td>YES, lactate</td>
<td>88 (42%)</td>
<td></td>
</tr>
<tr>
<td>YES, microcirculation with OPS/SDF imaging</td>
<td>4 (2%)</td>
<td></td>
</tr>
<tr>
<td>YES, a combination of indices</td>
<td>20 (9%)</td>
<td></td>
</tr>
<tr>
<td>YES, SvO$_2$</td>
<td>6 (3%)</td>
<td></td>
</tr>
<tr>
<td>YES, other</td>
<td>2 (1%)</td>
<td></td>
</tr>
</tbody>
</table>

NS, Not significant; FiO$_2$, Fractions of inspired Oxygen; OPS, Orthogonal Polarization Spectral; SDF, Sidestream Dark Field; SaO$_2$, Arterial Oxygen Saturation; SvO$_2$, Mixed Venous Oxygen Saturation
Presented with a patient whose arterial oxygen saturation ($\text{SaO}_2$) levels are low (<85%) or $\text{FiO}_2$ requirements are high, indices of tissue oxygenation were frequently assessed (Table 1). Differences between physicians and nurses approached statistical significance ($P=0.05$), with physicians favoring lactate assessment, and nurses being less likely to demand some assessment of tissue oxygenation. Nurses in training more often favored lactate assessment than senior ICU nurses ($P=0.01$).

**Adjustment of $\text{FiO}_2$ in specific clinical cases**

The proportions of ICU clinicians adjusting $\text{FiO}_2$ levels in specified clinical cases are listed in Table 2. Observed differences by profession were mainly restricted to questions regarding patients with untreatable anemia, where physicians generally favored higher $\text{FiO}_2$ levels than nurses. Only minor differences within the clustered categories of physicians (comparison between physicians, fellows, residents) and nurses (ICU nurses, nurses in training) were observed.

**Data derived from ABG measurements and ventilator settings**

**Descriptive data**

A total of 107,888 ABG results with concurrent ventilator settings, covering 5,565 patient admissions, were retrieved and included for analysis over a 1-year period prior to the survey in three hospitals. Median interval between two consecutive ABG samples was 214 min (IQR 130 to 331), and the median number of ABG samples per patient was 7 (IQR 4 to 19). Mean $\text{PaO}_2$ was 12.9 kPa (SD 5.1) or 96.8 mmHg and median $\text{PaO}_2$ was 11.7 kPa (IQR 9.9 to 14.3) or 87.8 mmHg. Overall, in 25.3% of ABG results, $\text{PaO}_2$ was in the self-reported range (7 to 10 kPa), 1.2% was lower and 73.4% was higher than the predefined range.

**Figure 1.** Self-reported tolerance limits for short-term (15 min, open bars) and longer term (24 to 48 h, closed bars) oxygenation.

Bars represent percentage of respondents ($n=200$). The presented case is a young to middle-aged ARDS patient in the ICU requiring mechanical ventilation. Ventilator settings (e.g., PEEP, airway pressures, I:E ratio, flow ratio) are optimized with respect to the $\text{PaO}_2$/$\text{FiO}_2$ ratio and hemodynamic indices. Lung injury due to high $\text{FiO}_2$ and/or ventilator settings is minimized. There is no evidence to indicate end-organ ischemia, and hemodynamics are stable.
### Table 2. Percentages of respondents adjusting FiO2 levels in specified clinical conditions with presented levels of arterial oxygenation

<table>
<thead>
<tr>
<th>Clinical condition</th>
<th>ARDS</th>
<th>Cardiac ischemia</th>
<th>Cerebral ischemia</th>
<th>Sepsis</th>
<th>Untreatable anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>FiO2 response</td>
<td>Higher</td>
<td>Unchanged</td>
<td>Lower</td>
<td>Higher</td>
<td>Unchanged</td>
</tr>
<tr>
<td>SaO2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80-85%</td>
<td>97.4</td>
<td>2.6</td>
<td>0.0</td>
<td>100</td>
<td>0.0</td>
</tr>
<tr>
<td>85-90%</td>
<td>61.5</td>
<td>38.5</td>
<td>0.0</td>
<td>96.4</td>
<td>3.6</td>
</tr>
<tr>
<td>90-95%</td>
<td>4.1</td>
<td>78.5</td>
<td>17.4</td>
<td>42.6</td>
<td>54.9</td>
</tr>
<tr>
<td>95-100%</td>
<td>0.0</td>
<td>17.4</td>
<td>82.6</td>
<td>2.6</td>
<td>61.0</td>
</tr>
<tr>
<td>PaO2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 kPa</td>
<td>96.6</td>
<td>3.4</td>
<td>0.0</td>
<td>98.3</td>
<td>1.7</td>
</tr>
<tr>
<td>9 kPa</td>
<td>9.0</td>
<td>85.3</td>
<td>5.6</td>
<td>60.1</td>
<td>38.2</td>
</tr>
<tr>
<td>12 kPa</td>
<td>0.6</td>
<td>27.1</td>
<td>72.3</td>
<td>5.6</td>
<td>60.7</td>
</tr>
<tr>
<td>16 kPa</td>
<td>0.0</td>
<td>2.3</td>
<td>97.7</td>
<td>2.2</td>
<td>10.1</td>
</tr>
</tbody>
</table>

All clinical situations represent patients in the ICU, who have been invasively mechanically ventilated for at least 5 days, with FiO$_2$ set at 50%. ARDS, patient with acute respiratory distress syndrome and pneumonia; Cardiac ischemia, patient with signs of cardiac ischemia (ST-depressions in the anterior leads [max 3 mm]) and pneumonia; Cerebral ischemia, patient with recent cerebral ischemia and one-sided hemiplegia; Sepsis, patient with a liver abscess and sepsis; Untreatable anemia, Jehovah’s Witness with stable hemoglobin of 1.8 mmol/L after gastric bleeding. Higher, i.e. increase FiO$_2$, higher than current 50%; Unchanged, i.e. maintain FiO$_2$ at current 50%; Lower, i.e. decrease FiO$_2$, lower than current 50%.
Mechanical ventilation settings showed a mean PEEP of 6.1 cm H$_2$O (SD 4.3), and median PEEP was 5 (IQR 5 to 8). Mean FiO$_2$ was 0.45 (SD 0.14), and median FiO$_2$ was 0.40 (IQR 0.40 to 0.50). Only small differences were observed between the three participating hospitals.

**Recorded FiO$_2$ adjustments following ABG analysis**

After exclusion of spontaneously breathing and non-invasively ventilated patients, 62,875 ABG records derived from 4,264 mechanically ventilated patients were included for analysis of FiO$_2$ adjustments in response to ABG samples.

Analyzing every first registered ABG sample in the ICU, 62,222 PaO$_2$ measurements covering 3,791 patients were retrospectively categorized in predefined ranges and were followed by a recorded FiO$_2$ adjustment. The subsequently registered PaO$_2$ measurement was compared with the first registered PaO$_2$ (Table 3).

Table 4 shows that quantity, direction, and magnitude of ventilator adjustments in response to high arterial oxygen levels are considerably influenced by the level of FiO$_2$. In 58.3% of cases with PaO$_2$ higher than the upper level of the commonly self-reported acceptable oxygenation (10 kPa or 75 mmHg), neither FiO$_2$ nor PEEP levels had been lowered when the next ABG sample was taken.

**Table 3. FiO$_2$ adjustment following ABG analysis and its effects on oxygenation measured in the next ABG**

<table>
<thead>
<tr>
<th>PaO$_2$ (%) [n=107,888]</th>
<th>Adjustment of FiO$_2$ (%) [n=62,222]</th>
<th>Higher (Delta PaO$_2$)</th>
<th>Unchanged</th>
<th>Lower (Delta PaO$_2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7 kPa (1.2)</td>
<td>Higher (34.7)</td>
<td>96.6% (+5.3)</td>
<td>0.4%</td>
<td>3.0% (-0.5)</td>
</tr>
<tr>
<td></td>
<td>Unchanged (46.9)</td>
<td>87.4% (+5.6)</td>
<td>3.2%</td>
<td>9.4% (-0.6)</td>
</tr>
<tr>
<td></td>
<td>Lower (18.4)</td>
<td>95.1% (+7.9)</td>
<td>2.4%</td>
<td>2.5% (-0.9)</td>
</tr>
<tr>
<td>7–10 kPa (25.3)</td>
<td>Higher (27.9)</td>
<td>76.3% (+3.1)</td>
<td>2.7%</td>
<td>21.0% (-0.9)</td>
</tr>
<tr>
<td></td>
<td>Unchanged (56.0)</td>
<td>66.3% (+2.0)</td>
<td>4.3%</td>
<td>29.4% (-0.8)</td>
</tr>
<tr>
<td></td>
<td>Lower (16.1)</td>
<td>61.3% (+2.6)</td>
<td>3.6%</td>
<td>35.1% (-1.0)</td>
</tr>
<tr>
<td>&gt;10 kPa (73.4)</td>
<td>Higher (10.8)</td>
<td>48.6% (+4.6)</td>
<td>2.1%</td>
<td>49.3% (-3.1)</td>
</tr>
<tr>
<td></td>
<td>Unchanged (62.0)</td>
<td>44.7% (+2.1)</td>
<td>3.1%</td>
<td>52.2% (-2.3)</td>
</tr>
<tr>
<td></td>
<td>Lower (27.2)</td>
<td>23.5% (+2.4)</td>
<td>1.7%</td>
<td>74.8% (-4.6)</td>
</tr>
<tr>
<td>Total (100)</td>
<td>–</td>
<td>46.3% (+2.6)</td>
<td>2.7%</td>
<td>51.0% (-2.9)</td>
</tr>
</tbody>
</table>

Data presented as percentages of total and irrespective of adjustment of other ventilator settings (e.g. PEEP, I:E ratio). Delta, mean difference between two successive ABG samples; PaO$_2$, any recorded PaO$_2$ stratified by self-reported ranges; Successful PaO$_2$, PaO$_2$ from successfully registered ABG sample; Higher, i.e. increased FiO$_2$ (column 2) or PaO$_2$ (column 3), higher than previous level; Unchanged, i.e. FiO$_2$ or PaO$_2$ equal to previous level; Lower, i.e. decreased FiO$_2$ or PaO$_2$ lower than previous level. A total of 62,222 PaO$_2$ measurements from 3,791 patients (57.7% of all 107,888 ABG samples) in the database is followed by an adjustment of ventilator settings, and 98.2% of PO$_2$ measurements is followed by a successive PO$_2$ measurement (n=61,073) in the same patient when adjustment of FiO$_2$ is also measured.
### Table 4. Adjustment of mechanical ventilation settings following ABG analysis.

<table>
<thead>
<tr>
<th>PaO₂ range (kPa)</th>
<th>FiO₂ 25-40% (n=37,172)</th>
<th>FiO₂ 40-60% (n=23,466)</th>
<th>FiO₂ 60-80% (n=4,318)</th>
<th>FiO₂ 80-100% (n=2,041)</th>
<th>Total (n=68,222)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO₂</td>
<td>13.4 (4.1)</td>
<td>12.6 (5.2)</td>
<td>12.3 (6.6)</td>
<td>16.0 (13.7)</td>
<td>13.1 (5.2)</td>
</tr>
<tr>
<td>SpO₂</td>
<td>98.0 (2.9)</td>
<td>96.5 (3.8)</td>
<td>94.3 (6.3)</td>
<td>89.7 (12.5)</td>
<td>96.9 (4.6)</td>
</tr>
<tr>
<td>PEEP</td>
<td>5.6 (3.4)</td>
<td>7.3 (4.4)</td>
<td>9.1 (5.6)</td>
<td>9.0 (6.3)</td>
<td>6.5 (4.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PaO₂ range (kPa)</th>
<th>Delta FiO₂ (%)</th>
<th>Delta PEEP (cm H₂O)</th>
<th>No decrease in FiO₂ or PEEP (%)</th>
<th>Delta FiO₂ (%)</th>
<th>Delta PEEP (cm H₂O)</th>
<th>No decrease in FiO₂ or PEEP (%)</th>
<th>Delta FiO₂ (%)</th>
<th>Delta PEEP (cm H₂O)</th>
<th>No decrease in FiO₂ or PEEP (%)</th>
<th>Delta FiO₂ (%)</th>
<th>Delta PEEP (cm H₂O)</th>
<th>No decrease in FiO₂ or PEEP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7</td>
<td>+6.1 (13.8)</td>
<td>+0.3 (3.2)</td>
<td>87.6</td>
<td>+5.4 (13.2)</td>
<td>+0.7 (3.7)</td>
<td>81.3</td>
<td>+2.0 (14.5)</td>
<td>+0.6 (6.0)</td>
<td>86.3</td>
<td>-7.0 (16.8)</td>
<td>+1.0 (6.7)</td>
<td>76.9</td>
</tr>
<tr>
<td>7-10</td>
<td>+2.6 (6.7)</td>
<td>+0.1 (3.1)</td>
<td>81.9</td>
<td>+1.6 (7.3)</td>
<td>+0.2 (4.0)</td>
<td>80.3</td>
<td>-0.2 (9.4)</td>
<td>+0.3 (5.2)</td>
<td>80.8</td>
<td>-6.7 (14.8)</td>
<td>+0.1 (5.9)</td>
<td>76.5</td>
</tr>
<tr>
<td>10-15</td>
<td>+0.6 (4.9)</td>
<td>-0.2 (2.7)</td>
<td>72.9</td>
<td>-1.5 (6.6)</td>
<td>-0.2 (3.8)</td>
<td>48.2</td>
<td>-5.2 (9.2)</td>
<td>+0.1 (4.9)</td>
<td>33.7</td>
<td>-15.6 (19.2)</td>
<td>+0.4 (5.7)</td>
<td>31.1</td>
</tr>
<tr>
<td>15-20</td>
<td>-0.3 (5.1)</td>
<td>-0.3 (2.7)</td>
<td>65.0</td>
<td>-4.8 (7.2)</td>
<td>-0.3 (3.3)</td>
<td>25.1</td>
<td>-11.2 (11.4)</td>
<td>+0.1 (4.7)</td>
<td>13.5</td>
<td>-20.4 (20.5)</td>
<td>+0.0 (4.7)</td>
<td>23.6</td>
</tr>
<tr>
<td>20-25</td>
<td>-1.2 (6.4)</td>
<td>-0.2 (2.4)</td>
<td>54.2</td>
<td>-6.1 (9.0)</td>
<td>-0.4 (3.0)</td>
<td>22.1</td>
<td>-12.7 (12.4)</td>
<td>-0.4 (5.3)</td>
<td>11.8</td>
<td>-25.9 (21.7)</td>
<td>-0.1 (4.8)</td>
<td>21.3</td>
</tr>
<tr>
<td>25-30</td>
<td>-1.6 (7.0)</td>
<td>-0.4 (2.8)</td>
<td>51.6</td>
<td>-7.2 (9.6)</td>
<td>-0.3 (2.7)</td>
<td>18.8</td>
<td>-19.0 (12.1)</td>
<td>-0.4 (3.8)</td>
<td>9.2</td>
<td>-25.3 (21.6)</td>
<td>-0.1 (4.8)</td>
<td>22.9</td>
</tr>
<tr>
<td>&gt;30</td>
<td>-1.0 (6.6)</td>
<td>-0.4 (4.0)</td>
<td>69.8</td>
<td>-3.5 (9.6)</td>
<td>-0.4 (4.5)</td>
<td>43.0</td>
<td>-15.4 (15.8)</td>
<td>+0.3 (5.7)</td>
<td>24.8</td>
<td>-33.6 (23.2)</td>
<td>-0.4 (4.0)</td>
<td>14.3</td>
</tr>
</tbody>
</table>

Data are means (±SD), unless stated otherwise. Delta, difference between two successive ABG samples.
DISCUSSION

In accordance with accumulating laboratory evidence for the toxic effects of oxygen in pulmonary injury (1, 35-38), the majority of surveyed ICU physicians and nurses consider prolonged hyperoxic exposure to be associated with an increased risk for lung injury, although a lower risk than high tidal volumes and inspiratory pressures. In contrast, in actual clinical practice, the majority of PaO₂ values recorded in ICU patients are higher than recommended targets under comparable conditions and are generally accepted by ICU physicians and nurses without adjustment of ventilator settings.

Compared with previous studies from other countries, more respondents identified oxygen toxicity as a major threat to lung injury in ICU patients (59% compared with 26% and 51% in studies from Australia and Canada, respectively) (27, 28). Similar proportions of respondents considered high inspiratory oxygen concentrations a more important risk than high tidal volumes or inspiratory pressures, and a similar heterogeneity in self-reported attitudes regarding oxygen therapy was observed (27, 28, 39). The current results show generally higher minimum allowable SaO₂ ranges than data from Canadian intensivists (28), which may indicate that clinicians’ beliefs have changed over the last decade or it may merely reflect geographical differences in oxygen therapy.

It appears that clinicians’ opinions regarding optimal oxygen therapy are more variable in case SaO₂ is presented compared to PaO₂ as marker of oxygenation. For PaO₂, the vast majority of clinicians choose 7 to 10 kPa (52.5 to 75mmHg), whereas the preferred targets for saturation varied between 85% and 95%. Assuming that oxygenation targets should be in line with the best evidence in available guidelines, these preferred ranges may be triggered by recommendations and protocols providing comparable PaO₂ targets (30, 40). However, caution is urged when interpreting pulse oximetry to differentiate between hyperoxemia and normoxia. Saturation levels above 95% require special attention, since the corresponding PaO₂ levels usually cover a wide range and may substantially exceed target levels (24, 41).

According to the results from our questionnaire, the vast majority of respondents stated they would lower FiO₂ levels if PaO₂ was higher than 12 kPa (90 mmHg) or SaO₂ was higher than 95% in ARDS patients. The proportion of respondents that would lower FiO₂ is much lower if patients were presented with sepsis, cardiac and cerebral ischemia, or untreatable anemia. Unfortunately, we do not know whether respondents believe that oxygen is specifically harmful in patients with pre-existing acute lung injury or that higher oxygen levels are considered desirable in patients with ischemia or anemia. The latter hypothesis appears plausible, even though hyperoxemia has been reported to induce important vasoconstriction, which may lead to a paradoxical decrease in oxygen delivery (4, 42).

The self-reported low tolerance for higher PaO₂ or SaO₂ than target levels appears to be in contrast with actual treatment of patients in the same three ICUs where the survey was conducted. Neither FiO₂ nor PEEP was changed in the majority of cases when PaO₂ was higher than 15 kPa (112.5 mmHg) and FiO₂ was 40% or lower. In cases when FiO₂ was 40% to 100%, ventilator settings were adjusted more often, but even in these circumstances, hyperoxemia was accepted in approximately 20%. Considering the absence of definitive guidelines and robust controlled clinical evidence, this behavior in itself may still be justifiable (43). However, the contrast between self-reported attitudes...
towards oxygen therapy on the one hand and actual treatment by the same healthcare workers on the other hand is striking.

The findings about oxygenation in ICU patients are consistent with previous findings from single center studies, showing that hyperoxemia was frequently present in mechanically ventilated patients and seldom led to adjustment of ventilator settings (31, 32). Clinicians may have specific reasons not to adjust ventilator settings when PaO₂ levels are higher than the target range. Indeed, we identified a considerable number of cases in which a presumed inadequate adjustment ultimately proved reasonable in the subsequent ABG sample (e.g., high PaO₂ followed by an increase in FiO₂ but resulting in a lower PaO₂). These cases may reflect scenarios in which clinicians anticipate deterioration in oxygenation or otherwise consider PaO₂ values as erroneous (e.g., arguably high PaO₂ – see Table 4, row PaO₂ > 30) or not representative for the current situation of a patient. Alternatively, it may be argued that hypoxemia harbors greater inherent hazards than hyperoxemia (3).

The differences between self-reported attitudes and actual treatment of patients should be interpreted with caution. First, the cases presented to the respondents included only limited details and do not reflect the complexity of clinical situations in daily practice. Further, we presented SaO₂ and PaO₂ categorized in ranges that were arbitrarily chosen. This may have influenced interpretation of the hypothetical cases. Second, ICU clinicians may have given more favorable responses in the online questionnaire due to social desirability and attention bias, although this is less likely as anonymous evaluation was secured. Third, the respondents were asked for the minimum allowable range in a specific ARDS case vignette, which may not reflect their beliefs regarding oxygen therapy in general. In the analysis of actually achieved oxygenation, we studied all patients independent of admission diagnosis. Also, response rates for the survey were relatively modest. However, the profession distribution in the group of respondents closely reflects a typical staff constitution in a general ICU in the Netherlands, which reduces the chance of sampling bias. In the Dutch clinical setting where respiratory therapists are not available, it is often the bedside nurse that responds first to changes in oxygenation. Therefore, the opinions of ICU nurses about oxygen therapy are important in the actual care of critically ill patients (39). Finally, some ABG samples, taken shortly after ICU arrival, may reflect oxygen therapy initiated on the operating room and influenced by anesthesiological ventilation strategies. However, successive ventilator adjustments were all recorded on the ICU and were supervised by critical care physicians. Therefore, high PaO₂ values in the direct postoperative period are not a plausible explanation for the low proportion of hyperoxic ABG samples not followed by adaptation of the ventilator settings.

Strengths of this study include the large sample of questionnaire responses and the extensive set of ABG data, derived from the same ICUs where the questionnaire was conducted. This facilitated a comprehensive comparison between self-reported attitudes and actual practices of oxygen therapy for both physicians and nurses. Further, the design of the present questionnaire closely resembles previous surveys from Canada and Australia, thereby exploring geographical patterns and trends in time concerning oxygen therapy. Our study extends these data as we have assessed objective data in our analysis including the successively measured PaO₂ after FiO₂ adjustment. This
allows further estimation of the effects of recorded FiO₂ adjustments in comparison with previous data (32).

**CONCLUSIONS**

This study shows that most clinicians acknowledge the potential adverse effects of prolonged exposure to hyperoxia, in accordance with emerging evidence for pulmonary toxicity and increased risk of poor outcome in both humans and animals caused by excessive oxygenation (2, 4, 6, 8, 16, 18, 20, 35, 44). However, objective data also suggest that clinicians did not consistently accommodate this conception in actual clinical practice and a large proportion of patients was exposed to arterial oxygen levels higher than self-reported as acceptable by nurses and physicians. Additional education, feedback, and implementation strategies, aimed at careful titration of oxygen, may therefore be an effective approach for strict adherence to oxygenation targets (45). Studies on the effects of different target ranges for PaO₂ on clinically relevant endpoints are needed to guide ICU professionals on how much oxygen should be administered to their patients.

**LIST OF ABBREVIATIONS**

ABG, arterial blood gas; FiO₂, fractions of inspired oxygen; ICU, intensive care unit; PaO₂, partial arterial oxygen pressure; PDMS, patient data management system; PEEP, positive end-expiratory pressure; SaO₂, arterial oxygen saturation
REFERENCES


