Efficiency of goal-directed oxygen delivery in ICU patients

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Abstract

Background: Current clinical practice guidelines promote a goal-directed approach for oxygen delivery with respect to SpO₂ objectives. We evaluated the efficiency of a strategy based on goal-directed O₂ delivery in the ICU.

Methods: A group of 30 patients (Group 1) with a proven history of chronic obstructive pulmonary disease suffering from acute hypercarbic exacerbation was compared to 2 other groups of patients admitted for acute respiratory failure with no history of pulmonary disease: 30 patients requiring oxygen supply and/or non-invasive ventilation (Group 2) and 30 requiring invasive ventilation (Group 3). The delivery of oxygen was based on SpO₂ measurement: 88−94% for Group 1 and 90−96% for others. The time spent with an SpO₂ below, within and above the prescribed limits was collected.

Results: The mean time spent within the prescribed range was for Groups 1, 2 and 3, respectively as follows: 61.9% [60.5−63.2], 63.7% [62.3−65] and 56.4% [55.3−57.6] (P < 0.001 for each group). A history of chronic obstructive pulmonary disease was not correlated with better results (P = 0.11), while invasive ventilation was related to the time spent out of the prescribed range (P < 0.001; OR 1.3 [1.22−1.28]) especially in hyperoxaemia (40.7% [39.6−41.8] P < 0.001). Efficiency seems unrelated to nursing workload or night team exhaustion (r = −0.09, P = 0.77).

Conclusions: Goal-directed oxygen delivery based on SpO₂ objectives in ICU patients ensures that in only approximately 64% of the time, SpO₂ stays within the prescribed range.

Key words: hyperoxaemia; hypoxaemia; pulse oximetry; oxygen therapy; mechanical ventilation; nurse protocol; goal-oriented therapy

Current scientific opinion emphasizes titration of oxygen delivery to avoid the side-effects of both hypoxaemia and hyperoxaemia in emergency and intensive care units [1−4]. Indeed, the risks related to hypoxaemia are widely known. However, complications related to excessive oxygenation preoccupy practitioners less often [5]. In acute myocardial infarction, high oxygen concentrations result in the reduction of coronary blood flow as a consequence of a vasoconstriction and may lead to an increase in infarct size and a greater mortality [6, 7]. In brain strokes recent guidelines emphasize that oxygen should only be used in strokes in the presence of hypoxaemia for the same reasons [8]. In post-resuscitation adult patients, both out of hospital and in the ICU, hyperoxia seems to be linked to a worse outcome in terms of one’s neurological state and risk of death [9, 10]. Neonatal Resuscitation Program guidelines recommend initial resuscitation of asphyxiated term newborns with 21% oxygen due to higher neonatal mortality with high flow oxygen [11]. In patients with chronic obstructive pulmonary disease (COPD), the hypercarbic effect of hyperoxia has been widely known for over 50 years [12, 13]. Further studies showed that oxygen therapy in the prehospital setting was very often excessive and lead to an increase in adverse outcomes including non-invasive and invasive ventilation uses, prolonged ICU stay and a higher mortality rate [1, 14].
Since 1967, Nash et al. [15] reported that prolonged high FiO$_2$ in mechanically ventilated patients worsens gas exchange and produces tracheobronchitis, interstitial oedema, alveolar protein leakage, infiltration by neutrophils, fibrosis and atelectasis [16]. Protective ventilation should also limit oxygen delivery to the required amount of oxygen; no more no less [17]. However, the efficiency of O$_2$ delivery prescription based on goal-directed pulse oximetry is not known.

The aim of this study was as follows: the evaluation of the efficiency of prescribed oximetry-guided oxygen delivery in the ICU; the identification of differences, if any, between COPD/non COPD patients and a mechanical ventilation/non-mechanical ventilation situation; as well as the identification of reasons for non-optimal adjustments.

METHODS

The study protocol was approved by the Institutional Review Board of the French Learned. Society for Respiratory Medicine — Société de Pneumologie de Langue Française (N°2014-041).

We performed a retrospective review of medical records from patients admitted to our ICU between September 2012 and January 2013. Our unit is a 24-bed mixed ICU in a second-level hospital with 1500 to 1700 admissions per year. We selected three groups of patients:

- Group 1: A history of COPD, hospitalized in the ICU for acute hypercapnic exacerbation and treated with oxygen alone or oxygen plus non-invasive ventilation (NIV).
- Group 2: No history of COPD or prior/actual status of smoker, receiving oxygen or NIV for acute respiratory failure.
- Group 3: No history of COPD, treated with mechanical ventilation through a tracheal tube whatever the indication.

The following patients were excluded: those without a blood gas sample within the 2 first hours of admittance; with an ICU stay less than 48 hours; aged under 18; enrolled in another research trial; without known pulmonary or smoker status; or with treatment limitation status. We included patients admitted to our ICU from the emergency department of our institution or from an external medical team. For Group 3, patients had to be intubated before admission. Patients suffering carbon monoxide poisoning or an acute event in sickle cell disease were excluded because of the probable need for supranormal oxygen rates. In addition, black-skinned people were not included because of the described inaccuracy between pulse and arterial oximetry [18]. In addition, 30 patients in Group 1 were identified and subsequently compared to 60 patients admitted for acute respiratory failure with no history of chronic pulmonary disease randomly selected during the same period.

Blood gas samples at admission, the number of modifications in oxygen dose delivery (i.e. FiO$_2$ or O$_2$ flow) during ICU stay, prognostic severity scores and basic epidemiologic data were collected anonymously. Pulse oximetry, heart rate and mean arterial pressure (measured invasively or not) were collected every 30 minutes for all of the included patients using a BeneView T8® Monitor (Mindray®, Shenzhen, China). In our ICU, pulse oximetry objectives are prescribed daily by physicians with a target range of 88–94% in COPD patients (corresponding to Study Group 1) and 90–96% in others (Groups 2 and 3). The time spent in each range was estimated by the following ratio: the number of SpO$_2$ measurements in the chosen range/total number of SpO$_2$ measurements. Likewise, emergency hospital or prehospital supplies always use pulse oximetry from varied but validated devices. Modifications are regularly made by physicians or nurses on the basis of pulse oximetry.

It is worth noticing that nurses and physicians were not informed of the study and all the data were collected directly from a computerized database, avoiding observational bias, thereby better reflecting real clinical practice. Although nurses are not aware of the hyperoxaemia question during their initial education, they regularly receive upgrade training in our ICU. For physicians, this knowledge depends on their initial and continuing education. This is sometimes emphasized during their medical rounds.

We evaluated the potential role of the nurse workload that would prevent optimal adaptation in oxygen supply. For Group 1, we compared the time spent in the different ranges of SpO$_2$ (below 88%, within 88–94% and above 94%) between 2 periods of a different patient/nurse index. In our ICU, the patient/nurse ratio is 2.7 from 8AM to 8PM (day team) and 4 from 8PM to 8AM (night team) while nurses work on a twelve-hour shift basis.

STATISTICAL ANALYSIS

The patient’s characteristics on admission and during their ICU stay were compared using the chi-square test for qualitative data and the Mann-Whitney test for quantitative data. Comparisons of the number of SpO$_2$ measurements for each group, both within and out of the range, were performed with the chi-square test. Linear regression was performed to search for a correlation between the time of day and the SpO$_2$ range. Calculations were performed with XLSTAT® Software (Microsoft Corporation®, Redmond, USA). Moreover, we performed a randomised patients’ sampling for Groups 2 and 3, stratified based on age, in order to equilibrate the number of cases in each group, using the same XLSTAT® software. Values are n (%), means ± SD [95% confidence interval], median [inter-quartile range] or percentages [95% confidence interval]. A P value of < 0.05 was considered to be significant.
RESULTS

During the study period 726 patients were admitted in the Department of Intensive Care Medicine (Fig. 1). Of these, 471 patients were excluded because of a lack of certainty regarding their pulmonary status (i.e. unknown or unreliable antecedents, past or present smoker status without a pulmonary function test), because of their origin from another hospital ward and due to the absence of oxygen therapy. In addition, 30, 163 and 62 patients achieved the requirements for inclusion into Groups 1, 2 and 3, respectively.

ADMISSION RESULTS

Patients’ characteristics at ICU admission are summarized in Tables 1 and 2. There was no difference in age or sex ratio among the three study groups. As expected, patients in Group 3 were more severe than others regarding SAPS II and SOFA scores ($P < 0.001$ within both groups) because of the weight of invasive ventilation and associated conditions (coma, emergency surgery). By definition of the groups, patients in Group 1 had more hypercapnic acidosis than other groups ($P < 0.001$ for $\text{PaCO}_2$ and bicarbonate). Although there was no statistically significant difference in pH between COPD-patients and invasive ventilation-patients ($P = 0.22$), the arterial amount of bicarbonate was lower in the third group resulting in metabolic acidosis ($\text{HCO}_3^- 35.5 \pm 9.6 \text{ mmol L}^{-1}$ in Group 1 versus $20.5 \pm 7.9 \text{ mmol L}^{-1}$ in Group 3, $P < 0.001$).

After emergency care all groups at ICU-admission presented a median saturation beyond the required ranges, respectively 96%, 98% and 99% for Groups 1, 2 and 3 (Table 1). As expected, admission oximetries were significantly lower in Group 1 than in Groups 2 or 3 ($P < 0.001$).

DURING ICU STAY

These results are presented in Table 3. Heart rate and mean arterial pressure were similar within the three groups. For each group, the mean saturation was within the prescribed range. As expected, the values were significantly lower in Group 1 compared to Groups 2 and 3 (92.8% ± 3.4, 94.2% ± 3.9 and 95.6% ± 3, respectively; $P < 0.001$). The group treated with mechanical ventilation (Group 3) had the highest oxygenation.

We collected 5,156 measures in Group 1, 4,721 in Group 2 and 7,424 in Group 3. The time spent below, within and above the prescribed range of $\text{SpO}_2$ for each group is presented in Figure 2. The time spent within the prescribed range is only 61.9% [95% CI 60.5−63.2%], 63.7% [62.3−65%] and 56.4% [55.3−57.6%], for Groups 1, 2 and 3, respectively. If the time spent below the objective was always less than 10%, the time above the objective was considered important with 32% [95% CI 30.7−33.3%] for Group 1, 27.6% [95% CI 26.3−28.9%] for Group 2 and even 40.7% [95% CI 39.6−41.8%] for Group 3 ($P < 0.001$) [Unclear meaning of sentence]. The overall distributions of time spent within the different saturation range (in, below or above) within
Table 1. Patients’ characteristics at admission. Data are expressed: n (%); median [inter-quartile range]; mean ± SD (median)

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>21 (70)</td>
<td>16 (53.3)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>70 [64–80]</td>
<td>78 [52–82]</td>
</tr>
<tr>
<td>Pulse or arterial oximetry (%)</td>
<td>95.2 ± 3.7 (96)</td>
<td>97.3 ± 2.3 (98)*</td>
</tr>
<tr>
<td>Arterial PCO₂ (mm Hg)</td>
<td>75.8 ± 23 (72)</td>
<td>39.4 ± 14.6 (38)**</td>
</tr>
<tr>
<td>pH</td>
<td>7.27 ± 0.07 (7.28)</td>
<td>7.39 ± 0.11 (7.42)**</td>
</tr>
<tr>
<td>Arterial HCO₃ (mmol L⁻¹)</td>
<td>35.5 ± 9.6 (33.1)</td>
<td>23.4 ± 6.8 (25.1)**</td>
</tr>
</tbody>
</table>

*P < 0.05 vs. Group 1; **P < 0.001 vs. Group 1; †P < 0.05 vs. Group 2; ††P < 0.001 vs. Group 2; SAPS II — Simplified Acute Physiology Score II; SOFA — Sequential Organ Failure Assessment score

Table 2. Patients’ admission patterns. Data are expressed: n (%)

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hypercarbic decompensation of COPD</td>
<td>30 (100)</td>
<td>10 (36.7)</td>
</tr>
<tr>
<td>Infectious hypoxemic pneumopathy</td>
<td>10 (36.7)</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Septic shock</td>
<td>5 (16.7)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>2 (6.7)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Voluntary drug intoxication</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>2 (6.7)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Polytrauma</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Acute liver failure</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>9 (30)</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Peritonitis</td>
<td>5 (16.7)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Acute pulmonary cardiogenic oedema</td>
<td>3 (10)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Infectious hypoxemic pneumopathy</td>
<td>2 (6.7)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Voluntary drug intoxication</td>
<td>2 (6.7)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Tetanus</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Blunt chest trauma</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Status epilepticus</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
</tbody>
</table>
| COPD — chronic obstructive pulmonary disease

Table 3. Patients’ characteristics during ICU stay. Data are expressed: mean ± SD (median)

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (min⁻¹)</td>
<td>86.2 ± 15.9 (85)</td>
<td>85.7 ± 18.3 (85)</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>84.2 ± 17.4 (81)</td>
<td>83.4 ± 16.3 (82)</td>
</tr>
<tr>
<td>Respiratory rate (min⁻¹)</td>
<td>20.8 ± 6.2 (20)</td>
<td>20 ± 5.8 (19)*</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>92.8 ± 3.4 (93)</td>
<td>94.2 ± 3.9 (95)*</td>
</tr>
<tr>
<td>Daily modifications in O₂ support (n)</td>
<td>4.1 ± 2 (3.9)</td>
<td>1.53 ± 1.1 (1.3)*</td>
</tr>
</tbody>
</table>

*P < 0.001 vs. Group 1; †P < 0.001 vs. Group 2
the three groups were statistically different ($P < 0.001$), especially with Group 3 where there was a clear trend towards hyperoxygenation. The frequency of daily modification in $O_2$ support was broadly higher in Group 1 than in the others ($4.1 \pm 2$ times per day for Group 1 vs. $1.53 \pm 1.1$ and $1.09 \pm 0.55$ in Groups 2 and 3) with $P < 0.001$ between Group 1 and Groups 2 or 3.

Indeed, when comparing times spent within and out of the prescribed range, invasive ventilation appears to be a risk factor for out-of-range saturation ($P < 0.001$; OR 1.3 [95% CI 1.22–1.38]). In contrast, COPD status does not appear to be associated with time spent within and out of the prescribed range ($P = 0.11$; OR 0.9 [0.8–1]).

A comparison of oximetry distributions between the day team (low patient/nurse ratio) and night team (high ratio) is reported in Figure 3. There is a significant difference between the day period and the night period: for the day period — $SpO_2$ 92.6% ± 3.5 [92.5–92.7] with time spent below, in and above the range at 7.3%, 62.5% and 30.2%, respectively; for the night period — $SpO_2$ 93% ± 3.3 [92.9–93.1] with time spent below, in and above the range at 4.9%, 61.3% and 33.8%, respectively ($P < 0.001$). When we divide each 12-hour period into 6-hour periods the only statistically significant difference remains between the fourth period (2AM to 8AM) and the others ($P < 0.05$). It shows that for 6-hour periods in which there is a different patient/nurse ratio, prescription adherence does not vary, except in the fourth period of "deep night". Thus, this is probably not a result of an increased nurse workload due to a lower patient/nurse ratio. In the fourth period, there is no statistical correlation between the time during this period of night and the mean oxygen saturation of patients ($r = −0.09$; $P = 0.77$). However, this test does not seem significant enough to invalidate the role of increasing tiredness linked to working through the night. Although, performance tests may be more accurate, this period with fewer nurses and less medical support remains critical.

**DISCUSSION**

Current guidelines support oxygen delivery titration both in hospital or prehospital emergency units and in the ICU [1, 5, 19]. In our study, emergency hospital and prehospital teams to deliver more oxygen supplementation than recommended [3].

During their ICU stay, patients receiving oxygen supply appear mostly within the prescribed saturation range, but not more than 55 to 62% of the time despite large objective intervals. A history of COPD with acute exacerbation does not enhance the trend to stay within the range. Furthermore, invasive ventilation is associated with out-of-range status, especially in hyperoxia. The nurse workload linked to the patient/nurse ratio does not appear to be responsible for prescription violations. Moreover, there is no evidence in our study whether a higher out-of-range time during the second part of the nightshift can be related or not to staff exhaustion. One explanation could be that oxygen delivery is adjusted by nurses and physicians, knowing that in the fourth period physicians are less present than in others. This may explain the statistical difference between periods 3 and 4. Searching for differences in the rate of oxygen modifications by nurses and physicians within these periods may answer this question. Unfortunately, our study was not designed to evaluate such a hypothesis.

Another possible explanation could be the “more is better” culture in oxygen supplementation that may not lead to decreased gas delivery for patients’ quiet and sleeping time, associated with the idea that hyperoxia is more “comfortable” or less harmful than hypoxaemia and even less harmful than normoxia in mechanically ventilated patients. Indeed, some nurses questioned on these findings brought up patients’ but also the medical teams’ comfort and security. Supplemental oxygen is regarded as safe and, because of a fear of giving too little, there has been almost no concern about giving too much. This has been already reported and seems to mainly affect invasively ventilated patients who, however, are the most severely affected patients regarding severity scores. Indeed, a Dutch study found that $PaO_2 > 120$ mm Hg in blood gas tests led to decreased $FiO_2$ in only 25%
of cases if FiO2 ≤ 0.4, advocating the authors to set up a protocol-driven titration [5]. Suzuki et al. [20] examined 358 mechanical ventilation days in 51 ICU patients and found that half of all observations were judged as hyperoxic (i.e. SpO2 > 98%).

Moreover, Rachmale et al. [2] showed that 74% of mechanically ventilated patients were exposed to excessive FiO2 which was correlated with a worse oxygenation index in a dose-response manner. However, their definition of excessive FiO2 was FiO2 > 0.5 despite SpO2 > 92%; while exposure was considered appropriate if SpO2 > 92% with FiO2 < 0.5 or any FiO2 with SpO2 < 92%. PaO2 may be up to 200 mm Hg with an FiO2 < 0.5 (e.g. a PaO2/FiO2 ratio above 400 in a normal lung). In addition, the association between a worsened oxygen index and a high FiO2 may not be necessarily due to direct toxicity but maybe atelectasis [21].

Pulse oximetry devices are available in all French emergency units even in out-of-hospital teams thanks to medicalized French prehospital care. However, emergency care is often undertaken in poor conditions. Optimal oxygen delivery is sometimes not possible in often unstable patients. We also have to emphasize that Continuing Medical Education was, for a long time ago, not mandatory in our country.

Although nurses are not made aware of the hyperoxaemia question during their education, in our ICU they receive upgrade training each year. For physicians, the concept of oxygen titration is rather new. This has to be regularly emphasized in order to overcome the usual practices. These results have led us to advocate for better Continuing Medical Education which is now mandatory for physicians (but not regarding compulsory subjects) but still not for nurses. However, it is not obvious that educational enhancement would be sufficient to improve our results enough. Indeed, patients' needs for oxygen widely vary during the day and in favour of different intercurrent events. Manual correction of these fluctuations is a really time-consuming procedure while spending 100% of one's time monitoring the required oxygen saturation seems far from possible without an automatically controlled machine. Thus, automated closed-loop systems for oxygen flow delivery have been developed both in spontaneously breathing patients [22–24] and those mechanically ventilated [25] in adult or paediatric settings [26].

Although pilot studies seem promising with a reduction in hypoxia and hyperoxia periods, clinical trials need to be performed [22–24, 26]. One major limitation of these devices is the accuracy of pulse oximetry. Patients in shock with peripheral hypoperfusion, black-skinned people, and frequent signal disruptions are known for displaying inaccurate measurements [2, 18]. Moreover, electronic algorithms should take care of the use of a specific alarm. Another risk, partially avoided with the use of a specific alarm, could be a reduction in the attentiveness of caregivers and their delayed recognition of changes in respiratory function.

This study has several limitations. First, it is an open and retrospective trial. However nurses and physicians were not informed of the study and all the data were collected directly from a computerized database, avoiding “study effect” with results being too good. In a prospective non-blind study, results could be better but probably less applicable to a period without investigation where care practitioners are less careful. Although patients in Group 1 were consecutive entries in the ICU, patients in the other groups were randomly selected in the same period to reach 30 patients in each group. As we did not include all the consecutive patients in the statistical analysis, it is not possible to generalize the results for all ICU patients.

This study was performed in a polyvalent ICU of a second level [Unclear meaning] hospital while the results could have been different in other structures, perhaps according to patient/nurse index, staff education, patients' pathologies or expertise in respiratory care. One may also criticize the saturation ranges prescribed. General consensus statements are lacking and there is no evidence of a benefit for levels of saturation up to 96%. Likewise, there is no proven deleterious effect of saturation as low as 90% for non-COPD patients and 88% for COPD patients. In any case, FiO2 setting in ARDS ventilation is based on SpO2 objectives from 88 to 95% [17]. Here, prescribed saturation ranges were rather large (6 points between 88% and 94% or between 90% and 96%). Although this recommended target is different or smaller in some publications (88−92%, 90−94%, 94−96%) [1–3, 5, 9, 14], we consider that the accuracy of pulse oximetry is described as SpO2−SaO2 = 0% ± 2% in an interval of (SaO2 + SpO2)/2 between 88% and 100% [27]. Therefore, restricting the range would artificially lead to more patients being out of the good interval with, potentially, no real clinical threat.

Current guidelines promote reasoned reasonable oxygen delivery based on titration to reach a window of safe SpO2, probably between 88–90% to 94–96%. If mechanisms and thresholds of oxygen toxicity are still questionable, the futility of over-supplementation must lead to this practice. However, the efficiency of oxygen delivery based on prescribed objectives in ICU patients, manually performed by nurses and physicians, is disappointing with, at best, 64% of the time spent at the required level of SpO2. Inaccuracy is particularly relevant in patients with invasive mechanical ventilation. It seems to be linked to a lack of education when caregivers give too much oxygen in order to ensure one avoids hypoxaemia. Although educational enhancement, both in initial and continuing training, must be carried out, it is likely that only the development of automated-adapting oxygen concentration devices could significantly improve these results.
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