ORIGINAL ARTICLE

Moderate concentrations of supplemental oxygen worsen hypercapnia in obesity hypoventilation syndrome: a randomised crossover study

Carly Ann Hollier,1,2 Alison Rosemary Harmer,2 Lyndal Jane Maxwell,3 Collette Menadue,1 Grant Neville Willson,4 Gunnar Unger,5 Daniel Flunt,1 Deborah Ann Black,4 Amanda Jane Piper1,5

ABSTRACT

Introduction In people with obesity hypoventilation syndrome (OHS), breathing 100% oxygen increases carbon dioxide (PCO₂), but its effect on pH is unknown. This study investigated the effects of moderate concentrations of supplemental oxygen on PCO₂, pH, minute ventilation (VE) and physiological dead space to tidal volume ratio (Vd/Vt) among people with stable untreated OHS, with comparison to healthy controls.

Methods In a double-blind randomised crossover study, participants breathed oxygen concentrations (FiO₂) 0.28 and 0.50, each for 20 min, separated by a 45 min washout period. Arterialised-venous PCO₂ (PavCO₂) and pH, VE and Vd/Vt were measured at baseline, then every 5 min. Data were analysed using general linear model analysis.

Results 28 participants were recruited (14 OHS, 14 controls). Among OHS participants (mean±SD arterial PCO₂ 6.7±0.5 kPa; arterial oxygen 8.9±1.4 kPa) FiO₂ 0.28 and 0.50 maintained oxygen saturation 98–100%. After 20 min of FiO₂ 0.28, PavCO₂ change (ΔPavCO₂) was 0.3±0.2 kPa (p=0.013), with minimal change in VE and rises in Vd/Vt of 1±5% (p=0.012). FiO₂ 0.50 increased PavCO₂ by 0.5±0.4 kPa (p=0.012), induced acidemia and increased Vd/Vt by 3±3% (p=0.012). VE fell by 1.2±2.1 L/min within 5 min then recovered individually to varying degrees. A negative correlation between ΔVE and ΔPavCO₂ (r=−0.60, p=0.024) suggested that ventilatory responses were the key determinant of PavCO₂ rises. Among controls, FiO₂ 0.28 and 0.50 did not change PavCO₂ or pH, but FiO₂ 0.50 significantly increased VE and Vd/Vt.

Conclusion Commonly used oxygen concentrations caused hyperventilation, PavCO₂ rises and acidemia among people with stable OHS. This highlights the potential dangers of this common intervention in this group.

INTRODUCTION

In obesity hypoventilation syndrome (OHS), chronic hypercapnia develops as a consequence of obesity. This condition is associated with alveolar hypoventilation, restricted pulmonary function, severe sleep-disordered breathing and higher rates of morbidity, mortality and healthcare costs compared with eucapnic obesity.1-4 OHS affects approximately 0.15–0.3% of the US population5 and over 50% of hospital inpatients with body mass index (BMI)>50 kg/m².1 Despite this, OHS frequently goes undiagnosed among hospital inpatients with obesity.1

Supplemental oxygen is a common medical intervention6 and may be administered to patients with OHS in a range of healthcare settings. British Thoracic Society guidelines on emergency oxygen prescription identify patients with OHS as a group among whom excessive concentrations of supplemental oxygen, causing hypoxemia, could increase carbon dioxide (CO₂) levels and lower pH.6 The basis of the guidelines relies upon expert opinion and data from COPD, because very few studies have investigated the effects of supplemental oxygen in OHS. Among patients with obesity and elevated transcutaneous CO₂ pressure (PCO₂), breathing 100% oxygen induced an average rise in transcutaneous PCO₂ of 0.7 kPa (with rises of >1.3 kPa in three patients).7 However, the effect of oxygen on pH, an important prognostic indicator,8 9 was not reported. Furthermore, 100% oxygen is rarely used in clinical practice.8 Hence, the clinical relevance of these data is uncertain.

During acute exacerbations of COPD, hyperoxia arising from supplemental oxygen worsens hypercapnia and pH, and has been linked to more
frequent admission to intensive care and increased hospital length of stay and mortality.9–11 Hypoxia-induced hypercapnia in COPD has been attributed to increased ventilation/perfusion (V/Q) inequality, mediated by the reversal of hypoxic vasoconstriction12–14; however recent evidence suggests that hyperventilation may be a quantitatively more important mechanism.15 16 Whether or not these mechanisms apply to OHS, which has a vastly different pathophysiology to COPD, has yet to be determined.

The aims of the present study were to document the time course of changes in PCO2, pH and respiratory variables in response to clinically relevant, moderate concentrations of supplemental oxygen among people with OHS in comparison to a healthy control group; and to examine physiological mechanisms that may explain any oxygen-induced changes in PCO2.

METHODS

Written informed consent was obtained from all participants. The study was approved by the Ethics Committees of Royal Prince Alfred Hospital (protocol no. X12-0067 and HREC/12/ RPAH/109) and the University of Sydney (Ref. 14935) and registered on the Australian and New Zealand Clinical Trials Registry (ACTRN1260800172303).

Participants

Patients referred to the Sleep Unit, Royal Prince Alfred Hospital with obesity and possible hypercapnia were screened for eligibility. Inclusion criteria were the combination of obesity (BMI ≥ 30 kg/m²) and daytime hypercapnia (arterial PCO2 (PaCO2) > 6 kPa). Patients were excluded in the case of any other potential cause of hypercapnia, current use of positive airway pressure, acute respiratory/cardiac illness within the previous month, acidemia or psychiatric illness. A control group was recruited concurrently from a sample of convenience. Each control participant was age (±3 years) and gender matched with an OHS participant, non-smoking, with BMI < 30 kg/m², normal spirometry and no history of cardiorespiratory disease.

Study design and protocol

Using a double-blind randomised crossover design (figure 1), each participant breathed two fractions of inspired oxygen (FiO2 0.28 and 0.50 in random order (sequence 1 or 2), via a breathing circuit, after a circuit acclimatisation period. Each test began with a 10 min period of breathing room air via the circuit (baseline), followed by a 20 min period of supplemental oxygen (FiO2 0.28 or 0.50), and then a 10 min period of breathing room air (recovery). A 45 min washout period separated the two supplemental oxygen tests.

Randomisation of sequence was generated using an online randomisation programme (http://www.randomization.com), with allocation concealed via sealed opaque envelopes. The chief investigator and participants remained blinded throughout. An unblinded con investigator operated equipment and instructed participants. Testing began between 8:30am and 10:00am. All participants had fasted and abstained from caffeine from midnight.

Instrumentation

The closed breathing circuit comprised a dry rolling-seal spirometer, a bias-flow generator, a soda-lime CO2 absorber and a T-connector at the participant interface. Gas was continuously sampled at the interface using oxygen/CO2 sensors. A stable FiO2 was maintained through titration of bottled air and oxygen using continuous real-time feedback from the oxygen sensor. Immediately after each FiO2 change, the circuit was flushed to allow stabilisation at the new FiO2 within 2 min. Participants breathed through the circuit via a nasal mask (dead space 175 mL) with the mouth closed (n=25), or in the case of nasal obstruction, via a mouthpiece (dead space 100 mL) with a nose peg (n=3).

Outcome measures

On the day of testing, baseline measures of height, weight, spirometry and arterial blood gases (ABGs) were performed. Arterialised-venous blood was repeatedly sampled to obtain surrogate measures of arterial PCO2 (PavCO2) and pH. We previously described and validated this method in OHS.17 An oximeter continuously measured pulse oxygen saturation (SpO2) (Radical, Masimo, Irvine, California, USA). Signals from the oxygen/CO2 sensors and spirometer were recorded by a computer programme and used to derive and/or display breath-by-breath minute ventilation (V̇E), tidal volume (V̇T) and respiratory rate (RR). Breath-by-breath physiological dead space (V̇D/phys) was calculated using a CO2 expirgram method18 and adjusted by subtracting apparatus dead space, then divided by V̇T to obtain V̇D/phys to V̇T ratio (V̇D/phys/V̇T). Data affected by leak or artefact were systematically excluded. Subsequently, breath-by-breath data were averaged over 60 s. For final analysis, data obtained during the following periods were included: the final minute of the 10 min baseline, the final minute of each 5 min epoch of supplemental oxygen, and the final minute of the 10 min recovery. Arterialised-venous blood samples were drawn within the last 10 s of each of these periods.

Statistical analysis

Data are presented as mean±SD or median (IQR), and mean difference (MD) and 95% CI for between-group comparisons. A significance level of p<0.05 was used for all comparisons. Between-group MDs in baseline variables were compared using
independent t-tests. General linear model (univariate, repeated measures) analysis compared responses to supplemental oxygen between participant groups (factor: group; factor interaction: time-by-group) for primary (PavCO2) and secondary (pH, VE and VD/VT) outcomes; between baseline and supplemental oxygen (factor: time) for primary, secondary and tertiary (VT, RR, VD/Phys) outcomes; and between the two oxygen concentrations (factor: concentration) for PavCO2. For non-parametric data, the Friedman test was used to evaluate effects of time. To account for multiple comparisons the level of significance was adjusted (adj.p) using Holm’s Bonferroni procedure.19 Within the OHS group only, Pearson’s correlation coefficient was calculated to examine potential factors associated with the change in PavCO2 after 20 min (ΔPavCO2) of FiO2 0.50, including baseline PaCO2, bicarbonate (HCO3−) and arterial oxygen saturation (SaO2), ΔVd, and ΔVd/VT. The study was powered to detect a ΔPavCO2 of 0.4 kPa16 from baseline during supplemental oxygen within the OHS group, with an SD estimate of 0.45 kPa (using data from the first five OHS participants), power of 0.8, α of 0.05. A sample of 14 OHS participants (hence 14 matched controls) was required. Data were analysed using PASW 18 (IBM, Armonk, New York, USA).

RESULTS
Fourteen participants with OHS and 14 controls were recruited between August 2008 and February 2012 (figure 2). Baseline characteristics (table 1) show that groups were well matched for age and gender. Participants with OHS presented with super-obesity, mild hypercapnia and hypoxaemia, and mild pulmonary restriction.

Table 1 Participant characteristics, baseline arterial blood gases and spirometry

<table>
<thead>
<tr>
<th></th>
<th>OHS</th>
<th>Controls</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48±12</td>
<td>48±12</td>
<td>0.987</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>3/11</td>
<td>3/11</td>
<td>–</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>53±7</td>
<td>25±4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>154±21</td>
<td>73±15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pH</td>
<td>7.395±0.030</td>
<td>7.414±0.019*</td>
<td>0.055</td>
</tr>
<tr>
<td>PaCO2 (kPa)</td>
<td>6.7±0.5</td>
<td>5.5±0.4*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PaO2 (kPa)</td>
<td>8.9±1.4</td>
<td>14.3±1.1*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SaO2 (%)</td>
<td>92±3</td>
<td>98±1*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HCO3− (mmol/L)</td>
<td>30.3±1.7</td>
<td>25.8±1.2*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>A-aDO2 (kPa)</td>
<td>3.6±1.4</td>
<td>0.9±1.2*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>153±20</td>
<td>143±11</td>
<td>0.156</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>2.39±0.72</td>
<td>3.71±0.71</td>
<td>0.001</td>
</tr>
<tr>
<td>FEV1 % predicted</td>
<td>73±14</td>
<td>106±11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>3.03±0.85</td>
<td>4.54±0.77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FVC % predicted</td>
<td>77±14</td>
<td>107±13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>79±6</td>
<td>82±5</td>
<td>0.231</td>
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</table>

Data presented as mean±SD; p value represents two-tailed significance from independent t tests comparing control and OHS groups.

*Data reported from n=13, as arterial blood gas could not be performed in one control participant.

ΔaDO2, alveolar-arterial oxygen difference; BMI, body mass index; FEV1, forced expired volume in 1 s; FVC, forced vital capacity; HCO3−, bicarbonate; OHS, obesity hypoventilation syndrome; PaCO2, arterial partial pressure of CO2; PaO2, arterial partial pressure of O2.

Figure 2 Flow diagram of enrolment, randomisation/ allocation and analysis phases. OHS, obesity hypoventilation syndrome, PAP, positive airway pressure.
Figure 3  Time course of changes in \( \text{PavCO}_2 \), \( V_t \) and \( V_{D/V_t} \) during air/oxygen breathing tests for OHS group (open circles) and control group (closed circles), with results of general linear model analysis of between-group differences (factor: group, and group by time). *Adjusted p value=0.01; \( F_{O2} \), inspired oxygen fraction; NS, non-significant; OHS, obesity hypoventilation syndrome; \( \text{PavCO}_2 \), arterialised-venous carbon dioxide; \( V_t \), minute ventilation; \( V_{D/V_t} \), physiological dead space to tidal volume ratio.
There was a positive correlation between ΔPavCO2 (FiO2 0.50) and PaCO2 (r=0.60, p=0.023) and HCO3− (r=0.58, p=0.030), but not SaO2 (r=−0.48, p=0.08). Furthermore, a negative correlation between ΔPavCO2 and ΔVE was found (r=−0.60, p=0.024), but not ΔVD/VT (r=−0.42, p=0.18).

There was no significant change in VE when breathing FiO2 0.28 (table 2). In contrast, during FiO2 0.50 a consistent fall in VE of 1.2±2.1 L/min (12±22%) below baseline occurred within 5 min (figure 3). Thereafter, a varying recovery in VE was observed (figure 4C), such that after 20 min VE remained below baseline in six participants, returned to baseline in four participants and exceeded baseline VE by >5% in four participants. After 20 min, group mean VE was 3±20% below baseline, which became non-significant after adjustment (raw p=0.014, adj.p=0.224). Decreases in VE were attributable to significant falls in V̇E, as RR was unchanged.

During FiO2 0.28 and 0.50, V̇D/V̇T increased by 1±5% and 3±3%, respectively (adj.p=0.012), in the absence of significant changes in V̇Dphys.

Control group: responses to supplemental oxygen

Among the controls, there were no significant changes in PavCO2 or pH during either FiO2 (table 2, figure 3), and no significant differences for PavCO2 between concentrations. During FiO2 0.28 there were no significant changes in V̇E, V̇T or RR. However, breathing FiO2 0.50 increased V̇E by 15±11% after 20 min (adj.p=0.019), due to a slight, non-significant increase in RR (raw p=0.01, adj.p=0.170).

Significant increases in V̇D/V̇T of 1±3% and 4±3% were observed during FiO2 0.28 and 0.50 respectively (adj.p=0.012). This was accompanied by small rises in V̇Dphys which became non-significant after adjustment (raw p<0.001, adj.p=0.085).

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Table 3 Between-group comparisons of responses to supplemental oxygen

<table>
<thead>
<tr>
<th></th>
<th>MD (± at 20 min)*</th>
<th>95% CI</th>
<th>Raw p value</th>
<th>Adj. p value</th>
<th>Raw p value</th>
<th>Adj. p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PavCO2 (kPa)</td>
<td>0.31</td>
<td>0.13 to 0.49</td>
<td>&lt;0.001</td>
<td>0.010</td>
<td>&lt;0.001</td>
<td>0.014</td>
</tr>
<tr>
<td>pH</td>
<td>−0.014</td>
<td>−0.023 to −0.005</td>
<td>&lt;0.001</td>
<td>0.011</td>
<td>0.001</td>
<td>0.019</td>
</tr>
<tr>
<td>V̇E (L/min)</td>
<td>0.8</td>
<td>−1.3 to −0.38</td>
<td>0.045</td>
<td>0.585</td>
<td>0.051</td>
<td>0.612</td>
</tr>
<tr>
<td>V̇D/V̇T (ratio)</td>
<td>0.01</td>
<td>−0.03 to 0.01</td>
<td>0.085</td>
<td>0.850</td>
<td>0.128</td>
<td>&gt;0.999</td>
</tr>
</tbody>
</table>

Adj. p value: significance level from general linear model analysis, OHS versus controls, after Holm’s Bonferroni correction.

*MD: mean difference (OHS–control) for Δ values at 20 min.

OHS, obesity hypoventilation syndrome; PavCO2, arterialised-venous carbon dioxide; V̇D/V̇T, physiological dead space to tidal volume ratio; V̇Dphys, physiological dead space; V̇E, minute ventilation.

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Figure 4 Individual and group responses to supplemental oxygen concentration (FiO2) 0.28 and 0.50 for OHS group (A and C) and control group (A and B), showing change in arterialised-venous carbon dioxide from room air baseline (ΔPavCO2) (A and B), and change in minute ventilation from room air baseline (ΔV̇E) (C and D). Each figure includes individual changes at 20 min for FiO2 0.28 and group mean±SD on the left, and individual changes at 20 min for FiO2 0.50 and group mean±SD on the right. OHS, obesity hypoventilation syndrome.
DISCUSSION
To our knowledge, this is the first study to investigate the effects of clinically relevant, moderate concentrations of supplemental oxygen on PCO₂ and pH, V̇D/V̇T and V̇E and its determinants among people with OHS. In OHS, hyperoxia induced by breathing F₂O₂ 0.28 and F₂O₂ 0.50 caused significant rises in PavCO₂. Accordingly, pH decreased, resulting in acidemia during F₂O₂ 0.50. Breathing F₂O₂ 0.50 was accompanied by hypoventilation and increases in V̇D/V̇E. However, changes in V̇E were the key determinant of PavCO₂ rises. Breathing F₂O₂ 0.50 also increased V̇D/V̇T in the control group, but controls maintained a stable PavCO₂ and pH through a 15% increase in V̇E. The findings of the present study bring into question the safety of moderate concentrations of supplemental oxygen among patients with untreated OHS and provide evidence to substantiate current clinical guidelines on oxygen prescription.⁶

Among participants with OHS, hyperoxia induced by supplemental oxygen significantly worsened hypercapnia and lowered pH. In an earlier study, breathing 100% oxygen increased transcutaneous PCO₂ in obesity-associated hypercapnia,⁷ but the clinical relevance of this report was unclear because pH was not measured and transcutaneous PCO₂ was used, inherently adding potential errors to PCO₂ measures and preventing a definitive diagnosis of OHS.⁵ The present study provided further physiological detail and insight into the clinical relevance of the effects of hyperoxia in OHS. Although the minimal important difference for PCO₂ in OHS has not been defined, in the present study the rise in PavCO₂ during F₂O₂ 0.50 (0.5±0.4 kPa) was considered clinically significant because it induced acidemia. In patients with COPD, hyperoxia-related acidemia is associated with higher in-hospital morbidity,⁹ and this may apply to acutely unwell patients with OHS⁵ ⁶ but has not been addressed. Therefore, in light of the results of the present study, the influence of supplemental oxygen usage on morbidity, mortality and healthcare utilisation in people with OHS requires investigation.

Ventilatory responses to hyperoxia
Controls
Interestingly, V̇D/V̇T increased among the control group with both oxygen concentrations, with rises of the same magnitude as those of the OHS group (figure 3). Despite this, PavCO₂ and pH remained relatively stable, albeit with some individual variation (figure 4B). During F₂O₂ 0.50, stable PavCO₂ levels were achieved by a 15±11% increase in V̇E. This is consistent with previous observations among healthy controls breathing 100% O₂,¹⁰–²³ and is indicative of normal ventilatory control. Hyperoxic hyperventilation in healthy individuals is usually preceded by a fall in V̇E (~5–12%) within the first 30 s to 2 min of breathing 100% oxygen via inhibition of the peripheral chemoreceptors, which are tonically active within a normal PaO₂ range.²⁰–²³ However, the washout time of circuit gases prevented this being captured in the present study. Quickly thereafter, V̇E increases above baseline due to transient increases in PaCO₂ from initial hyperventilation,²² ²³ the Haldane effect,²² increases in V̇D/V̇T and possibly in part through direct stimulation of chemoreceptors.²²

Obesity hypoventilation syndrome
Participants with OHS also experienced increases in V̇D/V̇T during hyperoxia. However, unlike the controls, breathing F₂O₂ 0.50 was invariably characterised by marked hyperventilation for the first 5–10 min, followed by a partial recovery in V̇E. The recovery of V̇E was usually insufficient to overcome the increase in V̇D/V̇E, hence PavCO₂ was elevated after 20 min of F₂O₂ 0.50 in most participants (figure 4). There was a negative correlation between ΔV̇E and ΔPavCO₂, but ΔV̇D/V̇T was not associated with ΔPavCO₂. These results suggest that the PavCO₂ rises observed amongst OHS participants were largely a result of inadequate ventilatory control. Impaired respiratory chemosensitivity is a common feature of OHS²⁴–²⁶ and may explain why the initial decrease in V̇E during hyperoxia was of a larger magnitude, with much slower recovery, than that reported in controls.²¹ ²³ Blunted hypercapnic ventilatory responses could also explain why an elevation of PavCO₂ at 20 min was tolerated by most participants. However, hypercapnic ventilatory responses are highly variable between individuals with OHS and are sometimes within the normal range in patients with mild hypercapnia,²⁴–²⁶ which may explain the variability in ventilatory responses to hyperoxia in the OHS group. We did not test ventilatory responses and are therefore unable to confirm their role in the changes in PavCO₂ observed during hyperoxia.

Factors potentially influencing V̇D/V̇T in controls and OHS
In both groups, V̇D/V̇T increased significantly during hyperoxia, although the contribution of this small change towards potential PavCO₂ rises is uncertain. Increased V̇D/V̇T could arise from an increase in V̇Dphys, a decrease in V̇T or both. In studies measuring V/Q distributions in healthy controls,²⁷ and patients with OHS,²⁸ breathing 100% oxygen has been shown to increase perfusion to poorly ventilated regions of lung through the release of local hypoxic vasconstriction.²³ This result is underperfusion of well ventilated regions, thereby increasing V̇Dphys.²³ This mechanism is plausible among the control group, in whom a small increase in V̇Dphys was observed during F₂O₂ 0.50. However, this change became non-significant after statistical adjustment. In contrast, no change was observed in V̇Dphys among the OHS group. It has been shown that V̇Dphys has a proportional relationship with V̇T.²⁹ ³⁰ Therefore in OHS participants, increases in V̇Dphys occurring due to increased V̇Q inequality may have been offset by the concomitant fall in V̇T. Given the lack of increase in V̇Dphys during hyperoxia among OHS participants, rises in V̇D/V̇T are largely attributable to the reduction in V̇E (via the reduction in V̇T), which is consistent with previous observations in patients with obesity-associated hypercapnia whilst breathing 100% oxygen.⁷ However, we did not perform invasive V/Q measures and therefore were unable to characterise the complex interactions between pulmonary ventilation and perfusion, gas exchange and breathing pattern when patients were breathing moderate oxygen concentrations.

Clinical implications
Clinically important differences between the two concentrations of oxygen were observed in the present study, that is, hyperoxia induced by F₂O₂ 0.28 caused minimal changes in pH or V̇E, while F₂O₂ 0.50 caused hyperventilation and acidemia. Furthermore, compared with responses to F₂O₂ 0.50 in our OHS participants, even more marked changes in PCO₂ and V̇E occurred during 100% oxygen in obesity-associated hypercapnia.⁷ The mechanisms by which hyperoxia induces hyperventilation in OHS remain unclear. However, these findings suggest that a greater degree of respiratory depression occurs with higher oxygen concentrations. Therefore, in stable OHS, hyperoxia caused by breathing F₂O₂ 0.28 may be less harmful than F₂O₂ 0.50 or 1.0.

Substantial inter-individual variability in ΔPavCO₂ during hyperoxia was evident among the OHS group; as has been reported in obesity-associated hypercapnia⁷ and COPD.¹⁶
Therefore it would be clinically useful to identify features that may predict adverse responses to hyperoxia. Strong associations between ΔPavCO₂ and baseline PaCO₂ and HCO₃⁻ were observed, suggesting that patients with OHS and severe hypercapnia (and associated elevated HCO₃⁻ levels) are more likely to develop worsening hypercapnia during hyperoxia. This is plausible, given the tendency for people with OHS and a higher PaCO₂ to have lower hypercapnic ventilatory responses than those with lower PaCO₂. Elevated HCO₃⁻ may also directly blunt hypercapnic ventilatory responses in OHS, through an increased acid-buffering capacity. Previous data also suggest that people with more severe hypoxaemia may experience larger PCO₂ rises during hyperoxia, although this was not evident amongst our mildly hypoxaemic group.

Participants in the present study were clinically stable, with mild hypercapnia and hypoxaemia. Therefore our findings probably underestimate the dangers of hyperoxia in people with OHS with severe hypercapnia and/or acute cardiorespiratory illness. The effects of supplemental oxygen in this population warrant further investigation. Even so, the findings of the present study highlight the potential risks associated with the administration of moderate concentrations of supplemental oxygen among people with OHS. These findings also provide an evidence base for current guidelines, which recommend that in OHS, supplemental oxygen should be titrated to maintain SpO₂ 88–92%, thereby avoiding hyperoxia and hypoxaemia. Oxygen supplementation should also include close monitoring and periodic reassessment of ABGs.

Limitations In this study, we documented acute responses to breathing supplemental oxygen for 20 min. Based on the time course of PavCO₂ (figure 3), a plateau in PavCO₂ occurred after 10 min of breathing oxygen. However, due to the large capacity of the body for CO₂ storage, CO₂ equilibrium is not usually achieved until 20–30 min after a change in ventilation and therefore participants may not have reached CO₂ steady state. In clinical practice, patients are usually treated with supplemental oxygen for extended periods. Hence, the effects of longer periods of supplemental oxygen require evaluation to further strengthen clinical practice guidelines.

CONCLUSION Among people with mild, stable untreated OHS, breathing moderate concentrations of supplemental oxygen increased PavCO₂, sufficient to induce acidemia during F₂O₂ 0.50. These findings highlight the need for caution during supplemental oxygen administration among people with OHS and support current clinical guidelines which recommend targeting an SpO₂ range and monitoring of ABGs during supplemental oxygen administration.

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Ethics approval Respective ethics committees of Royal Prince Alfred Hospital and The University of Sydney, Sydney Australia.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES


