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ORIGINAL ARTICLE

Quantitation of oxygen-induced hypercapnia in respiratory pump failure

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Abstract
Purpose: To determine the likelihood that clinicians know carbon dioxide levels before administering supplemental oxygen to patients with neuromuscular disorders, to quantitate the effect of oxygen therapy on carbon dioxide retention, and to explore hypercapnia contributing to the need to intubate and use of continuous noninvasive ventilatory support to avert it.
Basic procedures: A retrospective chart review for patients with neuromuscular disorders intubated or having intubation averted by using continuous noninvasive ventilatory support with carbon dioxide known pre- and during oxygen administration.
Main findings: For only 2 of 316 patients who were intubated did clinicians know carbon dioxide levels prior to administering oxygen. For four cases, intubation was averted by continuous noninvasive ventilatory support and mechanical insufflation–exsufflation despite severe hypercapnia and acidosis. After initiating oxygen therapy, patients' carbon dioxide partial pressures increased 52.1 ± 42.0 mm Hg in over as little as 20 min.
Principal conclusions: Clinicians should attempt to use continuous noninvasive ventilatory support and mechanical insufflation–exsufflation rather than supplemental oxygen to normalize blood gases for neuromuscular ventilatory failure and should be prepared to intubate hypercapnic patients for whom oxygen is administered.

Abbreviations: ABG, arterial blood gas; CMV, continuous mandatory ventilation; CNVS, continuous noninvasive ventilatory support; CO_2, carbon dioxide; CTMV, continuous tracheostomy mechanical ventilation; EPAP, expiratory positive airway pressure; $EtCO_2$, end-tidal carbon dioxide; FEV1, forced expiratory volume-one second; FiO_2, fraction of inspired oxygen; ICU, intensive care unit; IPAP, inspiratory positive airway pressure; MIE, mechanical insufflation–exsufflation; NMD, neuromuscular disease; NVS, noninvasive ventilatory support; O_2, oxygen; O_2 sat, oxyhemoglobin saturation; $PaCO_2$, partial pressure of carbon dioxide in arterial blood; PaO_2, partial pressure of oxygen in arterial blood; PAP, positive airway pressure; SMA, spinal muscular atrophy; URI, upper respiratory tract infection; VC, vital capacity; Vt, tidal volume.

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Introduction

Although administering supplemental oxygen (O_2) to hypercapnic patients with cardiopulmonary disease can decrease dyspnea, pulmonary hypertension, polycythemia, exercise intolerance, permit greater ventilator-free breathing particularly for chronic lung disease patients, and prolong life,[1–5] it can also depress hypoxic ventilatory drive and exacerbate hypercapnia.[2,3] With the advancing respiratory muscle weakness of patients with neuromuscular disease (NMD), however, it can render noninvasive ventilation ineffective,[6] which can cause carbon dioxide (CO_2) narcosis, coma, and acute on chronic respiratory failure.

In intensive care units (ICUs), since it is far more common to encounter patients with lung disease than NMDs, it is generally assumed that O_2 administration is harmless for anyone with respiratory symptoms and that NMD patients must accommodate elevated baseline CO_2 levels anyway so emergency services tend to administer O_2 immediately to all such symptomatic patients without first determining CO_2 levels.[7] The only publication that has thus far quantitated O_2-induced hypercapnia in NMD is that of Gay and Edmonds in 1995,[8] and they could only identify the pre- and post-O_2 delivery CO_2 levels for eight patients including three with polymyositis, three with motor neuron disease, and one each with inflammatory motor neuropathy and chronic poliomyelitis. The patients received low-flow O_2 and within 0.8–144 h, three became obtunded and required intubation but subsequently recovered; and two died when intubation was declined. Neither noninvasive ventilatory support (NVS) nor mechanical insufflation–exsufflation (MIE) was used to either avoid intubation or facilitate successful extubation.

Bi-level positive airway pressure (PAP) is generally used in acute and chronic care at less than full ventilatory support settings. However, many patients with little or no vital capacity (VC) require continuous NVS (CNVS) at volume or pressure settings that fully support respiratory muscle function. Two studies reported 166 patients with respiratory pump failure who required intubation after having been administered O_2 supplementation.[9,10] Another 61 patients underwent tracheotomy after being intubated following O_2 administration for acute on chronic respiratory failure.[11] None of these 227 patients had been offered CNVS or MIE[10] to either prevent intubation or facilitate extubation prior to transfer to a specialized unit for extubation or decanulation to CNVS and MIE. The purpose of this case series is to determine the likelihood that clinicians obtain CO_2 levels before administering O_2 to patients with NMD, to quantitate subsequent CO_2 levels as a contributing factor in the need to intubate, and to describe the use of CNVS and MIE to reverse hypercapnia and avert invasive airway intubation.

Methods

Consecutive outpatients to a NMD clinic from 1996 to 2015 were screened for having received O_2 therapy, undergoing intubation then possibly tracheotomy, then being extubated or decanulated to CNVS and MIE. In addition, we screened for others whose hypercapnia had been documented either by arterial blood gas sampling or by end-tidal CO_2 ($EtCO_2$) measurements before O_2 therapy but who were spared intubation by using CNVS and MIE. The MIE was administered by both hospital staff via invasive airway tubes and by the patients' relatives post-extubation/decanulation in the acute care setting up to every 20–30 min during waking hours via oronasal interfaces at insufflation and exsufflation pressures of 50–60 cm H_2O until ambient air oxyhemoglobin saturation (O_2 sat) baseline remained greater than 94%.

Results

Of 2804 patients with NMD, 316 were identified who had undergone intubation, then 61 of 316 tracheotomy. All were subsequently extubated or decanulated to CNVS and MIE.[9–11] Of these, only nine cases had had CO_2 levels available both pre- and during O_2 administration, and for only cases 1 and 4 was the CO_2 known by the clinicians who administered the O_2 and intubated the patients. For cases 2, 3, 7, and 9 whose hypercapnia worsened during O_2 therapy, intubation was averted by using CNVS and MIE.

Case presentations

Case 1: A 27-year-old woman with nemaline rod myopathy had failed extubation following scoliosis surgery at age 10, but she was successfully extubated to CNVS and MIE upon transfer to our intensive care unit (ICU).[9,10] From age 10 to 27, she used bi-level PAP at an inspiratory (I)PAP of 18 cm H_2O, expiratory (E)PAP of 4 cm H_2O, and rate 13 breaths/min only during intercurrent upper respiratory tract infections (URI) despite having a VC as low as 340 mL. In December 2014, she presented to emergency services with a URI and partial pressure of CO_2 in arterial blood ($PaCO_2$) of 47 mm Hg despite continuous use of bi-level PAP. Then, she was started on supplemental O_2. Over a 2-h period, her $PaCO_2$ increased to 67 mm Hg. She became obtunded, was intubated, and failed one extubation attempt to IPAP 8 cm H_2O, EPAP 4 cm H_2O, and supplemental O_2. After nine total days of intubation, she was transferred to our ICU, where she was successfully extubated to CNVS and MIE. Her $PaCO_2$ remained below 40 mm Hg, and she was discharged home 4 days later, where she eventually weaned to nocturnal nasal NVS.

Case 2: A 32-year-old wheelchair-dependent man with Becker muscular dystrophy began to use nocturnal nasal NVS in November 2013 to treat fatigue, sleepiness, difficulty concentrating, and hypercapnia. He had a VC of 550 mL and an $EtCO_2$ of 77 mm Hg. His symptoms cleared and diurnal $EtCO_2$ decreased to 54 mm Hg, but since he refused to use NVS during daytime hours, he again developed mild confusion and presented to emergency services in February 2014. He was placed on 100% fraction of inspired O_2 (FiO_2) and became obtunded over the next 20 min. An arterial blood gas (ABG) revealed a $PaCO_2$ of 177 mm Hg, bicarbonate of 41 meq/L, and pH of 6.98. The patient was manually resuscitated and immediate intubation was recommended. However, the father insisted that the author (Bach) be called first, and when it was discovered that the patient's portable ventilator was in the trunk of his car, the father retrieved it and administered nasal CNVS at a volume-preset of 1150 mL and rate 12 breaths/min. A few minutes later, the patient transitioned to mouthpiece CNVS and, 20 min later, was discharged home with normal O_2 sat, fully coherent, and in no distress.

At his next outpatient visit in May 2014, now using CNVS, the patient's $EtCO_2$ remained below 40 mm Hg and ambient air O_2 sat was normal. When breathing unassisted for a few minutes, his $EtCO_2$ increased to 46 mm Hg.

Case 3: A 15-year-old boy with spinal muscular atrophy type 1 (SMA), who was CNVS-dependent with a VC of 10 mL and received all nutrition via a nasogastric tube since 8 months of age, was admitted to a pediatric ICU for respiratory distress despite pressure-controlled continuous mandatory ventilation (CMV) at 24 cm H_2O, rate 12 breaths/min. At 5 PM, his $PaCO_2$ was 21 mm Hg and partial pressure of O_2 in arterial blood (PaO_2) of 42 mm Hg. He was placed on FiO_2 of 32% along with CNVS. Thirteen hours later, his $PaCO_2$ increased to 56 mm Hg with a PaO_2 of 59 mm Hg. As his aspiration pneumonitis resolved, his FiO_2 was reduced to 28%. Two hours later, his $PaCO_2$ decreased to 49 mm Hg. He was discharged home with normal O_2 sat and $EtCO_2$ of 35 mm Hg. At a 2-week follow-up outpatient visit, his $EtCO_2$ was 30 mm Hg, which had been his baseline.

Case 4: A 4-year-old boy with SMA2, baseline VC of 480 mL, and $EtCO_2$ of 46 mm Hg was admitted to a pediatric ICU for distress due to a URI. He was using volume-preset CMV at 750 mL, rate 16 breaths/min. His $PaCO_2$ was 41 mm Hg. He was placed on FiO_2 of 50% and became disoriented over the next 2 h. A repeat ABG drawn on FiO_2 of 40% showed a $PaCO_2$ of 73 mm Hg and PaO_2 of 67 mm Hg. He was then intubated and his $PaCO_2$ normalized. Two days later, on FiO_2 of 21%, he was extubated back to CNVS on CMV at 20 cm H_2O, rate 16 breaths/min.

Case 5: A 60-year-old woman with facioscapulohumeral muscular dystrophy using nocturnal CMV (Vt 1000 mL, rate 12 breaths/min, FiO_2 21%) had a VC of 640 mL (sitting) and 480 mL (supine) and $EtCO_2$ of 39 mm Hg. On a routine visit to her pulmonologist, despite normal pulse oximetry, she was placed on 2 L/min O_2 and bronchodilators. Three weeks later, she was admitted for CO_2 narcosis, intubated, and underwent tracheotomy. She used continuous tracheostomy mechanical ventilation (CTMV) for 4 months until she was decanulated to CNVS on her previous settings. Her $EtCO_2$ remained 32–40 mm Hg using CNVS over the next six outpatient visits spanning 5 years despite her VC decreasing to 250 mL.

Case 6: A 7-year-old boy with SMA1 and CNVS dependence since 4 months of age, who had an $EtCO_2$ of 19–34 mm Hg over 11 outpatient visits and a VC of 15 mL, was hospitalized for gastroenteritis. Although he had no respiratory symptoms, he was placed on FiO_2 of 50%. Eleven hours later, on repeat ABG, his $PaCO_2$ had increased from 43 on admission to 62 mm Hg with a PaO_2 of 48 mm Hg, and he was intubated for 3 days. Once stabilized with normal O_2 sat and CO_2 on ambient air, he was extubated back to CNVS and discharged home 5 days later.

Case 7: A 32-year-old man with myotonic dystrophy using CNVS was admitted for aspiration pneumonia. On admission, with a $PaCO_2$ of 40 mm Hg and PaO_2 of 79 mm Hg, he was placed on FiO_2 of 32%. Three days later, his $PaCO_2$ was 58 mm Hg with PaO_2 53 mm Hg. Then, O_2 was discontinued and the $PaCO_2$ normalized to 39 mm Hg. Three days later, he was discharged home using nocturnal-only nasal NVS.

Case 8: A 71-year-old woman with post-poliomyelitis ventilatory insufficiency, baseline VC of 500 mL, and $EtCO_2$ 45 mm Hg was placed on 2 L/min O_2 to treat exertional dyspnea. Six weeks later, she was hospitalized for CO_2 narcosis with a $PaCO_2$ of 106 mm Hg. She was intubated, failed conventional weaning/extubation, and transferred for extubation to CNVS and MIE.[9,10] Three days later, she was discharged home using sleep NVS on CMV at Vt 950 mL, rate 12 breaths/min. At a 3-day follow-up, her $EtCO_2$ was 40 mm Hg with normal O_2 sat.

Case 9: A 12-month-old CNVS dependent infant with SMA type 1 used nasal CNVS at 20 cm pressure and her $PaCO_2$ ranged from 37 to 43 mm Hg over a 5-day period. Ventilator weaning was attempted, but her $PaCO_2$ increased to 59 mm Hg and O_2 sat decreased at which point she was placed back on CNVS with low-flow O_2. Three hours later, her $PaCO_2$ was 168 mm Hg. Intubation was averted by discontinuing the O_2, and use of CNVS quickly normalized her CO_2 level to 36 mm Hg.

Discussion

Consistent with the report of Gay and Edmonds,[8] who found a mean increase in CO_2 of 28.2 ± 23.3 mm Hg with O_2 therapy for eight patients with NMD, the CO_2 of our cases increased from 43.8 to 95.9 mm Hg or 52.1 ± 42.0 mm Hg (range of 21–59 to 56–177) over a mean 17.4 h (range of 20 min to 6 weeks). Whereas Gay and Edmonds did not use NVS or MIE, our cases 2, 3, 7, and 9 avoided intubation because of it.

Case 1 became hypercapnic because bi-level PAP settings were inadequate to fully rest or support a patient with little VC. Normally compliant lungs require full tidal volumes or pressure settings of 18–20 cm H_2O. While O_2 therapy exacerbates hypercapnia by suppressing hypoxic drive for patients breathing spontaneously, for nasal bi-level PAP or NVS users like cases 1, 3, 6, and 9, it resulted in increased ventilation leakage out of the mouth.[6] Patients with little or no VC can maintain normal lung ventilation during sleep by using open systems of NVS provided that ventilatory drive is adequate to reflexively prevent excessive air leakage to avoid severe hypercapnia. This reflex activity occurs at the nadir of O_2 desaturations and is suppressed by O_2 administration.[6] Other mechanisms for O_2-exacerbated hypercapnia include worsening ventilation-perfusion matching secondary to attenuation of hypoxic pulmonary vasoconstriction, depression of diaphragm function,[9] and decreased affinity of hemoglobin for CO_2 (Haldane effect), which results in increased bicarbonate and dissolved CO_2.[12] Although acute increases in $PaCO_2$ and H+ stimulate ventilation, as baseline $PaCO_2$ and bicarbonate levels increase,[13] further increases result in respiratory depression, obtundation, and agonal breathing as nasally insufflated air leaks out of the mouth. Likewise, nasal bi-level PAP is also less effective in the acute setting for patients receiving supplemental O_2 for lung disease[14–16] as it is for patients receiving heavy sedation or narcotics.[6]

A limitation of this study is that for cases 2 and 8, baseline $EtCO_2$ was compared with $PaCO_2$ during O_2 delivery. Since people with NMD generally have normal lung tissue diffusion, $EtCO_2$ differs minimally from $PaCO_2$. Reports suggest that $EtCO_2$ is 1[17] to 2–6 mm Hg less than $PaCO_2$ (*R*-value of 0.94–0.98) unless cardiac output and lung perfusion pressures are decreased.[18,19] Thus, $EtCO_2$ can be conveniently used for home sleep monitoring, whereas $PaCO_2$ necessitates indwelling arterial lines.

Administering O_2 and pressure-preset bi-level PAP rather than volume-preset NVS precludes the use of active lung volume recruitment (air stacking),[20] which along with failure to use MIE, prevented sufficient cough flows for cases 1 and 4 to avoid pneumonia and intubation. Cases 5 and 8 demonstrate that even chronic low-flow O_2 therapy (2 L/min) can result in CO_2 narcosis. Although CTMV dependent, decanulation to CNVS permitted case 5 to wean back to nocturnal-only NVS. This effect of weaning from CTMV to part-time NVS is especially pronounced when hyperventilated, hypocapnic CTMV users are decanulated to NVS.[21,22] Cases 1, 4, 5, 6, and 8 were all successfully extubated or decanulated to CNVS and MIE in ambient air despite having no ventilator-free breathing ability.

Conclusion

For only 2 of 316 intubated patients were CO_2 levels known to the clinician administering O_2 and intubating the patient. Physicians need to obtain CO_2 analyses before administering O_2 to NMD patients with respiratory distress and to attempt to resolve the problem by using CNVS and MIE. The O_2 should only be administered if CNVS and MIE have failed to normalize ambient air O_2 sat, in which case they should be prepared to intubate. Whereas hypercapnic lung disease patients have poor prognoses with a 5-year survival of 30% for patients whose forced expiratory volume-one second (FEV1) is less than 750 mL,[23] patients with NMD have been reported to have survived 20 to over 60 years using CNVS.[20] Thus, O_2 therapy should not be used as a substitute for NVS and MIE to maintain normal O_2 sat (>94%). Avoiding O_2 also permits oximetry to gauge hypercapnia, airway secretion encumbrance, and intrinsic lung disease as well as the effectiveness of NVS and MIE in treating them.[24]

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Conflicts of interest

The authors have no conflicts of interest to report.

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