Section Editor: **Richard C. Prielipp**

Effect of Apneic Oxygenation on Tracheal Oxygen Levels, Tracheal Pressure, and Carbon Dioxide Accumulation: A Randomized, Controlled Trial of Buccal Oxygen Administration

Andrew J. Toner, MD (Res),* Scott G. Douglas, FANZCA,* Martin A. Bailey, FANZCA,*† Hans J. Avis, PhD,* Arani V. Pillai, FRCA,*‡ Michael Phillips, MMedSci,*§ and Andrew Heard, FRCA*

BACKGROUND: Apneic oxygenation via the oral route using a buccal device extends the safe apnea time in most but not all obese patients. Apneic oxygenation techniques are most effective when tracheal oxygen concentrations are maintained >90%. It remains unclear whether buccal oxygen administration consistently achieves this goal and whether significant risks of hypercarbia or barotrauma exist.

METHODS: We conducted a randomized trial of buccal or sham oxygenation in healthy, nonobese patients (n = 20), using prolonged laryngoscopy to maintain apnea with a patent airway until arterial oxygen saturation (Spo_2) dropped <95% or 750 seconds elapsed. Tracheal oxygen concentration, tracheal pressure, and transcutaneous carbon dioxide (CO_2) were measured throughout. The primary outcome was maintenance of a tracheal oxygen concentration >90% during apnea.

RESULTS: Buccal patients were more likely to achieve the primary outcome ($P < .0001$), had higher tracheal oxygen concentrations throughout apnea (mean difference, 65.9%; 95% confidence interval [CI], 62.6%–69.3%; $P < .0001$), and had a prolonged median (interquartile range) apnea time with Spo_2 >94%; 750 seconds (750–750 seconds) vs 447 seconds (405–525 seconds); $P < .001$. One patient desaturated to Spo_2 <95% despite 100% tracheal oxygen. Mean tracheal pressures were low in the buccal (0.21 cm·H_2O; SD = 0.39) and sham (0.56 cm·H_2O; SD = 1.25) arms; mean difference, −0.35 cm·H_2O; 95% CI, 1.22–0.53; $P = .41$. CO_2 accumulation during early apnea before any study end points were reached was linear and marginally faster in the buccal arm (3.16 vs 2.82 mm Hg/min; mean difference, 0.34; 95% CI, 0.30–0.38; $P < .001$). Prolonged apnea in the buccal arm revealed nonlinear CO_2 accumulation that declined over time and averaged 2.22 mm Hg/min (95% CI, 2.21–2.23).

CONCLUSIONS: Buccal oxygen administration reliably maintains high tracheal oxygen concentrations, but early arterial desaturation can still occur through mechanisms other than device failure. Whereas the risk of hypercarbia is similar to that observed with other approaches, the risk of barotrauma is negligible. Continuous measurement of advanced physiological parameters is feasible in an apneic oxygenation trial and can assist with device evaluation. (Anesth Analg 2019;128:1154–9)

KEY POINTS

- **Question:** Does the early arterial desaturation sometimes observed during apneic oxygenation via the buccal route occur because the device fails to maintain high tracheal oxygen concentrations, and are any risks of hypercarbia or barotrauma posed?
- **Findings:** Buccal oxygenation reliably maintains tracheal oxygen concentrations >90%, without significantly influencing carbon dioxide accumulation or tracheal pressure levels.
- **Meaning:** Buccal oxygenation is a reliable and safe apneic oxygenation technique, but prolonged apnea should be accompanied by a carbon dioxide management plan.

Apneic oxygenation techniques extend the safe apnea time during intubation[1] and ventilation-free surgery.[2] Anesthesiologists are increasingly applying these approaches in clinical practice to minimize arterial desaturation during airway management and to facilitate airway surgery. However, a proportion of patients still exhibit early arterial desaturation during apneic oxygenation,[3–5] for reasons that remain unclear. Furthermore, harm can be caused through carbon dioxide (CO_2) accumulation[6] and barotrauma.[7]

From the *Department of Anaesthesia and Pain Medicine, Royal Perth Hospital, Perth, Australia; †Department of Anaesthesia and Pain Medicine, Fiona Stanley Hospital, Perth, Australia; ‡Department of Anaesthesia, Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom; and §Centre for Medical Research, University of Western Australia, Perth, Australia.

Accepted for publication August 14, 2018.

Funding: Royal Perth Hospital Department of Anaesthesia and Pain Medicine funded Fellows for trial recruitment and provided disposables. The Medical Research Fund of Royal Perth Hospital (http://www.rphmrf.org.au) supported the statistical analysis.

DOI: 10.1213/ANE.0000000000003810

The authors declare no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.anesthesia-analgesia.org).

Clinical trial number and registry URL: ACTRN12617000173392 (www.anzctr.org.au). Principal Investigator: Andrew J. Toner.

Reprints will not be available from the authors.

Address correspondence to Andrew J. Toner, MD (Res), Department of Anaesthesia and Pain Medicine, University of Western Australia, Royal Perth Hospital, Perth 6000, Australia. Address e-mail to toner@doctors.org.uk.

Computational modeling suggests that the clinical efficacy of apneic oxygenation is underpinned by the maintenance of high oxygen concentrations in the subglottic airways, and the benefits of increasing oxygen levels from 90% to 100% appear to exceed the benefits of increasing oxygen levels from 21% to 90%.[8] Because apneic oxygenation techniques have evolved from delivering oxygen directly into the trachea[6] toward delivering oxygen close to the body surface,[4,5,9–11] the subglottic oxygen concentrations achieved are uncertain. In a recent trial in obese patients, we showed that oxygen administration using a novel buccal (oral) approach was very effective overall, but a third of patients still desaturated before the full apneic duration of 750 seconds elapsed.[4] It is unknown whether this early desaturation reflects low tracheal oxygen concentrations or other pathophysiological mechanisms.

To fully evaluate the reliability and safety of buccal oxygen administration, we therefore set out to measure tracheal oxygen, tracheal pressure, and CO_2 accumulation during an apneic oxygenation trial. We hypothesized that buccal oxygen delivery would maintain tracheal oxygen concentrations >90% during prolonged apnea, without altering tracheal pressure levels or CO_2 accumulation.

METHODS

The study protocol was approved by the local Human Research Ethics Committee. Eligible patients were approached by the research team in the surgical admission unit, and informed consent was obtained for all participants. The trial was registered before patient enrolment with the Australia and New Zealand Clinical Trials Registry (ACTRN12617000173392, principal investigator: A.J.T., date of registration: February 2, 2017). Trial reporting was in accordance with the 2010 CONsolidated Standards Of Reporting Trials (CONSORT) statement.

Trial Design

We conducted an open-label randomized trial of buccal or sham oxygenation in healthy, nonobese patients (n = 20) at a single University Hospital site in Western Australia. Block randomization in a 1:1 ratio occurred by computerized sequence generation and the sealed opaque envelope method. Twenty patients were recruited between March 7, 2017 and October 3, 2017 (Supplemental Digital Content, Figure 1, http://links.lww.com/AA/C587). Eligibility criteria included the following: patients ≥18 years of age requiring general anesthesia with endotracheal intubation for scheduled surgery, body mass index (BMI) between 20 and 30, and American Society of Anesthesiologists physical status I or II. Patients were deemed ineligible if they had chronic respiratory disease, arterial hemoglobin saturation <98% after preoxygenation, previous or anticipated difficult intubation, uncontrolled hypertension, ischemic heart disease, congestive heart failure, increased intracranial pressure, gastroesophageal reflux disease, known allergy or contraindication to study drugs (propofol, remifentanil, fentanyl, rocuronium, or midazolam), or an anatomical feature precluding adequate positioning of the buccal device.

Conduct of Anesthesia

In the preoperative holding area, patients had vascular access secured. After 2 patients exhibited secretions during apnea (see Results), a protocol amendment was approved, and from the eighth participant onward, intravenous (IV) glycopyrrolate was administered in the holding area (4 μg/kg; maximum, 400 μg). Thereafter, the conduct of anesthesia followed the protocol outlined in our original trial of buccal oxygenation.[4] In brief, monitoring was established on the operating table before induction of anesthesia, including processed electroencephalogram (State Entropy, GE Healthcare, Helsinki, Finland), 3-lead electrocardiogram, arterial oxygen saturation (Spo_2), and noninvasive blood pressure set at 1-minute cycles. The final preoperative theater checklist was completed, and then IV midazolam (2 mg) was administered. The buccal oxygen delivery device, an adapted 3.5-mm internal diameter, south-facing Ring-Adair-Elwin (RAE) tube, was applied to the left internal cheek and connected to the auxiliary oxygen outlet of the anesthetic machine.[4] Preoxygenation to an end-tidal oxygen target ≥80% was conducted with patients in the supine position, spontaneously ventilating with the adjustable pressure limiting (APL) valve fully open and a continuous capnography trace. Supplemental oxygen via the buccal device was then started in the intervention arm only, at a flow rate of 10 L/min. Total IV anesthesia was commenced with propofol (7.0 μg/mL, Schnider model, effect-site concentration) and remifentanil (4.0 ng/mL, Minto model, effect-site concentration) or fentanyl (2–3 μg/kg) if the former was unavailable. Time zero was recorded, and the theatre stop clock began at the point all planned total IV anesthesia infusions were running. Thereafter, rocuronium 0.9 mg/kg was injected at the 1-minute point, and laryngoscopy was performed 2.5 minutes into the study with a C-MAC (Macintosh style blade; Karl Storz Ltd, Tuttlingen, Germany) video laryngoscope. A video-assisted laryngeal view consistent with straightforward intubation was required for study continuation. A Cormack and Lehane 2B view on the C-MAC monitor was then maintained with prolonged laryngoscopy until a study end point of Spo_2 <95% or 12.5 minutes was reached. At study end, patients were briefly facemask ventilated with 100% oxygen and the APL valve set between 20 and 30 cm·H_2O before proceeding to intubation and the scheduled surgery.

Data Collection

The primary outcome was maintenance of a tracheal oxygen concentration >90% throughout the apneic period. Secondary outcomes were tracheal pressure and CO_2 accumulation rates. Patient age, sex, weight, height, BMI, and American Society of Anesthesiologists grade were also documented on the case report form (CRF). The apparatus and data collection processes are outlined in detail below.

Measurement Apparatus. A 12F, 20-cm length central venous catheter (CVC) with 12-gauge proximal and medial ports and a 16-gauge distal port (Teleflex Medical Ltd, Mascot, Australia; product number CS-15123-F) was preformed within an 8.0-mm internal diameter south-facing RAE tube, by inserting to a depth of 18 cm for ≥10 minutes (Figure 1). The inflow and return-flow hubs of a G210 oxygen analyzer (Bedfont Scientific Ltd, Maidstone, United Kingdom, manufacturer accuracy reported as ±[1% of range + 2% of reading]) were connected to the medial and proximal ports of the CVC, respectively, using gas sampling tubing (GE Healthcare, Helsinki, Finland) and a 0.45 Micron filter (Meditech Systems Ltd, Shaftesbury, United Kingdom). The G210 oxygen analyzer has a default

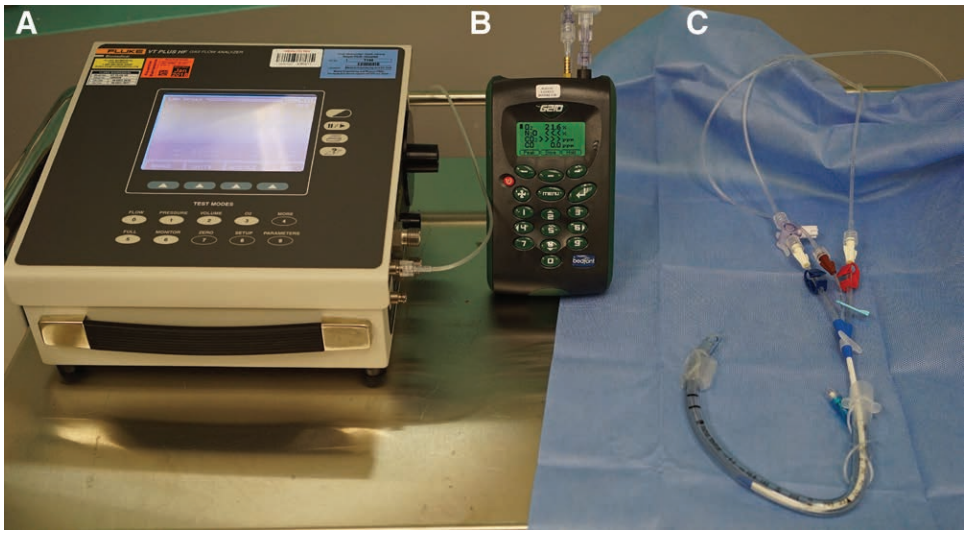

Figure 1. Apparatus setup for tracheal measurements. A–C, VT Plus HF pressure monitor; G210 oxygen analyzer; and triple lumen central venous catheter preformed at a depth of 18 cm within an 8.0-mm internal diameter south-facing RAE tube. RAE indicates Ring-Adair-Elwin.

gas extraction rate of 100 mL/min, and a maximal "flow fail" setting of +16 was used to allow ongoing gas extraction in the event of partial sampling tube blockage. Importantly, the G210 return-flow feature allows for analyzed gas to be returned to the sampling source at the same flow rate that it is being extracted. Before use, the G210 oxygen analyzing system and sampling lines were primed with 100% oxygen.

The remaining distal CVC port was connected to a VT Plus HF pressure analyzer (Fluke Biomedical, Everett, WA; manufacturer span accuracy reported as ±2.04 cm·H_2O) with gas sampling tubing. When switched on, the VT Plus HF pressure analyzer underwent the full automated warm-up period (5 minutes). The analyzer was then set to measure the low-pressure range in cm·H_2O via the "gas or fluid" inlet port and was zeroed to atmospheric pressure. The complete tracheal measurement apparatus setup before induction of anesthesia is illustrated in Figure 1.

Tracheal Oxygen and Pressure Measurements. At laryngoscopy, the tip of the preformed CVC was placed 3 to 5 cm below the vocal cords using a bougie-style insertion technique. Once in position, the G210 oxygen analyzer commenced gas extraction and return, in the process providing a continuous measurement of tracheal oxygen concentration without modifying the gas mixture or pressure levels in the trachea. The first oxygen percentage was recorded on the CRF 3 minutes into the study and at 30-second intervals thereafter. If delays inserting the CVC were encountered, the first useable oxygen percentage was recorded. Just after CVC insertion, the minimum, maximum, and average pressure read-outs from the VT Plus HF pressure monitor were reset to zero, and these parameters were then recorded on the CRF between 3 and 5 minutes and between 3 and 10 minutes if an end point had not been reached. At study end, the maximal tracheal pressure sensed during facemask ventilation was also recorded on the CRF, to evaluate the responsiveness of the pressure measurement system.

CO_2 Measurements. A TCM5 transcutaneous CO_2 monitor (Radiometer Pacific Pty Ltd, Mt Waverley Vic, Australia) was applied to participants in the holding area before surgery. The probe was placed in the subclavicular region and the 10-minute warming and capillary arterialization process was initiated. The monitor remained connected for transfer to the operating theatre, and an event marking the study start was entered manually. At study end, data files containing transcutaneous CO_2 values at 1-second intervals were exported to Microsoft Excel and analyzed offline.

Statistical Analysis

The primary outcome was analyzed with a linear longitudinal mixed-effects model with an independent covariance structure for the 2-level model. Fractional polynomial transformations were used to accommodate nonlinearity over time with the set of powers examined between −2 and 3 giving 44 models. Kaplan–Meier curves were combined with the log-rank test. For comparison with preceding studies, safe apnea times with Spo_2 ≥95% were reported in each arm, and differences were assessed with the exact test. Mean apneic tracheal pressure was compared with an unpaired t test. CO_2 accumulation in each arm during apnea was similarly analyzed with a linear mixed-effects model, also with fractional polynomial transformations. Analyses were performed on an intention-to-treat basis using the Stata statistical package (Stata Statistical Software, release 15; StataCorp LLC, College Station, TX), with $P < .05$ (2-tailed) regarded as statistically significant.

Sample size was calculated for a comparison of 2 proportions. Extrapolating from our original buccal oxygenation trial,[4] we anticipated that 80% of patients receiving buccal oxygen would maintain tracheal oxygen concentrations >90%, compared to ≤10% of sham controls. To detect such a difference with 90% power and a significance level of 0.05, 9 patients in each group were required. To allow for a 10% withdrawal rate, the sample size was set at 20 patients.

RESULTS

Twenty patients were recruited with no exclusions for Spo_2 <98% after preoxygenation or unanticipated difficult laryngoscopy. Patient characteristics were similar in the 2 arms (Table), and the preoxygenation end-tidal oxygen target of ≥80% was consistently achieved. There were no adverse events related to physiological monitoring, buccal oxygenation, or prolonged laryngoscopy. Tracheal oxygen and pressure data were successfully measured in all 20 patients, and

the first reading was obtained at a median (range) study time of 180 seconds (180–300 seconds). Transcutaneous CO_2 was successfully measured in 19 of 20 patients; a technical fault was encountered in a single patient (study ID 04) after randomization but before commencement of the study protocol. Two patients exhibited secretions and intermittent sample line blockage which resolved with line flushing or replacement. After an amendment to administer preoperative IV glycopyrrolate was approved by the Human Research Ethics Committee, no further secretions were observed.

Patients in the buccal oxygen arm were more likely to maintain a tracheal oxygen concentration >90% for the full duration of the apneic period (log-rank χ^2 = 240.2; P < .0001; Figure 2). Tracheal oxygen concentrations with buccal oxygen administration were higher overall (mean difference, 65.9%; 95% confidence interval [CI]s, 62.6%–69.3%; P < .0001) and increased over time toward 100% (0.109% per second; 95% CI, 0.085–0.133; P < .001; Figure 3). In the sham arm, tracheal oxygen concentrations declined rapidly toward 21% within a minute of the first reading, with the exception of 1 patient (study ID 07) who exhibited sampling line blockage and a marginally slower rate of oxygen decline (Supplemental Digital Content, Figure 2A, http://links.lww.com/AA/C587). These findings are consistent with a prolonged median (interquartile range) apnea time with Spo_2 >94%; 750 seconds (750–750 seconds) vs 447 seconds (405–525 seconds; exact test, P < .001).

In the buccal oxygenation arm, a single patient did not complete the full apnea test (study ID 03), reaching the study end point of Spo_2 <95% at 9.5 minutes despite 100% tracheal oxygen (Supplemental Digital Content, Figure 2B, http://links.lww.com/AA/C587). This patient was at the upper limit of the BMI eligibility criteria (BMI = 29.9). In another patient (study ID 04), tracheal oxygen concentrations initially fell <50% until examination of the oral cavity revealed the buccal oxygen device in an incorrect position, causing occlusion of the distal end by soft tissue. After the correct position was established, the tracheal oxygen concentration returned toward 100% and Spo_2 stayed >94% for the full 750-second study duration. A sensitivity analysis removing these results did not materially change the mixed model analysis results.

Table. Patient Characteristics

	Sham Oxygen (n = 10)	Buccal Oxygen (n = 10)
Age, y	43 ± 21 (18–75)	50 ± 16 (27–73)
Weight, kg	75 ± 15 (51–88)	72 ± 11 (57–89)
Height, cm	173 ± 14 (151–192)	168 ± 8 (155–182)
BMI	25 ± 2 (21–28)	25 ± 3 (21–30)
Female, n (%)	4 (40)	6 (60)
ASA I/II, n	5/5	1/9

Data are presented as mean ± standard deviation (range).
Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index.

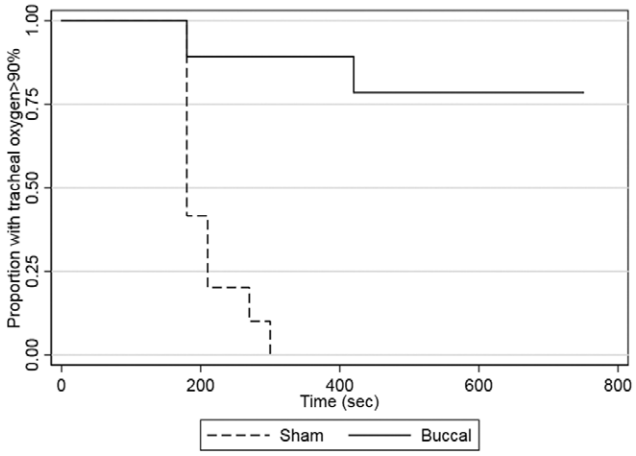

Figure 2. Proportion of patients with tracheal oxygen ≥90% during 750 s of apnea.

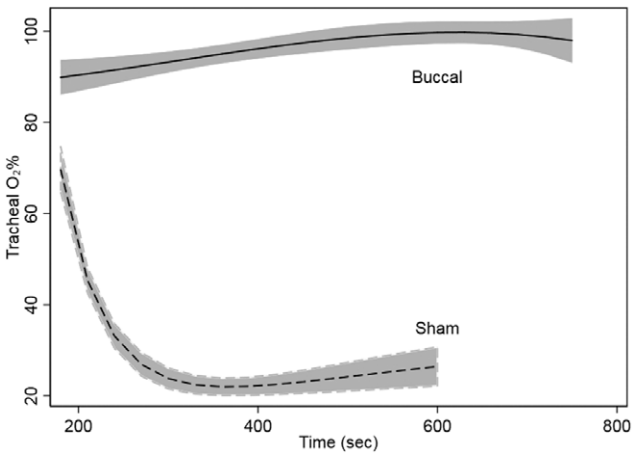

Figure 3. Linear mixed model of tracheal oxygen concentration during 750 s of apnea (shaded area shows the 95% confidence interval).

Mean tracheal pressures were low in the buccal (0.21 cm·H_2O; SD = 0.39) and sham (0.56 cm·H_2O; SD = 1.25) arms; mean difference, −0.35 cm·H_2O; 95% CI, 1.22–0.53; P = .41. Tracheal pressure traces during facemask ventilation confirmed a responsive pressure measurement system (Supplemental Digital Content, Figure 3, http://links.lww.com/AA/C587), with mean (SD) maximum pressures of 17.45 cm·H_2O (6.92 cm·H_2O), that were consistent with the settings of the APL valve (20–30 cm·H_2O) and some system leak.

CO_2 accumulation during early apnea before any study end points were reached (≤230 seconds) was linear and marginally faster in the buccal arm (3.16 vs 2.82 mm Hg/min; mean difference, 0.34; 95% CI, 0.30–0.38; P < .001; Figure 4). Prolonged apnea in the buccal arm revealed nonlinear CO_2 accumulation that declined over time (P < .001 for interaction) and averaged 2.22 mm Hg/min (95% CI, 2.21–2.23; Figure 5).

DISCUSSION

This is the first apneic oxygenation trial to use continuous measurement of subglottic physiological parameters, revealing a number of unique insights into the strengths and weaknesses of the buccal approach.

Foremost, buccal oxygen delivery with a patent airway reliably maintains tracheal oxygen concentrations in the most effective range, >90%. This is consistent with clinically significant extensions of the safe apnea time observed in this study and our original description of the technique.[4] According to a landmark computational analysis,[8] maintenance of such high tracheal oxygen should allow for very prolonged apnea without desaturation in patients with low pulmonary shunt. Thus, prolonged ventilation-free surgery

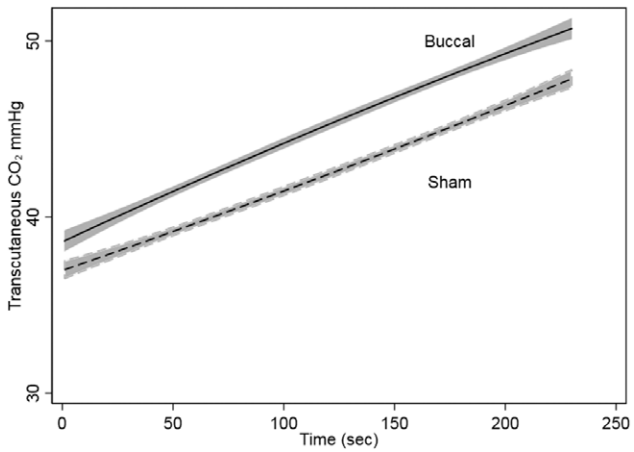

Figure 4. Linear mixed model of transcutaneous CO_2 during 230 s of apnea (shaded area shows the 95% confidence interval). CO_2 indicates carbon dioxide.

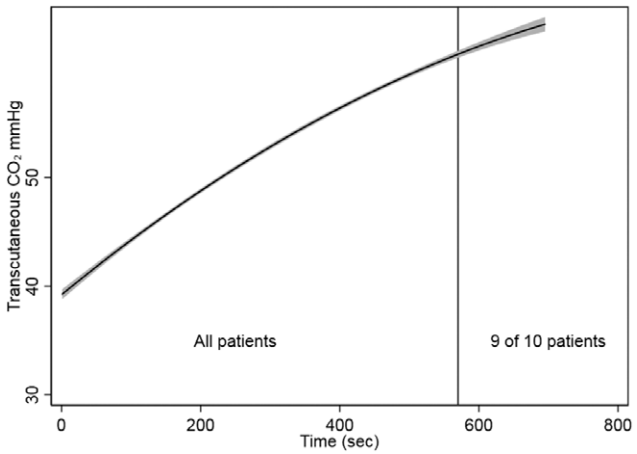

Figure 5. Linear mixed model of transcutaneous CO_2 during 750 s of apnea in buccal patients only (shaded area shows the 95% confidence interval). CO_2 indicates carbon dioxide.

may be feasible in selected patients with buccal oxygenation, alongside a CO_2 management plan (see below).

In our original study with no subglottic measurements, arterial desaturation before the full apneic test period elapsed (750 seconds) occurred in 7 of 20 obese patients (median BMI = 34.4), and we speculated this may be due to mechanisms other than a failure of the device to maintain high tracheal oxygen. In this respect, the development of atelectasis and pulmonary shunt is common after induction of anesthesia,[12] positively correlated with BMI,[13] and is proven in animal models to drive rapid arterial desaturation during apneic oxygenation.[14] The data described here support this view, especially because early arterial desaturation occurred in 1 patient (BMI = 29.9) despite 100% tracheal oxygen. Importantly, animal studies also imply that apneic oxygenation in the presence of pulmonary shunt remains beneficial despite early rapid desaturation to an equilibrium point.[14] Consequently, desaturation during effective apneic oxygenation will occur in some high-risk patients, but this should not prompt technique abandonment unless a device is impeding the execution of airway rescue algorithms.

This study has also confirmed our previously stated hypothesis[4] that buccal oxygenation does not generate any appreciable positive airways pressure because the guaranteed oral escape route provides a low resistance pathway for oxygen egress. This is both a strength and a weakness. The risk of barotrauma or gastric insufflation is negligible, but there is no capability to prevent atelectasis and pulmonary shunt.[13] The pressure measurement apparatus in this study was rapidly responsive during facemask ventilation across a clinically important range, and this approach may therefore be suitable to assess devices that are hypothesized to generate positive airway pressure. Devices that can be shown to reliably and predictably generate optimal pressure levels (around 5–10 $cm{\cdot}H_2O$) during apnea would offer a distinct advantage in patients at risk of developing atelectasis and pulmonary shunt.

The rate of rise of transcutaneous CO_2 (an accurate surrogate of arterial values[2]) during the first 4 minutes of apnea was relatively high in the buccal oxygenation arm (3.16 mm Hg/min or 0.42 KPa/min) and marginally exceeded the sham arm (mean difference, 0.34 mm Hg/min). There is no clear explanation for this finding, other than perhaps an imbalance in baseline health factors in a relatively small sample size (Table) and the use of a highly powerful statistical approach. Moreover, CO_2 accumulation was shown to be nonlinear in the buccal arm, declining as time progressed and averaging a much lower rate over 12.5 minutes (2.22 mm Hg/min or 0.29 KPa/min). Overall, this study provides clarity that normal precautions to avoid the sequelae of hypercarbia during buccal oxygenation should be used. In this respect, we currently conduct prolonged apneic oxygenation with a CO_2 management plan that constitutes intubation and ventilation to normalize CO_2 every 15 minutes or when transcutaneous values exceed 70 mm Hg. By confirming the nonlinear nature of CO_2 rises during apnea that has been described elsewhere,[2,15] this study also demonstrates that accumulation rate values reported with apneic oxygenation devices are partly determined by the duration of apnea experienced. This may explain why recent case series of prolonged apneic oxygenation report low CO_2 accumulation rates relative to historical controls,[9] but thus far, direct comparisons within randomized trials have reported equivalence.[16,17]

Although this study supports buccal oxygenation as a safe and effective technique, it must be realized that the approach uses adapted airway equipment and is vulnerable, albeit rarely, to incorrect positioning. In 1 participant in particular, we observed a rapid fall in tracheal oxygen concentration with incorrect positioning, with rapid resolution when this was addressed. Therefore, it is important that the natural curvature of the buccal RAE tube faces toward the midline after it is secured in position, and that the RAE tube is shortened if necessary to prevent the abutment of deeper tissue. A purpose-built device may overcome such limitations by incorporating redundancy in the oxygen delivery pathways and having a range of available sizes.

Physiological measurements provided a number of key insights into the performance of the buccal oxygen device, but also significant challenges. First, this was a resource-intensive study requiring at least 2 senior investigators to be present for every patient recruited. Second, model-based training was necessary to ensure prompt placement of the CVC monitoring device into the trachea under video

laryngoscope guidance. Third, 2 patients exhibited secretions and intermittent sampling line blockage. Although lines were flushed and changed, some of the tracheal pressure and oxygen measurements in these patients may have been rendered inaccurate. Secretions were not observed after an amendment to administer IV glycopyrrolate preoperatively, and this should be a standard for future studies. Finally, in line with many other apneic oxygenation trials, the sham group airway management deviated substantially from standard clinical practice. Patient risks in this respect were minimized by the trial design and eligibility criteria.

This work has a number of other limitations. The tracheal oxygen measurement system had an appreciable equilibration time, taking approximately 1 minute to read accurately when moving from 21% to 100% oxygen, or vice versa (bench data, not shown). Thus, in the sham oxygen arm, it is likely that the fall in tracheal oxygen concentration observed between the third and fourth minute of the study (Figure 3) represents the equilibration time, rather than the true tracheal readings. Furthermore, the tracheal oxygen and pressure apparatus were not recalibrated at study end, precluding an estimate of measurement drift. The span accuracy of the pressure apparatus (VT Plus) is defined by the manufacturer as ±2.04 cm·H_2O, which may also limit the detection of small but clinically important differences in tracheal pressure between devices. Finally, this study evaluated the performance of buccal oxygenation in the presence of a patent airway during prolonged laryngoscopy (grade 2B view). A common concern among clinicians is the benefit conferred by apneic oxygenation when the airway is less patent during genuine difficulty. The rapid feedback from physiological monitoring allows this to be addressed in future study designs.

In conclusion, buccal oxygen reliably maintains a high tracheal oxygen concentration during apnea, but early arterial desaturation can still occur through mechanisms other than device failure. Whereas the risk of hypercarbia is similar to that observed with other approaches, the risk of barotrauma or gastric insufflation is negligible. This extends our previous findings[4] with respect to efficacy and safety and highlights the pitfalls of prematurely abandoning apneic oxygenation in the face of early desaturation. Continuous measurement of advanced physiological parameters is feasible in an apneic oxygenation trial and can assist with device evaluation. ■

ACKNOWLEDGMENTS

Radiometer Pacific Pty Ltd (Mt Waverley Vic, Australia) provided a no-obligation loan of the TCM5 transcutaneous carbon dioxide monitor for the duration of participant enrollment.

DISCLOSURES

Name: Andrew J. Toner, MD (Res).
Contribution: This author helped conceive the study design, develop the protocol and standard operating procedures, register the trial, enroll the participants, analyze the data, and write and revise the manuscript.
Name: Scott G. Douglas, FANZCA.
Contribution: This author helped enroll the participants and revise the manuscript.
Name: Martin A. Bailey, FANZCA.
Contribution: This author helped enroll the participants and revise the manuscript.
Name: Hans J. Avis, PhD.
Contribution: This author helped enroll the participants and revise the manuscript.
Name: Arani V. Pillai, FRCA.
Contribution: This author helped develop the protocol, register the trial, and revise the manuscript.
Name: Michael Phillips, MMedSci.
Contribution: This author helped conduct the statistical analyses.
Name: Andrew Heard, FRCA.
Contribution: This author helped conceive the study design, develop the protocol, enroll the participants, analyze the data, and revise the manuscript.
This manuscript was handled by: Richard C. Prielipp, MD, MBA.

REFERENCES

1. Wong DT, Yee AJ, Leong SM, Chung F. The effectiveness of apneic oxygenation during tracheal intubation in various clinical settings: a narrative review. *Can J Anaesth*. 2017;64:416–427.
2. Gustafsson IM, Lodenius Å, Tunelli J, Ullman J, Jonsson Fagerlund M. Apnoeic oxygenation in adults under general anaesthesia using Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) - a physiological study. *Br J Anaesth*. 2017;118:610–617.
3. Achar SK, Pai AJ, Shenoy UK. Apneic oxygenation during simulated prolonged difficult laryngoscopy: comparison of nasal prongs versus nasopharyngeal catheter: a prospective randomized controlled study. *Anesth Essays Res*. 2014;8:63–67.
4. Heard A, Toner AJ, Evans JR, Aranda Palacios AM, Lauer S. Apneic oxygenation during prolonged laryngoscopy in obese patients: a randomized, controlled trial of buccal RAE tube oxygen administration. *Anesth Analg*. 2017;124:1162–1167.
5. Ramachandran SK, Cosnowski A, Shanks A, Turner CR. Apneic oxygenation during prolonged laryngoscopy in obese patients: a randomized, controlled trial of nasal oxygen administration. *J Clin Anesth*. 2010;22:164–168.
6. Frumin MJ, Epstein RM, Cohen G. Apneic oxygenation in man. *Anesthesiology*. 1959;20:789–798.
7. Yao HH, Tuck MV, McNally C, Smith M, Usatoff V. Gastric rupture following nasopharyngeal catheter oxygen delivery-a report of two cases. *Anaesth Intensive Care*. 2015;43:244–248.
8. McNamara MJ, Hardman JG. Hypoxaemia during open-airway apnoea: a computational modelling analysis. *Anaesthesia*. 2005;60:741–746.
9. Patel A, Nouraei SA. Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE): a physiological method of increasing apnoea time in patients with difficult airways. *Anaesthesia*. 2015;70:323–329.
10. Steiner JW, Sessler DI, Makarova N, et al. Use of deep laryngeal oxygen insufflation during laryngoscopy in children: a randomized clinical trial. *Br J Anaesth*. 2016;117:350–357.
11. Teller LE, Alexander CM, Frumin MJ, Gross JB. Pharyngeal insufflation of oxygen prevents arterial desaturation during apnea. *Anesthesiology*. 1988;69:980–982.
12. Magnusson L, Spahn DR. New concepts of atelectasis during general anaesthesia. *Br J Anaesth*. 2003;91:61–72.
13. Gander S, Frascarolo P, Suter M, Spahn DR, Magnusson L. Positive end-expiratory pressure during induction of general anesthesia increases duration of nonhypoxic apnea in morbidly obese patients. *Anesth Analg*. 2005;100:580–584.
14. Engström J, Hedenstierna G, Larsson A. Pharyngeal oxygen administration increases the time to serious desaturation at intubation in acute lung injury: an experimental study. *Crit Care*. 2010;14:R93.
15. Eger EI, Severinghaus JW. The rate of rise of PaCO2 in the apneic anesthetized patient. *Anesthesiology*. 1961;22:419–425.
16. Humphreys S, Lee-Archer P, Reyne G, Long D, Williams T, Schibler A. Transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) in children: a randomized controlled trial. *Br J Anaesth*. 2017;118:232–238.
17. Riva T, Pedersen TH, Seiler S, et al. Transnasal humidified rapid insufflation ventilatory exchange for oxygenation of children during apnoea: a prospective randomised controlled trial. *Br J Anaesth*. 2018;120:592–599.