Original Article

Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE): a physiological method of increasing apnoea time in patients with difficult airways

A. Patel[1,2] and S. A. R. Nouraei[3]

1 Consultant Anaesthetist, The Royal National Throat Nose and Ear Hospital, London, UK
2 Consultant Anaesthetist, 3 Specialist Registrar in Academic Otolaryngology, University College Hospital NHS Foundation Trust, London, UK

Summary

Emergency and difficult tracheal intubations are hazardous undertakings where successive laryngoscopy–hypoxaemia–re-oxygenation cycles can escalate to airway loss and the 'can't intubate, can't ventilate' scenario. Between 2013 and 2014, we extended the apnoea times of 25 patients with difficult airways who were undergoing general anaesthesia for hypopharyngeal or laryngotracheal surgery. This was achieved through continuous delivery of transnasal high-flow humidified oxygen, initially to provide pre-oxygenation, and continuing as post-oxygenation during intravenous induction of anaesthesia and neuromuscular blockade until a definitive airway was secured. Apnoea time commenced at administration of neuromuscular blockade and ended with commencement of jet ventilation, positive-pressure ventilation or recommencement of spontaneous ventilation. During this time, upper airway patency was maintained with jaw-thrust. Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) was used in 15 males and 10 females. Mean (SD [range]) age at treatment was 49 (15 [25–81]) years. The median (IQR [range]) Mallampati grade was 3 (2–3 [2–4]) and direct laryngoscopy grade was 3 (3–3 [2–4]). There were 12 obese patients and nine patients were stridulous. The median (IQR [range]) apnoea time was 14 (9–19 [5–65]) min. No patient experienced arterial desaturation < 90%. Mean (SD [range]) post-apnoea end-tidal (and in four patients, arterial) carbon dioxide level was 7.8 (2.4 [4.9–15.3]) kPa. The rate of increase in end-tidal carbon dioxide was 0.15 kPa.min^{-1}. We conclude that THRIVE combines the benefits of 'classical' apnoeic oxygenation with continuous positive airway pressure and gaseous exchange through flow-dependent deadspace flushing. It has the potential to transform the practice of anaesthesia by changing the nature of securing a definitive airway in emergency and difficult intubations from a pressured stop–start process to a smooth and unhurried undertaking.

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Correspondence to: A. Patel
Email: anil.patel@uclh.nhs.uk

Introduction

The principal objective of airway management during anaesthesia is maintenance of oxygenation. As the patient transitions from wakefulness to anaesthesia and receives neuromuscular blockade, the anaesthetist is afforded a finite time ('apnoeic window') during which to secure a definitive airway. Failure to do so normally results in recommencement of facemask ventilation, re-oxygenation and a further attempt at securing a definitive airway. In some patients, the combination of

unfavourable pharyngolaryngeal anatomy and reduced apnoea time due to cardiorespiratory decompensation makes this stop-start approach hazardous. Multiple attempts at difficult laryngoscopy increase the risk of airway trauma, which in turn makes subsequent attempts at laryngoscopy and facemask ventilation more difficult [1]. This can deleteriously impact on human factors that are intrinsic to a highly pressured clinical scenario [2], and can readily cascade into a 'cannot intubate, cannot ventilate' scenario with significant attending morbidity and mortality [3, 4].

The mainstay method of increasing the apnoeic window is through pre-oxygenation, which entails spontaneous facemask ventilation with 100% oxygen [5]. Pre-oxygenation denitrogenises the lungs and creates an alveolar oxygen reservoir [6]. The size of this reservoir can be increased by reducing dependent atelectasis through head-up patient positioning [7] and raising mean airway pressure [8] but ultimately, the size of the oxygen reservoir is fixed at the end of pre-oxygenation and once apnoea begins, it does not get replenished.

Aventilatory mass flow (AVMF) [9] is a physiological phenomenon in which, provided that a patent air passageway exists between the lungs and the exterior, the difference between the alveolar rates of oxygen removal and carbon dioxide excretion generates a negative pressure gradient of up to 20 cmH_2O [10] that drives oxygen into the lungs [9, 11–16]. The clinical application of this phenomenon is known in modern anaesthetic practice as apnoeic oxygenation (i.e. AVFM and apnoeic oxygenation are synonymous). Apnoeic oxygenation has been used both experimentally and clinically as a strategy to extend the apnoeic window by providing a pharyngeal oxygen reservoir [9, 11–14, 16, 17]. We report our early experience with OptiFlow™, a commercial transnasal humidified oxygen delivery system (Fisher and Paykel Healthcare Limited, Panmure, Auckland, New Zealand) to increase apnoea time in difficult airway patients undergoing general anaesthesia.

Methods

Between 2013 and 2014, 25 adult patients presenting for surgery, in whom the presence of a difficult airway was known based on previous anaesthetics or strongly anticipated based on unfavourable pharyngolaryngeal anatomy, and whose BMI or underlying cardiorespira-

tory disease made rapid arterial oxygen desaturation at induction of anaesthesia likely, were clinically judged as likely to benefit from using the Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) technique. Patients were undergoing surgery for laryngotracheal stenosis, vocal fold pathology and obstructive sleep apnoea, and benign and malignant hypopharyngeal obstruction.

All patients were pre-oxygenated at 40 degrees of head-up inclination with the OptiFlow nasal cannula (Fig. 1) at a rate of 70 l.min^{-1} for 10 min. Intravenous induction of anaesthesia then commenced with boluses of 2–3 mg.kg^{-1} propofol, 1–2 µg.kg^{-1} fentanyl, and 0.5 mg.kg^{-1} rocuronium, followed by a peripheral infusion of propofol at a rate of 0.2–0.3 mg.kg^{-1}.min^{-1}. Jaw-thrust was performed immediately the patient became unconscious and was maintained throughout the apnoeic period, to ensure upper airway patency. Facemask ventilation was confirmed and discontinued. The patient's angle of inclination was reduced to 20 degrees for laryngoscopy. The first attempt at laryngoscopy was with a standard metal Macintosh laryngoscope and if this was unsuccessful, an A.P. Advance™ videolaryngoscope (Venner Medical Deutschland GmbH, Dänischenhagen, Germany) with a Macintosh blade was used. If this also proved unsuccessful, an A.P. Advance difficult airway blade was used. Meticulous care was taken in all laryngoscopies not to traumatise the airway. Nasal oxygenation was maintained at the same rate of 70 l.min^{-1} until the definitive airway was secured. Apnoea time referred to the time between administration of neuromuscular blockade and commencement of jet ventilation, positive-pressure ventilation or recommencement of spontaneous ventilation.

Information about patients' age, sex, ASA grade, burden of general morbidities (which was quantified using the Charlson co-morbidity score [18]), BMI, indication for and the nature of the procedure undertaken, and Mallampati [19] and Cormack-Lehane direct laryngoscopy grades [20] were recorded. Duration of apnoea was determined by clinical need in all cases and the nature of the airway placed at the end of the apnoeic period and procedure were recorded. Maximum heart rate and minimum oxygen saturations during apnoea, and end-tidal carbon dioxide levels
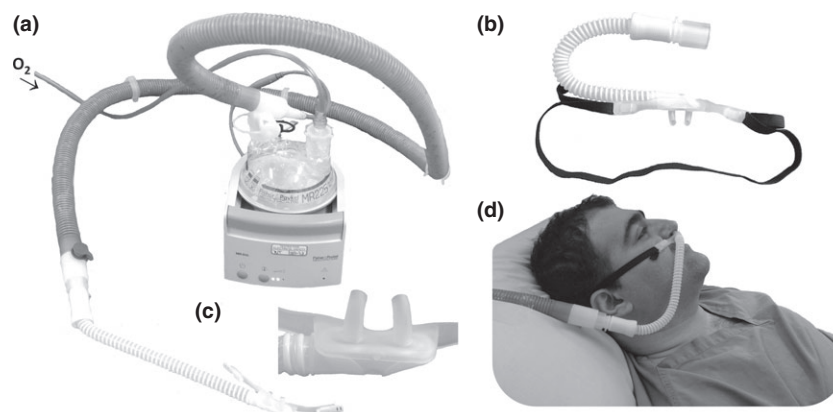
Figure 1 The OptiFlow high-flow humidified oxygen delivery system. The oxygen humidification unit (a) receives oxygen from a standard oxygen regulator and delivers humidified oxygen to a custom-built transnasal oxygen cannula (b and c) like a standard nasal oxygen cannula (d).

once a definitive airway had been placed, were recorded from the anaesthetic record. In four patients with longer apnoea times and in whom arterial cannulation had been required, arterial blood gases were also measured. The correlation between carbon dioxide levels at the end of apnoea and apnoea time was assessed with simple correlation. Data were analysed using MedCalc (MedCalc Software bvba, Ostend, Belgium). As data were collected as part of delivering standard care following introduction of a new technique into clinical practice, formal ethical committee approval was not sought. However, we consulted the Caldicott guardian for approval to analyse the data and present the study.

Results

Twenty-five patients underwent induction of anaesthesia using the THRIVE technique between 2013 and 2014. There were 15 males and 10 females and mean age (SD [range]) at treatment was 49 (15 [25–81]) years. The median (IQR [range]) ASA grade was 3 (2–3 [1–4]). The median (IQR [range]) BMI was 30 (23–36 [18–52]) kg.m^{-2}. The median (IQR [range]) age-adjusted Charlson co-morbidity index was 2 (0–4 [0–5]). Ten patients underwent treatment for benign laryngeal conditions, two patients had surgery for obstructive sleep apnoea and four patients had treatment for benign or malignant head and neck conditions. Nine patients had acute airway compromise with stridor on presentation. The median (IQR

[range]) Mallampati grade was 3 (2–3 [2–4]) and direct laryngoscopy grade was 3 (3–3 [2–4]). The median (IQR [range]) apnoea time was 14 (9–19 [5–65]) min. No patient experienced arterial desaturation < 90% (Fig. 2).

The surgical procedures required different forms of definitive airway management: in 14 patients the definitive airway was suspension laryngoscopy and jet ventilation; and four patients were tracheally intubated. Furthermore, four patients had a laryngeal mask airway placed after THRIVE, one patient had a tracheostomy, and for two patients, THRIVE was the sole mode of ventilation throughout the procedure.
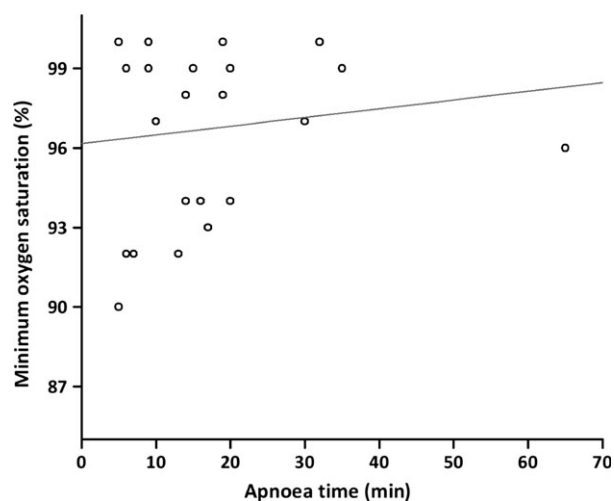
Figure 2 The relationship between apnoea time and oxygen saturation levels (n = 25). The line represents linear regression with r = 0.136 and p = 0.51.
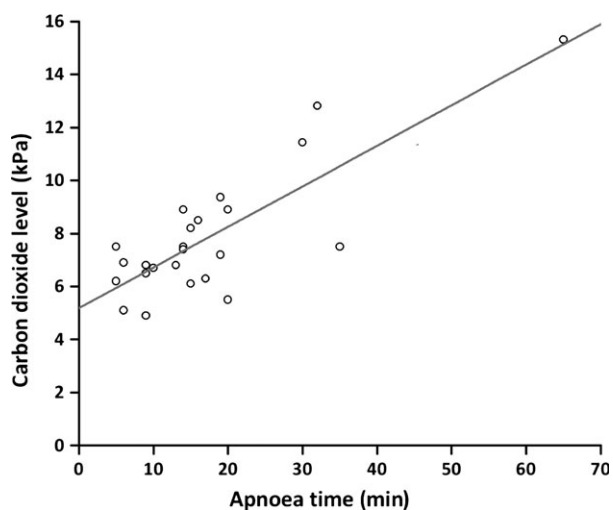
Figure 3 illustrates the relationship between duration of apnoea and carbon dioxide levels at the end of the apnoeic period.

Discussion

We found deployment of THRIVE beneficial in extending apnoea time in our patients with difficult airways undergoing general anaesthesia [1, 21]. There were no desaturations below 90%, despite an average apnoea time of 17 min and none of the patients developed cardiac arrhythmias or other complications suggestive of carbon dioxide toxicity [13, 22].

High-flow nasal oxygenation has successfully been used, predominantly in intensive care [23] but also in emergency department [24] settings, to treat acute respiratory failure [25–29], to prevent postoperative atelectasis [30], and to alleviate dyspnoea in acute heart failure [31]. Interest is also emerging in the use of this technique to increase the apnoeic window in the context of tracheal intubation in the intensive care unit [32]. Our findings extend the application of this technique to managing patients with difficult airways undergoing general anaesthesia.

In 23 of 25 of our patients, termination of apnoea was planned and THRIVE made securing the definitive airway a smooth and unpressured undertaking. One

Figure 3 The relationship between apnoea time and end-tidal (and in four patients, arterial) carbon dioxide levels (n = 24). The line represents linear regression with r = 0.82 and p < 0.0001. The regression equation was $CO_2 = (5.2 \pm 0.5) + (0.15 \pm 0.02) \times$ apnoea time.

stridulous patient with acute airway compromise due to severe tracheobronchomalacia and a BMI of 34 kg.m^{-2} desaturated to 92% at 7 min after induction and is likely to have done so sooner without THRIVE, and a second patient with spasmodic dysphonia and a BMI of 52 kg.m^{-2} desaturated to 90% after 5 min of apnoea. In both of these cases, the modestly extended apnoeic window allowed suspension laryngoscopy and jet ventilation to be atraumatically established and saturations returned to 99% once jetting commenced. In two other patients, THRIVE was used throughout the procedure; these patients had apnoea times of 32 and 65 min, and this allowed pharyngolaryngeal surgery to be performed.

The physiological nomenclature for describing 'apnoeic oxygenation' has changed several times since the phenomenon was described by Volhard in 1908 [10]. It has been described as 'diffusion respiration' by Draper and Whitehead [33], as 'AVMF' by Bartlett et al. [9] and as 'apnoeic oxygenation' by Frumin et al. [13]. What all of these studies describe is oxygenation using only the difference in the rates of excretion of carbon dioxide and absorption of oxygen as the driver of gaseous flow. It was rapidly recognised that while apnoeic oxygenation alone could largely match the oxygen demands of the subject, it did not prevent a potentially rapid and dangerous rise in carbon dioxide concentration. In Frumin et al.'s experiments, two of eight human trials were prematurely terminated owing to development of ventricular arrhythmias [13], and in Draper et al.'s experiments, one of the 12 dogs died, most likely from carbon dioxide toxicity [11]. There were also early suggestions of patients' death and altered cerebral function following 'classical' apnoeic oxygenation [34, 35]. Joels and Samueloff demonstrated that classical apnoeic oxygenation causes a progressive respiratory acidosis that rapidly overwhelms the blood's buffering mechanisms and progresses into a mixed acidosis that proves fatal [36]. Death is principally due to limited tolerance of the myocardial contractile [37] and conductive [22] mechanisms to acidosis. Joels and Samueloff's experiments placed the upper limit of the 95% CI for occurrence of death due to acidosis at a pH of 6.9 [36].

We provide further evidence that classical apnoeic oxygenation provides little clearance of carbon dioxide.

We have plotted the rate of rise of carbon dioxide in three studies of classical apnoeic oxygenation [13, 15, 16], along with one study by Stock et al., who measured the rate of increase in carbon dioxide during airway obstruction (Fig. 4) [38]. In all of these studies, the rate of rise of carbon dioxide levels was between 0.35 and 0.45 $kPa.min^{-1}$, suggesting that classical apnoeic oxygenation provides a similarly low level of carbon dioxide clearance to that if the airway was obstructed.

It seems, therefore, that 'apnoeic oxygenation', while almost certainly a contributor to oxygenation during THRIVE, is an incomplete description for the technique. Perhaps, there is a contribution from a high-flow pre-oxygenation element, since very high flows of oxygen before or at induction may reduce rebreathing and maximise oxygen stores [39]. Moreover, we believe that a better explanation for the physiology that is being clinically observed can be derived from Meltzer and Auer's 'respiration without respiratory movements' experiments [40]. They maintained prolonged ventilation, apparently without carbon dioxide toxicity, through continuous insufflation of oxygen into the trachea [40]. They chose the calibre of the cannula to be smaller than tracheal diameter to allow gases to be exchanged with the exterior. We believe

that continuous insufflation is the critical component of THRIVE, which achieves a continuous positive airway pressure of approximately 7 cmH_2O [41] that splints the upper airways and reduces shunting [42, 43]. Continuous insufflation facilitates oxygenation [17, 44] and carbon dioxide clearance through gaseous mixing and flushing of the deadspace. Evidence for the existence of flow-dependent, non-rhythmic ventilatory exchange can be provided by comparing the increase in rise of carbon dioxide under different continuous insufflation apnoeic conditions. Rudolf and Hohenhorst [45] performed a study in which ventilation was achieved through an intratracheal catheter delivering oxygen at a rate of 0.5 $l.min^{-1}$. This achieved a rate of carbon dioxide increase of 0.24 $kPa.min^{-1}$. Watson et al. used a high-flow tracheal cannula at 45 $l.min^{-1}$ and achieved a steady-state carbon dioxide level within 5 min of the start of apnoea [46]. With THRIVE, the rate of carbon dioxide increase was 0.15 $kPa.min^{-1}$ (Fig. 3) and a steady-state carbon dioxide level was not reached.

Our study was limited by the fact that it was observational and cross-sectional, and we only maintained THRIVE until a definitive airway had been secured. Furthermore, we only recorded those measurements of oxygenation and carbon dioxide
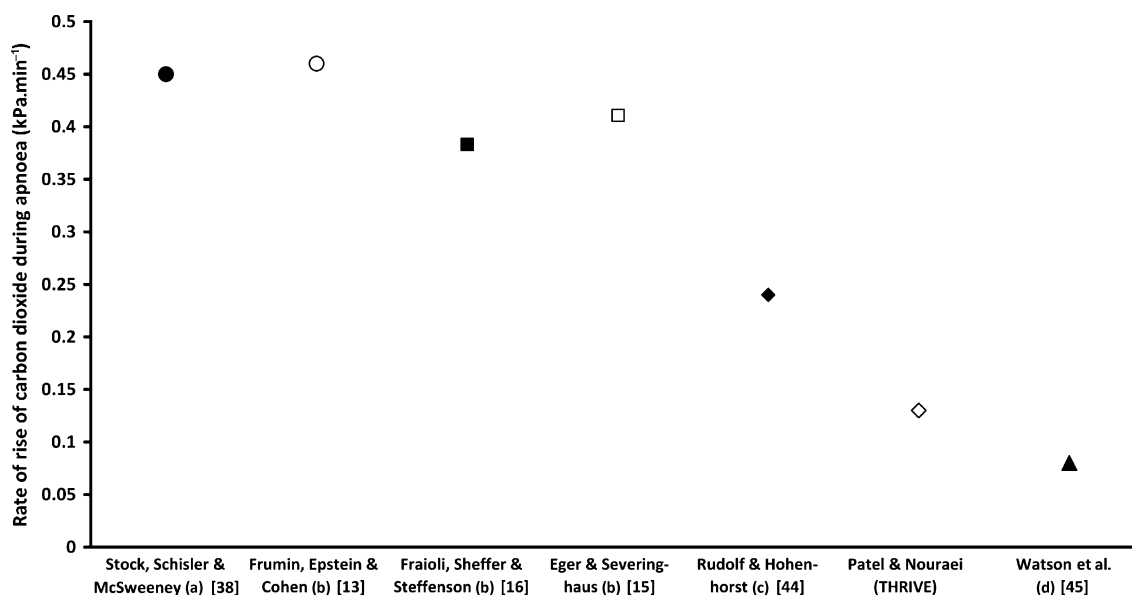
Figure 4 Rate of rise of carbon dioxide levels under different apnoea conditions undertaken within the study referred to: (a) airway obstruction; (b) classical apnoeic oxygenation; (c) low-flow intra-tracheal cannula and (d) high-flow intratracheal cannula.

excretion that were necessary as part of delivering routine clinical care. Furthermore, experimental studies are needed to characterise safe upper limits of THRIVE in different patient groups. We encountered two instances of desaturation, although not hypoxaemia. One case occurred in the presence of severe obesity and a second in the presence of severe tracheobronchomalacia and obesity. We are mindful of the fact that the apnoeic window, while extended through post-oxygenation compared with pre-oxygenation alone, is unlikely to be the same in obese as in non-obese patients. Based on our preliminary findings, the safe upper limit of apnoea in the presence of morbid obesity can be as low as 5 min, but this needs to be confirmed through an experimental human physiology study. It is also unlikely that THRIVE can readily rescue those patients who have total airway obstruction and its use in the presence of a known or suspected cranial base fracture is also not advised.

In conclusion, we have shown that THRIVE, as currently administered through a standard commercially available nasal high-flow oxygen delivery system, could maintain oxygen saturations after commencement of apnoea to levels that could change the nature of difficult intubations from a hurried stop-start, potentially traumatic undertaking, to a smooth event undertaken within an extended safe apnoeic window.

Competing interests

No external funding or competing interests declared. AP has contributed to the design of the A.P. Advance videolaryngoscopy system.

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