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High-flow nasal oxygenation for anesthetic management

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High-flow nasal oxygenation (HFNO) is a promising new technique for anesthesiologists. The use of HFNO during the induction of anesthesia and during upper airway surgeries has been initiated, and its applications have been rapidly growing ever since. The advantages of this technique include its easy set-up, high tolerability, and its abilities to produce positive airway pressure and a high fraction of inspired oxygen and to influence the clearance of carbon dioxide to some extent. HFNO, via a nasal cannula, can provide oxygen both to patients who can breathe spontaneously and to those who are apneic; further, this technique does not interfere with bag-mask ventilation, attempts at laryngoscopy for tracheal intubation, and surgical procedures conducted in the airway. In this review, we describe the techniques associated with HFNO and the advantages and disadvantages of HFNO based on the current state of knowledge.

Keywords: Airway management; Airway surgery; Apneic oxygenation; Endotracheal intubation; High-flow nasal oxygenation; Hypercapnea; Hypoxemia; Preoxygenation.

Introduction

Airway management is an essential skill that all anesthesiologists require. As the current airway management methods are still not optimal, anesthesiologists need to be continuously updated with new developments related to airway devices and techniques [1]. Among these developments, high-flow nasal oxygenation (HFNO) is particularly prominent. Although the use of this technique is spreading globally, there are some controversies regarding its indications and the advantages of having the required skills to use it. Therefore, in this narrative review, we focus on the new emerging airway management skill of performing HFNO, and we describe the potential role of HFNO based on the current state of knowledge.

High-flow Nasal Oxygenation (HFNO)

HFNO is a method that provides oxygen at a high flow rate of over 15 L/min (which is the maximum flow rate for a conventional nasal cannula) through a patient's nasal opening [2]. The device is able to titrate the fractional inspired oxygen (FiO_2) to up to 1.0 and to consistently deliver a highly oxygenated flow to the alveoli because of its ability to provide higher flow rates than that of the usual inspiratory flow and to reduce the entrainment of room air [2]. HFNO generates a low level of continuous positive airway pressure of 2.7–7.4 cmH_2O, facilitates the washout of the nasopharyngeal dead space, reduces the nasopharyngeal resistance, increases alveolar recruitment, decreases the work of breathing, and prevents the development of atelectasis and bronchospasm [2–4]. Specially designed equipment is required for HFNO because the oxygen flow should be at adequately high temperatures and humidity levels, which prevents the feeling of

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dryness in the nasal cavity of patients and promotes tolerance for the high-flow rate [3]. Additionally, humidified and heated inspired oxygen lessens the energy cost involved in gas conditioning [5], prevents mucociliary damage, and facilitates mucociliary clearance [3,6].

Traditional use of HFNO

HFNO has proven highly effective for patients admitted to the intensive care unit (ICU) [7] or to the post-anesthetic care unit after surgery [3]. It is evident that HFNO enhances oxygenation in patients who develop hypoxemic acute respiratory failure and that it helps to avert the need for reintubation after extubation in the ICU [3]. A meta-analysis reported that HFNO, when employed postoperatively, reduced the length of hospital stay for adult patients [8]. Following this meta-analysis report, another study confirmed that postoperative HFNO reduced the length of hospital stay and the incidence of re-admission to the ICU in the case of cardiac surgical patients with pre-existing respiratory diseases [7].

The reported side effects from the trials were minor, such as being sensitive to noise, feeling hot, and developing a runny nose [3]. The nasal interface of the HFNO system is composed of soft silicone with a wider bore compared to that of traditional nasal prongs. HFNO is generally well tolerated compared to other means of oxygen supplementation, such as a low-flow nasal cannula or a facemask [9]; further, patients can tolerate HFNO with a flow rate of up to 100 L/min without experiencing any discomfort, and some may even fall asleep [4].

HFNO has potential contraindications, including in cases involving severe nasal obstruction, copious nasal bleeding, recent nasal trauma, recent nasal surgery, significantly raised intracranial pressure, and base-of-skull fractures [10].

Use for anesthesia management

Recently, HFNO has been applied during anesthesia management, including during the anesthesia induction period and intraoperative period (Fig. 1). For this purpose, a system with different characteristics (Optiflow™; Fisher & Paykel Healthcare, New Zealand) has been developed. Optiflow consists of a flow meter, humidifier, heating system, heated non-condensing circuit, nasal cannula, head strap, and an oxygen connector for gas supply (Fig. 2). It is different from the Airvo system (Airvo™ system, Fisher & Paykel Healthcare Ltd., New Zealand) in its use in the ICU as the FiO_2 is fixed at 1.0 in order to facilitate the installation of the device within 2–3 min [11]. The oxygen flow rate can be increased to up to 70 L/min, which is more than that of Airvo (2–60 L/min). Due to the FiO_2 of 1.0 and its higher flow rate, Optiflow is mostly indicated for adults and children who weigh more than 10 kg. Airvo is more appropriate than Optiflow for children who weigh less than 10 kg due to the proper titration of FiO_2 to less than 1.0 (range: 21–100%) and the flow rate of less than 20 L/min. The heating and active humidifying of oxygen flow performed in Optiflow are similar to those in Airvo (37℃ and 44 mgH_2O/L). It is recommended that this equipment be turned on approximately 5 min before its use to ensure adequate humidification and heating [10].

Conventional Oxygenation Methods

When general anesthesia is induced and a neuromuscular blocking agent is administered, the risk of hypoxemia arises after the induction of anesthesia if the facemask ventilation is inadequate and if tracheal intubation is difficult or has failed. In the case of difficult oxygenation during the induction of anesthesia, a high risk of severe complications, such as hemodynamic instability, dysrhythmias, hypoxic brain injury, cardiac arrest, and even death, develops [12]. One effective method to minimize hypoxemia-related complications during the induction of anesthesia is adequate oxygenation.

The oxygenation process during the induction of anesthesia can be divided into 2 phases based on the time points at which they are performed: preoxygenation and peroxygenation. Pre-

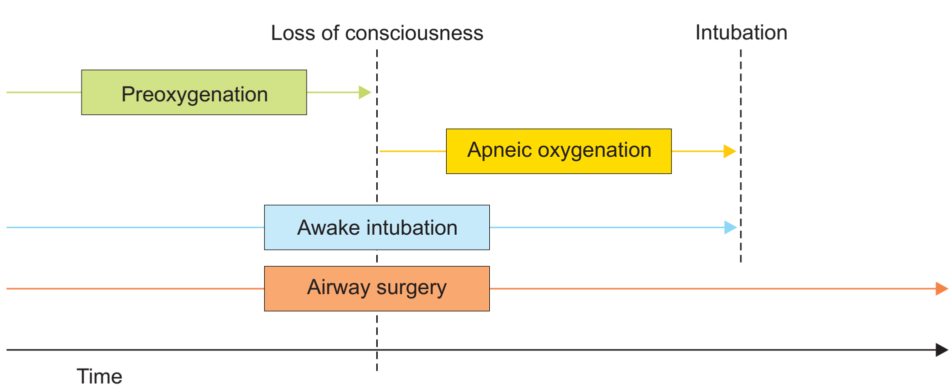

Fig. 1. Recent areas of use for high-flow nasal oxygenation, including during the anesthetic induction period and intraoperative period.

Fig. 2. Equipment for high-flow nasal oxygenation (Optiflow™, Fisher & Paykel Healthcare, New Zealand). (A) Optiflow™ consists of a flow meter, humidifier, heating system, heated non-condensing circuit, nasal cannula, head strap, and an oxygen connector for gas supply. (B) Nasal cannula. (C) Humidifier and heating system (© Fisher & Paykel Healthcare 2018. Used with permission).

oxygenation is defined as the administration of oxygen before the induction of anesthesia, and its purpose is to maximize the amount of a 'safe' apnea time (apnea time without hypoxemia) after the induction of anesthesia and to delay the onset of hypoxemia if airway management is unexpectedly difficult [12,13]. Peroxygenation is the oxygenation performed from the time point at which anesthesia is induced until when the airway is completely secured. After the induction of anesthesia, a patient's spontaneous breathing can either be maintained or stopped. In the latter case, the usual method is the application of intermittent positive pressure ventilation via a facemask. If this is not possible, an alternative method is the insufflation of oxygen into the pharyngeal cavity, and this method is called 'apneic oxygenation.'

Preoxygenation via a facemask

For adults, the conventional method of preoxygenation is to provide oxygen using an FiO_2 of 1.0 with a flow rate of 10–12 L/min through a tightly fitting facemask placed over a patient's nose and mouth [14,15]. The duration of preoxygenation should be titrated to denitrogenate the expiratory reserve and residual lung volume [16]. It is recommended to then confirm adequate preoxygenation via an end-tidal oxygen partial pressure (EtO_2) that exceeds 90%. In healthy adults, this endpoint can be achieved within 3–5 min when using tidal volume breathing through a facemask [17].

During preoxygenation, the method via which the patient breathes is crucial, and this affects the time needed for adequate oxygenation [16]. The 2 most representative methods are tidal volume breathing for 3 min and vital capacity breathing for 8 breaths within 60 s [18]. Adequate preoxygenation enables a healthy adult to endure apnea for approximately 7–10 min without developing hypoxemia [18].

Apneic oxygenation

Apneic oxygenation can be employed to further delay the onset of desaturation. Employing apneic oxygenation can result in additional time to consider and attempt alternative airway management options when the airway cannot easily be secured. While the patient is in this less stressful condition, it is critical for the physician to focus on preventing an emergency situation and on making the right decision for the patient's safety.

The concept of apneic oxygenation was established in 1908.[1)] The underlying physiology involves the passive movement of oxygen from the nasopharynx or the oropharynx to the alveoli; consequently, oxygen is taken up into the bloodstream even without active lung expansion [19,20]. This gas movement occurs because oxygen and carbon dioxide differ in the flow rates associated with their absorption and excretion between the alveoli and bloodstream (O_2: 250 ml/min and CO_2: 8–20 ml/min). This creates a sub-atmospheric pressure in the alveoli and a pressure gradient between the upper airway and the alveoli. Owing to this, oxygen is drawn from the pharynx into the alveoli. Therefore, if oxygenation were insufflated through the nasal or oral (buccal) route, it would prevent rapid desaturation even when a patient is apneic [21]. There are several available devices, such as nasal prongs, nasopharyngeal catheters, oropharyngeal catheters, an adapted Ring-Adair-Elwin (RAE) tube, and a modified laryngoscope, that currently exist for this purpose.

Oxygenation insufflation via a nasal cannula or prongs

Apneic oxygenation through a nasal catheter or via prongs, with an oxygen flow rate of 3–10 L/min, is generally useful in delaying desaturation in adult patients with physical statuses of American Society of Anesthesiologists (ASA) 1 or 2 [22]. In a retrospective study involving 728 patients [23], the incidence of desaturation (peripheral capillary oxygen saturation [SpO_2] < 93%) was decreased from 23% to 17% by the implementation of apneic oxygenation (with an oxygen flow rate of 15 L/min) via a nasal cannula. Likewise, in a study involving 127 patients with intracranial hemorrhage who required rapid-sequence induction of anesthesia in the emergency department [24], nasal prongs with an oxygen flow of 5–15 L/min during apnea reduced the incidence of desaturation (SpO_2 < 90%) from 29% to 7%. In obese patients (with a mean body mass index [BMI]: 31.2 kg/m^2), nasal prongs with an oxygen flow of 5 L/min extended the safe apnea time (SpO_2 ≥ 95%) from 3.5 to 5.3 min [25]. An oxygen flow of 10 L/min via nasal prongs together with an oxygen flow of 15 L/min via a facemask for 3 min increased the EtO_2 even in the case of a gas leakage around the facemask [26].

Oxygenation insufflation via a pharyngeal tube

A previous study [27] involving 56 adult patients classified as ASA 1–2 demonstrated that the administration of 5 L/min of oxygen via a nasopharyngeal catheter was a superior method in preventing desaturation compared to providing oxygenation via nasal prongs; the possible reason for this is that a nasopharyngeal catheter delivers oxygen more effectively to the alveoli because of the shorter distance from the oxygen outlet to the laryngeal inlet. The insufflation of oxygen at a flow rate of 10 L/min via a RAE tube with its tip placed into the oral cavity (buccal route) extended the median safe apnea time (tracheal oxygen concentrations > 94%) from 447 to 750 s in adult patients [28]. However, in 1 out of 10 patients, the SpO_2 decreased to less than 95% at the 9.5 min time point, and in another patient, the SpO_2 fell to less than 50% due to the soft tissues occluding the tip of the RAE tube [28]. A similar study was performed on obese patients with BMIs of 30–40 kg/m^2 in which apneic oxygenation with a flow rate of 10 L/min via a RAE tube having an internal diameter of 3.5 mm extended the median safe apnea time (SpO_2 ≥ 95%) from 296–750 s [29]. In infants and small children without cardiopulmonary diseases, oxygen insufflation at a rate of 4 L/min through a tube attached to the side channel of a videolaryngoscope extended the safe apnea time (SpO_2 ≥ 95%) by an average of 30 s (mean time: from 131 to 166 s) [30].

Limitations of conventional apneic oxygenation

Apneic oxygenation devices that provide oxygen at a flow rate of less than 15 L/min have several limitations. First, the resulting FiO_2 is unpredictable and limited due to the entrainment of room air [21]. Second, the airflow is cold and dry, impairing the mucociliary function and thereby leading to a risk of triggering bronchoconstriction. Third, the tip of a nasopharyngeal catheter or of a RAE tube can be misplaced or occluded by the surrounding tissues, thereby resulting in unexpected desaturation. Fourth, oxygen insufflation via a tube that is attached to the side channel of a laryngoscope can be performed only when the laryngoscope is placed in the patient's oropharynx. Lastly, when oxygen insufflation is performed while the patient is apneic, the clearance of carbon dioxide from the body cannot be expected [31].

HFNO during the Induction of Anesthesia

The efficacy of HFNO therapy in extending the safe apnea time before the airway is secured has been examined via several clinical studies, the focus of which could be categorized into the following topics: preoxygenation, induction of general anesthesia, rapid-sequence induction, and awake tracheal intubation (Table 1).

Preoxygenation

Non-obese adults

One of the benefits of HFNO is that it can easily and comfortably be applied to a patient who is awake until anesthesia is induced. A study compared HFNO with an oxygen flow of 60 L/min for 3 min with oxygenation via a facemask (with an oxygen

[1)] Volhard F. Uber kunstliche Atmung durch Ventilation der Trachea und eine einfache Vorrichtung zur hytmischen kunstlichen Atmung. München Medizinische Wochenschrift 1908; 55: 209-11.

Table 1. Characteristics of the Clinical Studies on High-flow Nasal Oxygenation (HFNO) Performed during the Induction of Anesthesia

Year, author, design	Number of patients, location, inclusion (I), exclusion (E)	Intervention	Comparator	Outcome and results, Intervention group (I), Comparator (C)
Preoxygenation				
Pillai et al. (2016), prospective study [32]	(n = 10) I: healthy adult volunteers E: respiratory or cardiac disease	(n = 10) OIA: HFNO at 60 L/min for 3 min (with mouth closed and open)	(n = 10) OIA: FM at 10 L/min for 3 min	1) EtO_2, mean (SD) (P = 0.001): I (mouth closed): 85.6 (6.4) kPa I (mouth open): 48.7 (26.4) kPa C: 88.5 (6.2) kPa 2) Transcutaneous oxygen partial pressures, mean (SD) (P = 0.03): I (mouth closed): 36.4 (6.5) kPa I (mouth open): 25.5 (15.7) kPa C: 34.6 (5.4) kPa
Ang et al. (2017), prospective pilot study [33]	(n = 21) I: healthy adult volunteers	(n = 21) OIA: HFNO at 70 L/min for 30, 60, 90, 120, 150, and 180 s	No control	1) EtO_2, median (IQR) [range]: I (30 s): 72% (66–79%) [45–82%] I (60 s): 79% (71–86%) [65–89%] I (90 s): 84% (77–88%) [64–91%] I (120 s): 87% (80–91%) [72– 93%] I (150 s): 88% (83–90%) [75–94%] I (180 s): 86% (84–90%) [78–92%]
Heinrich et al. (2014), prospective RCT [39]	(n = 33) OR I: morbidly obese adult patients scheduled for laparoscopic bariatric surgery. (BMI ≥ 35 kg/m^2) E: patients with severe pulmonary disorder, known or anticipated difficult airway	(n = 11) OIA: HFNO at 50 L/min with FiO_2 of 1.0 for 7 min (mouth closed)	(n = 11) OIA: FM at 12 L/min with FiO_2 of 1.0 for 7 min	1) PaO_2, median (IQR): I: 380 (339–443) mmHg C: 337 (295–390) mmHg
Hengen et al. (2017), case report [11]	(n = 1) OR I: 27-year-old non-obese pregnant patient with acute respiratory distress syndrome and heart failure.	(n = 1) OIA: HFNO of 70 L/min with FiO_2 of 1.0 for 5 min. OIS, OIL: HFNO of 70 L/min with FiO_2 of 1.0	No control	1) SpO_2: 98% during endotracheal intubation.
Tan et al. (2019), prospective observational study [35]	(n = 73) I: ASA 2 pregnant women E: Patients with significant nasal pathology, severe cardiac or respiratory disease, pre-eclampsia, sepsis	(n = 73) OIA: HFNO at 30 L/min for 30 s, then at 50 L/min for 150 s. (deep breathing, with mouth closed)	No control	1) EtO_2, median (IQR) [range]: I: 91% (83–93%) [58–96%]

Table 1. Continued 1

Year, author, design	Number of patients, location, inclusion (I), exclusion (E)	Intervention	Comparator	Outcome and results, Intervention group (I), Comparator (C)
Apneic oxygenation				
Ng et al. (2018), prospective RCT [10]	(n = 48) OR I: ASA 1–3 adult patients E: Patients with BMI > 35 kg/m^2, known or anticipated difficult airway, rapid sequence induction, significant raised intracranial pressure, active nasal bleeding, base of skull fracture	(n = 24) OIA: HFNO at 30 L/min for 30 s, then at 50 L/min for 270 s	(n = 24) OIA: FM 10 L/min for 5 min.	1) PaO_2, median (IQR) [range] (P = 0.01): I: 471 (429–516) [185–550] mmHg C: 357 (324–450) [183–550] mmHg
Lee et al. (2018), case report [44]	(n = 1) Adult Patients with emergent endotracheal intubation for acute epiglottitis	(n = 1) OIA: HFNO at 50 L/min with FiO_2 of 1.0 OIS, OIL: HFNO at 70 L/min with FiO_2 of 1.0 (Spontaneous respiration, no neuromuscular relaxation)	No control	$SpO_2 \geq 96\%$ $EtCO_2$: 39 mmHg
Humphreys et al. (2017), prospective RCT [46]	(n = 48) OR I: healthy children (age: 0–6 months, 7–24 months, 2–5 yr and 6–10 yr old)	(n = 24) OIS: bag-mask ventilation for 3 min. OIL: HFNO 0–15 kg, 2 L/kg/min; 15–30 kg, 35 L/min; 30–50 kg, 40 L/min; and > 50 kg, 50 L/min	(n = 24) OIS: bag-mask ventilation for 3 min OIL: no oxygenation	1) Apnea time mean (P < 0.001): I: 192 s (0–6 months), 237 s (7–24 months), 320 s (2–5 yr), 430 s (6–10 yr). C: 109.2 s (0–6 months), 147.3 s (7–24 months), 190.5 s (2–5 yr), 260.8 s (6–10 yr). 2) SpO_2, mean [range]: I: 99.6% [97–100%] C: 92% [92%]
Riva et al. (2018), prospective RCT [47]	(n = 60) OR I: ASA 1–2 children (age: 1–6 yr, weight: 10–20 kg) E: Patients with known or anticipated difficult airway, congenital heart or lung disease, obesity (BMI > 30 kg/m^2), risk of aspiration	(n = 20, FiO_2 1.0) OIS: bag-mask ventilation OIL: HFNO at 2 L/kg/min with FiO_2 of 1.0 (n = 20, FiO_2 0.3) OIS: bag-mask ventilation OIL: HFNO at 2 L/kg/min with FiO_2 of 0.3	(n = 20) OIS: bag-mask ventilation OIL: HFNO 0.2 at L/kg/min with FiO_2 of 1.0	1) Apnea time, median (IQR) [range] (P < 0.001): I (FiO_2 1.0): 7.6 (6.2–9.1) [5.2–10.0] min I (FiO_2 0.3): 3.0 (2.4–3.7) [0.2–5.3] min C: 6.9 (5.7–7.8) [2.8–10.0] min
Rapid sequence induction				
Lodenius et al. (2018), prospective RCT [36]	(n = 80) OR I: Adult patients who required rapid sequence induction E: Patients with BMI > 35 kg/m^2	(n = 40) OIA: HFNO at 40 L/min, then at 70 L/min with FiO_2 of 1.0 for 3 min. OIS, OIL: HFNO at 70 L/min with FiO_2 of 1.0	(n = 40) OIA: FM at 10 L/min with FiO_2 of 1.0 for 3 min. OIS: FM at 10 L/min, no bag-mask ventilation. OIL: no oxygenation.	1) lowest SpO_2, median (IQR) [range] (P = 0.097): I: 99% (99–100%) [96–100%] C: 99% (97–100%) [70–100%]
Mir et al. (2017), prospective RCT [48]	(n = 40) OR I: Adult patients who required rapid sequence induction E: Patients with severe respiratory disease	(n = 20) OIA: HFNO at 30 L/min, then at 70 L/min for 3 min. OIS, OIL: HFNO at 70 L/min	(n = 20) OIA: FM at 12 L/min for 3 min. OIS: FM at 12 L/min, no bag-mask ventilation. OIL: no oxygenation.	1) PaO_2, mean (SD) (P = 0.722): I: 43.7 (15.2) kPa C: 41.9 (16.2) kPa

Table 1. Continued 2

Year, author, design	Number of patients, location, inclusion (I), exclusion (E)	Intervention	Comparator	Outcome and results, Intervention group (I), Comparator (C)
Miguel-Montanes et al. (2015), prospective before-after study [52]	(n = 101) ICU I: Adult patients who required rapid sequence induction E: Patients with cardiac arrest, severe hypoxemia (defined as SpO_2 < 95% under a NRM with an oxygen flow of 15 L/min), patients already receiving HFNO, and patients under NIV	(n = 51) OIA: HFNO at 60 L/min with FiO_2 of 1.0 for 3 min OIS, OIL: HFNO at 60 L/min with FiO_2 of 1.0	(n = 50) OIA: NRM at 15 L/min for 3 min. OIS: NRM at 15 L/min OIL: nasopharyngeal catheter at 6 L/min	1) lowest SpO_2, median (IQR) ($P < 0.0001$): I: 100% (95–100%) C: 94% (83–98.5%)
Vourc'h et al. (2015), prospective RCT [55]	(n = 119) ICU I: Adult patients who required rapid sequence induction with acute hypoxemic respiratory failure E: Patients with cardiac arrest, asphyxia, nasopharyngeal obstacle, grade 4 glottis exposure on the Cormack–Lehane scale	(n = 62) OIA: HFNO at 60 L/min with FiO_2 of 1.0 for 4 min OIS, OIL: HFNO of 60 L/min with FiO_2 of 1.0	(n = 57) OIA: FM at 15 L/min for 4 min OIS: FM at 15 L/min OIL: no oxygenation	1) lowest SpO_2, median (IQR) ($P = 0.44$): I: 91.5 % (80–96%) C: 89.5 % (81–95%)
Simon et al. (2016), prospective RCT [34]	(n = 40) ICU I: Adult patients who required rapid sequence induction with hypoxemic respiratory failure E: Patients with nasopharyngeal obstruction or blockage, suspected or known difficult airway	(n = 20) OIA: HFNO of 50 L/min with FiO_2 of 1.0 OIS, OIL: HFNO of 50 L/min with of FiO_2 1.0	(n = 20) OIA: bag-valve mask at 10 L/min OIS: bag-valve mask at 10 L/min OIL: no oxygenation	1) lowest SpO_2, mean (SD) ($P = 0.56$): I: 89 (18)% C: 86 (11)%
Jabor et al. (2016), prospective RCT [56]	(n = 49) ICU I: Adult patients who required rapid sequence induction with acute hypoxemic respiratory failure E: Patients with cardiac arrest, nasopharyngeal obstruction, usual contraindications to NIV	(n = 25) OIA: HFNO of 60 L/min with FiO_2 of 1.0 with NIV for 4 min OIS: HFNO at 60 L/min with FiO_2 of 1.0 with NIV OIL: HFNO at 60 L/min with FiO_2 of 1.0	(n = 24) OIA: NIV with FiO_2 of 1.0 for 4 min OIS: NIV with FiO_2 of 1.0 OIL: no oxygenation.	1) lowest SpO_2, median (IQR) ($P = 0.029$): I: 100% (95–100) % C: 96% (92–99) %
Doyle et al. (2016), prospective observational study [37]	(n = 71) ICU, OR, ED I: Adult patients requiring intubation	(n = 71) OIA: HFNO at 60 L/min for 3 min. OIS, OIL: HFNO at 60 L/min	No control	1) Incidence of desaturation (reduction of SpO_2 > 10%): I: 5 patients (7%)

ASA: American Society of Anesthesiologists, BMI: body mass index, FiO_2: fraction of inspired oxygen, FM: face mask oxygenation, HFNO: high-flow nasal oxygenation, ICU: intensive care unit, IQR: interquartile range, NIV: non-invasive ventilation, NRM: non-rebreathing bag reservoir face mask, OIA: oxygenation-in-awake, OIL: oxygenation-in-laryngoscopy, OIS: oxygenation-in-sedative state, OR: operating room, PaO_2: partial pressure of arterial oxygen, RCT: randomized controlled trial, SpO_2: peripheral capillary oxygen saturation, SD: standard deviation.

flow of 10 L/min) in 10 adult volunteers who were awake [32]. The resulting mean EtO_2 was similar between both techniques (86 kPa for HFNO and 89 kPa for a facemask). Nevertheless, in the case of HFNO, the EtO_2 decreased to 49 kPa when the volunteers opened their mouths, indicating that HFNO may be effective only with the mouth closed.

In another observational study, HFNO with an oxygen flow of 70 L/min was applied to 21 adult volunteers who were awake, and it was observed that while the volunteers were closing their mouths, the EtO_2 increased from 14–17% to 78–92% in 3 min [33]. Nevertheless, in half of the volunteers, the EtO_2 did not reach 90%. In addition, 1 patient experienced discomfort, and the test was stopped midway; further, an additional 4 patients reported experiencing moderate discomfort (5 or 6 on a visual analogue scale). Although it may be technically difficult to measure the EtO_2 accurately during HFNO, it is also possible that HFNO may not reliably increase the EtO_2 during preoxygenation for 3 min. In addition, patients in respiratory distress situations inevitably need to breathe with an open mouth, and it may be difficult for them to follow instructions requiring them to close their mouths [34]. The optimal parameters for the application of HFNO, such as the duration of preoxygenation, breathing pattern, or mouth status, need to be determined. In reported studies, different durations, ranging between 3–5 min, of HFNO were applied before the start of anesthesia induction [10,32,35–37]. To determine the optimal preoxygenation time with HFNO, apart from the EtO_2, new criteria, such as the oxygen reserve index sensor, should be considered in future clinical trials.

Obese adults

In obese patients, when preoxygenation is carried out through a facemask, the safe apnea time period is as short as 1–3 min following preoxygenation compared with 7–10 min in healthy adult patients [18,38]. This is due to obesity-related physiological changes such as decreased functional residual capacity, increased oxygen consumption, and increased closing volume [15]. In a study involving 33 morbidly obese patients (BMI ≥ 35 kg/m^2) [39], HFNO at a flow rate of 50 L/min with the patient's mouth closed was superior to facemask oxygenation in achieving a high arterial partial pressure of oxygen (PaO_2). After 3 min of preoxygenation with the patient in a 30° head-up position, the median PaO_2 was 380 mmHg in the HFNO group and 337 mmHg in the facemask group. None of the patients developed complications due to epistaxis or gastric aspiration when using HFNO. Therefore, in obese patients, the efficacy of HFNO is increased by placing the patient in a head-up position.

Pregnant women

In obstetric patients, it is particularly important to make sure that the EtO_2 reaches over 90% by employing at least 3 min of tidal volume breathing of 100% oxygen [19,40] because the rate at which difficult intubation occurs in these patients may be 10 times higher than in the general population [12,41]. In addition, the safe apnea time period is relatively short due to several pregnancy-related changes such as airway edema, decreased functional residual capacity, increased oxygen consumption, and a higher risk of aspiration, as well as due to emergency surgery [40].

A computational model that simulates the effects of apneic oxygenation during rapid-sequence induction of anesthesia in obstetric women has indicated that the increase in FiO_2 to up to 1.0 extends the safe apnea time [42]. The successful use of HFNO in a pregnant woman with severe cardiopulmonary disease has been reported in the case of a 27-year-old pregnant woman with acute respiratory distress syndrome and heart failure who required an emergency Cesarean section [11]. The patient had dyspnea and exhibited significant mouth breathing, and her SpO_2 was 80%. Oxygen at a flow rate of 9 L/min via a facemask increased the SpO_2 to 95%, and HFNO at a flow rate of 70 L/min with an FiO_2 of 1.0 further increased the SpO_2 to 98% within 5 min even though the patient breathed predominantly through her mouth. After the induction of anesthesia, tracheal intubation was successfully performed with the SpO_2 maintained at 98%.

In contrast, the results of another study have cast a doubt on the efficacy of HFNO [35] in pregnant women: following HFNO for 3 min (30 L/min for 30 s, followed by 50 L/min for 150 s), an EtO_2 of 90% was achieved in merely 44 out of 73 (60%) pregnant women. In addition, although HFNO received similar scores associated with the comfort of its use to those of a facemask, only 56% of women preferred HFNO to the facemask. These results are similar to those associated with non-pregnant patients.

HFNO for apneic oxygenation

After the induction of anesthesia and a neuromuscular blockade, oxygenation is usually performed by intermittent positive pressure ventilation via a facemask. When a facemask is used, the mask needs to be removed while attempting tracheal intubations, and thus, no oxygen is supplied during these attempts. If the time taken for tracheal intubation is prolonged and if difficulties, such as in advancing the tracheal tube over a fiber-optic bronchoscope (which has successfully been inserted into the trachea), are encountered while performing the mask ventilation, the risk of hypoxemia arises. Apneic oxygenation may be performed by the insufflation of oxygen through a RAE tube, a nasopharyngeal airway, or a short tracheal tube.

With HFNO, the nasal cannula does not need to be removed during attempts at laryngoscopy or fiber-optic bronchoscopy, or during the insertion of a supraglottic airway and this increases the stability of the oxygenation. Moreover, there is a low probability of the occurrence of problems that are associated with the incorrect positioning of the device, which are more likely to occur with a buccal RAE tube. This prevents the need for clinicians to abandon ongoing intubation attempts too early due to the occurrence of desaturation, and it allows for sufficient time for them to focus on performing the tracheal intubation and on any maneuvers required [43]. In addition, the nasal cannula used for HFNO does not interfere with the application of a facemask when additional mask ventilation is needed.

In adults

In 48 neurosurgical adult patients [10], the efficacy in increasing the PaO_2 between HFNO with an oxygen flow of 50 L/min and an oxygen flow of 10 L/min through a facemask was compared. After 5 min of preoxygenation, the median PaO_2 was significantly higher in the case of HFNO (471 mmHg) than in that of facemask oxygenation (357 mmHg). However, after the induction of anesthesia, the PaO_2 decreased significantly in the HFNO group but not in the facemask group in which bag-mask ventilation was performed. This suggests that HFNO is more efficient than facemask oxygenation in ensuring a high PaO_2 before the induction of anesthesia, but HFNO is less effective than facemask ventilation in maintaining a high PaO_2. Nevertheless, 7 patients in the facemask group required the use of airway adjuncts such as oropharyngeal airways, but none of the patients in the HFNO group required them, suggesting that HFNO is more easily incorporated.

A male patient who had acute epiglottitis requiring emergency tracheal intubation [44] exhibited the following characteristics: an airway assessed as a Mallampati score of 2, a thyromental distance of > 6 cm, poor dentition, adequate mouth opening and neck range of movement, and an easily palpable cricothyroid membrane. Despite the administration of intravenous antibiotics and steroids, the airway obstruction progressed rapidly and required airway intervention. HFNO at a flow rate of 70 L/min was used in combination with the target-controlled infusion (TCI) of propofol, thereby allowing spontaneous breathing. The minimum oxygen saturation was 96% following tracheal intubation.

Oxygenation can be more difficult to perform in obese patients because the incidences of difficult mask ventilation and tracheal intubation may increase with obesity. The head-up position is helpful to maximize the efficacy of apneic oxygenation by reducing atelectasis and the subsequent pulmonary shunting [12,29]. Another study conducted on obese patients demonstrated that HFNO at a flow rate of 50 L/min resulted in the highest PaO_2 value after 3–5 min of preoxygenation in morbidly obese patients and that the PaO_2 decreased as the preoxygenation duration was extended up to 7 min [39]. Therefore, the appropriate duration of preoxygenation using HFNO remains to be determined.

In children

Compared to adults, children are more prone to the risk of rapid desaturation in the order of seconds after the cessation of ventilation due to their decreased functional residual capacity, higher oxygen consumption, increased closing capacity, and higher risk of airway collapse [17,45]. A study has demonstrated that the mean desaturation time until the SpO_2 reached 90% was significantly shorter in children (160 s) than in adolescents (382 s), and it was substantially shorter in infants (97 s). In fact, the incidence of desaturation is common in children (4–10% during induction of anesthesia and 20% during tracheal intubation) [18]. Therefore, in children, optimal oxygenation strategies are crucial in order to extend the duration of safe apnea.

HFNO may extend the safe apnea time in children. In a study involving 48 children who were under 10 years with normal airways [46], in the facemask group, bag-valve ventilation was ceased and the jaw thrust was maintained whereas in the HFNO group, the flow rates of 2 L/kg/min, 35, 40, and 50 L/min were applied based on the body weight, and the jaw thrust method was performed during apnea. The main hypothesis was that the safe apnea time (time taken for the SpO_2 to reach 92%) in the case of HFNO would be more than double the length of the apnea time in the facemask group and the results confirm that this hypothesis was true.

In another study involving 60 children, aged 1–6 years, weighing 10–20 kg, HFNO at a flow rate of 2 L/kg/min with an FiO_2 of 1.0, HFNO at a flow rate of 2 L/kg/min with an FiO_2 of 0.3, and low-flow nasal oxygenation at a flow rate of 0.2 L/kg/min with an FiO_2 of 1.0 were compared [47]. Bag-valve mask ventilation was ceased when the target EtO_2 of > 90% was reached. Apnea was terminated when the SpO_2 was less than 95%, transcutaneous carbon dioxide ($tcCO_2$) reached 65 mmHg, or apnea duration reached 10 min. The SpO_2 had decreased to < 95% within 10 min in all the HFNO (FiO_2 0.3) patients and in 3 of the low-flow nasal oxygenation patients (17%), but it did not decrease in any of the HFNO (FiO_2 1.0) patients, indicating that HFNO at a flow rate of 2 L/kg/min with an FiO_2 of 0.3 is not effective. The $tcCO_2$ exceeded above 65 mmHg within 10 min in 16 (80%) HFNO patients with an FiO_2 of 1.0 and in 13 (72%) low-flow nasal oxygenation patients. In the case of HFNO with a flow rate of 2 L/kg/min and an FiO_2 of 1.0, the median safe apnea time was 7.6 min with a range of 5.2–10 min. Therefore, in children, HFNO with a flow rate of 2 L/kg/min and an FiO_2 of 1.0 can maintain the SpO_2 for 10 min; however, there is a higher risk of hypercapnea with this technique, and therefore, it may be useful for surgeries that last between 5–6 min. It is not known whether or not a higher flow rate (e.g., 4 L/kg/min) with an FiO_2 of less than 1.0 can be effective.

HFNO for rapid-sequence induction of anesthesia

In the operating rooms

HFNO may also have a potential role during rapid-sequence induction of anesthesia in the operating room. In a study involving 80 adults who were receiving rapid-sequence induction of anesthesia, the efficacy of oxygenation was compared between HFNO at a flow rate of 70 L/min and facemask oxygenation at a rate of 10 L/min [36]. The lowest SpO_2 up to 1 min after tracheal intubation was similar between the techniques, but the SpO_2 decreased to < 96% in 7 patients (18%) in the facemask group whereas this was not observed in the HFNO group. None of the patients developed complications, such as the regurgitation of gastric contents, and there was no significant difference in the duration of the safe apnea time between HFNO (median: 116 s) and facemask (median: 109 s).

In another study involving 40 adult patients receiving rapid-sequence induction of anesthesia for emergency surgery, the efficacy between HFNO at the rate of 70 L/min and facemask oxygenation at the rate of 12 L/min were compared [48]. In the HFNO group, HFNO was maintained throughout the induction period whereas in the facemask group, the jaw was kept thrust out without bag-mask ventilation. In all the patients, the trachea was intubated successfully and there were no significant differences in the PaO_2 between the groups. Nevertheless, it took significantly longer to intubate the trachea in the HFNO group (the mean of 248 s) than in the facemask group (123 s). The authors of the report state that this difference was not due to any apparent difference in procedural difficulty; however, the difference was quite marked. One of the reasons might be that the presence of a nasal cannula mechanically or psychologically facilitated a more careful time-consuming laryngoscopy and tracheal intubation.

These results indicate that HFNO with the jaw thrust is an efficient method to prevent desaturation within 3–4 min of apnea during rapid-sequence induction of anesthesia in adults even if cricoid pressure is being applied.

Outside the operating rooms

Securing the airway is frequently more difficult outside the operating rooms than inside [49,50]. This is because outside the operating room, the unstable physiological status of patients, such as being affected by a cardiopulmonary disease, having a low cardiac output, or being in hypermetabolic states, limits the efficiency of preoxygenation and peroxygenation. In addition, emergency procedures, poor planning, less skilled staff, and the inadequate availability of equipment increase the incidence of difficult intubation to up to approximately 12% [43,51,52]. Therefore, tracheal intubation is associated with a high incidence of hypoxemia, which is the most commonly associated complication (approximately 19–26%) [51,53] that is linked to hemodynamic deterioration, cardiac arrest, and death [12,54]. The incidence of death related to airway management has been reported to be 38-fold higher in the emergency department and 58-fold higher in the ICU than in the operating rooms [12].

Meta-analyses have shown that oxygenation through a nasal cannula at various flow rates is effective in preventing desaturation in patients who received emergency tracheal intubation [20,43]. In a study involving 101 adult patients who required rapid-sequence induction of anesthesia and intubation in the ICU [52], the efficacy of HFNO was compared with that of a non-rebreathing bag reservoir facemask combined with a nasopharyngeal catheter. For the HFNO group, HFNO at a flow rate of 60 L/min with an FiO_2 of 1.0 was used for 3 min before the induction of anesthesia (preoxygenation) and was continued after the induction of anesthesia and during tracheal intubation. For the facemask group, 15 L/min of oxygen was provided for at least 3 min before the induction of anesthesia, and after the induction, the facemask was removed, a nasal cannula was placed, and 6 L/min of oxygen was insufflated. The median of the lowest SpO_2 was significantly higher in the HFNO group (100%, range: 95–100%) than in facemask group (94%; 83–99%). Episodes of severe hypoxemia (SpO_2 < 80%) were significantly lower in the HFNO group (2%) than in facemask group (14%); further, 1 cardiac arrest due to hypoxemia occurred in the facemask group. A multivariate analysis indicated that HFNO was an independent factor that prevented severe hypoxemia.

Nevertheless, HNFO may not be effective in improving oxygenation when tracheal intubation is required in hypoxemic patients. In a study involving 119 patients who had acute hypoxemic respiratory failure that required rapid-sequence induction and intubation (respiratory rate > 30 breaths/min, FiO_2 requirement > 50%, PaO_2/FiO_2 < 300 mmHg) [55], either HFNO at a flow rate of 60 L/min with an FiO_2 of 1.0 or facemask oxygenation at a flow rate of 15 L/min was used. There was no significant difference in the lowest SpO_2 level (92% in HFNO group and 90% in facemask group) and in the occurrence of severe hypoxemia involving an SpO_2 < 80% during tracheal intubation (16 [26%] in the HFNO group and 13 [22%] in the facemask group).

Similarly, another study that compared the efficacy of HFNO at a flow rate of 50 L/min and that of bag-valve-mask ventilation at a flow rate of 10 L/min in 40 critically ill patients who suffered hypoxemic respiratory failure (PaO_2/FiO_2 < 300 mmHg) [34], the lowest mean SpO_2 during tracheal intubation and the occurrence of severe hypoxemia (SpO_2 < 80%) were similar between the groups.

In a report on 49 adult patients who required rapid-sequence induction due to severe acute hypoxemic respiratory failure in the ICU (respiratory rate > 30 breaths/min, FiO_2 requirement ≥ 50%, PaO_2/FiO_2 < 300 mmHg) [56], the efficacy of preoxygenation with HFNO at a flow rate of 60 L/min with an FiO_2 of 1.0 together with non-invasive ventilation was compared with that of non-invasive ventilation performed on its own. HFNO plus non-invasive ventilation resulted in improved oxygenation and less frequent episodes of desaturation (SpO_2 < 80%). Therefore, HFNO combined with non-invasive ventilation can reduce the incidence of severe hypoxemia during rapid-sequence induction of anesthesia in patients with severe acute hypoxemic respiratory failure.

In a prospective observational study that investigated the efficacy of HFNO at a flow rate of 60 L/min during emergency tracheal intubation in 71 adult patients in the ICU, in the operating room, or in the emergency department, the median (range) apnea time was 80 (30–480) s [37]. Significant desaturation (reduction in SpO_2 to > 10% after induction of anesthesia) occurred in 5 patients (7%) who underwent acute respiratory failure (2 patients) or who had difficulty maintaining airway patency during apnea (3 patients). There were no complications resulting from the use of HFNO.

In the ICU, patients' conditions in relation to their respiratory diseases and the techniques used in the control and intervention groups are varied. The intubation protocol including intubation equipment, patient positioning, preoxygenation approach, operators, and medications administered have not been standardized [57]. This may be a reason for the discrepancies among out-of-hospital studies. Moreover, the definitions of clinical outcomes vary between studies. For example, the standard that is taken into consideration to define hypoxemia is usually the SpO_2 value, which is the starting point of the steep slope on the oxygen dissociation curve of hemoglobin [58]. Nevertheless, desaturation can be defined differently, which may be another reason for the conflicting results. Therefore, the efficacy of apneic HFNO compared to that of low-flow nasal apneic oxygenation is still unclear in emergency airway management in the ICU [3,20]. At least it is now apparent that HFNO alone may not be beneficial to patients who suffer severe respiratory failure [34,55]. This may be because pulmonary shunting or easily collapsed airways diminish the benefits of HFNO. To overcome this limitation, other techniques that provide high positive airway pressure may be required [58].

Complications

Hypercapnea

One major potential problem in relation to apneic oxygenation via HFNO is excessive hypercapnea. A study has demonstrated that the partial pressure of carbon dioxide ($PaCO_2$) increased with the speed of 3 mmHg/min during apneic oxygenation via HFNO at a flow rate of 50 L/min [10]. The $PaCO_2$ was significantly higher during apnea with HFNO than during bag-mask ventilation, but the resultant rise in the $PaCO_2$ with HFNO seemed tolerable because the highest $PaCO_2$ value was approximately 65 mmHg after the completion of tracheal intubation. Flow rates of up to 70 L/min may be required to achieve the maximum clearance of carbon dioxide. In contrast, carbon dioxide accumulation was similar between HFNO and facemask preoxygenation during rapid-sequence induction during emergency surgery [36,48] potentially due to a short observation period and the increase in carbon dioxide at a more rapid rate during the first minute following the onset of apnea. The clearance of carbon dioxide during HFNO may be superior to that resulting from a low-flow oxygen delivery system [59].

In children aged up to 10 years [46], the mean $tcCO_2$ that was measured at the end of apnea was 62 mmHg (range 49–79 mmHg), and the mean rate of the increase in carbon dioxide was 2.4 mmHg/min (range 0.2–3.9 mmHg/min). However, the rate of increase in carbon dioxide was not significantly lower when HFNO was combined with the jaw thrust method compared to when jaw thrust was used in isolation during apnea. In a study involving children aged up to 6 years [47], the $tcCO_2$ increased at a median rate (range) of 4.1 (2.2–5.3) kPa/min in response to HFNO with an FiO_2 of 1.0, and the rate of increase in the $tcCO_2$ was similar to that observed in the low-flow nasal oxygenation group. It has also been demonstrated that the younger the child, the faster the increase in the $tcCO_2$ during apnea. These results imply that the efficiency in carbon dioxide clearance via HFNO is not prominent in children. This may be because the increase in carbon dioxide is higher in children than in adults and in younger children than in older children due to their higher metabolic demands.

The application of HFNO interrupts the earlier detection of a rise in carbon dioxide and of airway obstruction compared to when bag-mask ventilation is used. Therefore, the transcutaneous monitoring of carbon dioxide [10,46] and the use of oxygen reserve index sensors may help in minimizing this risk and in optimizing the utilization of HFNO.

Gastric insufflation

Gastric insufflation is a theoretical complication resulting from HFNO because HFNO generates positive airway pressure. The increase in the nasal flow rate to 10 L/min is known to cause a 1.2 cmH_2O increase in the nasopharyngeal airway pressure, as observed when healthy volunteers breathed with their mouths closed when HFNO was being used [4], and thus, the airway pressure would increase to around 3 cmH_2O at 30 L/min and to around 12 cmH_2O at 100 L/min.

No serious complications, such as gastric insufflation, regurgitation, or pulmonary aspiration of gastric contents, have so far been reported even in the case of morbidly obese patients [36,39]. The number of studies on this subject is still limited, and thus, the true risk of gastric insufflation associated with the use of HFNO during anesthesia remains to be elucidated.

Settings of HFNO for the induction of anesthesia

Flow rate

Reports on the use of HFNO have indicated various high-flow rates such as 50 L/min [10,34,35,39], 60 L/min [32,37,52,55,56], or 70 L/min [33,36,48]. One study has demonstrated that the median intratracheal FiO_2 significantly increased from 67% to 93% as the flow rate increased from 15 L/min to 45 L/min [60]. Similarly, another study has demonstrated that increasing the flow rate of HFNO from 10 L/min to 50 L/min can yield a higher FiO_2 [61]. Therefore, using a higher flow rate of greater than 50 L/min is advisable to obtain the maximal effects of oxygenation.

Generally, HFNO is well tolerated by patients who are awake [35,36], but some of them may experience moderate or severe discomfort when a flow of 50–70 L/min is used [10,33]. Therefore, it may be prudent to start HFNO with a relatively low flow rate (30–40 L/min) when a patient is awake and then to increase the flow rate (50–70 L/min). When a patient cannot tolerate a high flow, the flow should immediately be reduced to 30–40 L/min, and once the patient has lost consciousness, the flow should be increased back to 50–70 L/min [10,35,36,48]. Concerning children, the adequate flow rate has been indicated to be 2 L/kg/min for those weighing 0–15 (or 20) kg, 35 L/min for those weighing 15 (or 20) –30 kg, 40 L/min for those weighing 30–50 kg, and 50 L/min for those weighing > 50 kg [46,47].

FiO_2

As the FiO_2 increases, the safe apnea time gets extended. In addition, a study has demonstrated that an increase in the FiO_2 from 0.9 to 1.0 yielded a greater increase in the safe apnea time compared to an increase in the FiO_2 from 0.21 to 0.9 [62]. Therefore, the FiO_2 should usually be set to 1.0 in order to maximize the safe apnea time in adults including in morbidly obese patients [39] and in those requiring rapid-sequence induction of anesthesia [36,52].

In children, HFNO with an FiO_2 of 0.3 may not be as efficient in extending the safe apnea time when compared to HFNO with an FiO_2 of 1.0 [47]; therefore, when HFNO is used, the FiO_2 should be kept high.

Breathing method

There is still little evidence with regard to which breathing method is the best. In some studies, patients were asked to maintain normal breathing [32,33] whereas in other studies, deep breathing was preferred [35]. One clear characteristic is that the efficacy of HFNO in oxygenation is reduced when the patient's mouth is open [2]. In a study [63] in which HFNO with a flow rate of 35 L/min was applied in postoperative cardiac surgery adult patients, the mean nasopharyngeal positive airway pressure was 2.7 cmH_2O when the patient's mouth was closed whereas it was only 1.2 cmH_2O when the mouth was open. Similarly, in another study [64], the increase in the flow rates of HFNO resulted in increased mean airway pressures of 0.7 cmH_2O per every 10 L/min when the mouth was closed, and the increased rate of airway pressure significantly reduced to 0.4 cmH_2O when the mouth was open. Further [60], the median of mean airway pressure significantly increased from 0.4 cmH_2O to 2 cmH_2O as the oxygen flow was increased from 15 L/min to 45 L/min, but significantly decreased from 2 cmH_2O to 0.6 cmH_2O when the mouth was open. However, the FiO_2 was not significantly different between when the mouth was closed or open with HFNO at a flow rate of 45 L/min [60]. In a study in which the EtO_2 was measured during HFNO at a flow rate of 60 L/min [32], HFNO increased the EtO_2 when the patient's mouth was closed (86 kPa) whereas it failed to increase the EtO_2 when the patient's mouth was open (49 kPa).

Another crucial point to consider during HFNO is that the patency of the upper airway is essential to provide adequate oxygenation [17]. The patency of the upper airway needs to be maintained using a head tilt [37], jaw thrust [36,37,46–48], chin lift [36,37], or the insertion of a pharyngeal airway [47].

Theoretically, deep breathing through the nose with the mouth shut would be the best patient status for preoxygenation [32,33,35,39].

HFNO for Awake Intubation

Awake tracheal intubation is another technique for securing the airway for which HFNO may be valuable. Patients undergoing awake fiber-optic intubation are at risk of desaturation due to underlying airway diseases, obesity, or sudden complete airway obstruction that can be caused by oversedation or topicalization [65]. The use of HFNO has a theoretical advantage with regard to providing oxygenation during awake fiber-optic intubation. This was confirmed by an observational study involving 50 adult patients [66] in which HFNO at a flow rate of 50–70 L/min was used during awake fiber-optic intubation. HFNO increased the median (range) of SpO_2 from the baseline value of 98 (83–100)% to 100 (93–100)%, and none of the patients exhibited desaturation below the baseline SpO_2 during the procedure. The median (range) of the $EtCO_2$ was 4.8 (3.5–6.7) kPa after securing the airway. HFNO was also successfully used during surgical tracheostomy performed on a sedated patient with upper airway obstruction secondary to an infective acute leukemic mass [67].

HFNO for Airway Surgery

Upper airway surgery often requires repetitive tracheal intubations and extubations during the procedure to allow access to the surgical field and to allow the manipulation required. It is therefore necessary to use specialized methods to reduce stressful conditions by extending the safe apnea time and by preventing hypoxemia [68]. There are several oxygenation techniques for airway surgery, such as transtracheal or transglottic jet ventilation, controlled mechanical ventilation using a small sized tracheal tube, and intermittent apneic ventilation [69]. Among these techniques, jet ventilation is the least preferred compared to the other techniques due to a resulting higher risk of barotrauma. The ideal method may be the tubeless technique that enables an optimal view of the surgical field and prevents tracheal tube-related injuries to the airways. The use of HFNO is a revolutionary oxygenation technique for airway surgery and it may replace the use of a tracheal tube during laryngomicrosurgery (Table 2).

Reported use

Patel and Nouraei [59] were the first to report the use of HFNO during airway surgery. They used the technique in 25 adult patients who were undergoing hypopharyngeal or laryngotracheal surgeries, such as for benign laryngeal conditions, for obstructive sleep apnea, or for benign or malignant head and neck conditions. Their study included 12 obese patients and 9 patients with stridor. The median BMI (range) was 30 (18–52) kg/m^2. The median apnea time was 14 min, with the longest duration being 65 min. None of the patients exhibited desaturation, i.e., an SpO_2 of < 90%, when HFNO at a flow rate of 70 L/min was used. Further, none of the patients experienced complications, such as cardiac arrhythmia, due to an increase in carbon dioxide during apnea.

Booth et al. [70] employed a 'traditional' use of HFNO during airway surgery by maintaining spontaneous breathing. In 30 adult patients who underwent laryngotracheal surgeries due to laryngotracheal stenosis or papilloma, HFNO at a rate of 70 L/min was applied while anesthesia was maintained with TCI propofol, thereby maintaining spontaneous breathing. The median duration of spontaneous breathing (range) was 44 (18–100) min. Only 1 patient experienced desaturation due to a miscalculated remifentanil overdose, and tracheal intubation was required during the surgery. In another 3 patients, the SpO_2 decreased to less than 90% during laser surgery when the FiO_2 was reduced to 0.3. Nevertheless, the SpO_2 increased rapidly when the FiO_2 was increased back to 1.0.

In another report on 28 adult patients who were undergoing airway surgeries, apneic oxygenation was provided via a unique system called the Perioperative Insufflatory Nasal Therapy system at a flow rate of 80 L/min [71]. In 4 patients, the SpO_2 decreased to 85–90%, lasting for less than 2 min at several time points, following the injection of rocuronium. The oxygen saturation was increased by the jaw thrust method and by increasing the flow rate to 120 L/min following the removal of the suspension laryngoscope or the insertion of a supraglottic airway. A different HFNO system (Optiflow) has a maximal flow rate of only 70 L/min; therefore, the rescue technique of increasing the flow rate to up to 120 L/min is not feasible with this system.

HFNO has also been successfully used in patients with difficult airways. For example, in a 55-year-old male who had severe supraglottic-pharyngeal stenosis, HFNO with a flow rate of 70 L/min and an FiO_2 of 1.0 was applied, and the patient remained apneic for 26 min with the use of propofol, remifentanil, and rocuronium [72]. After the scar tissue was transected along the lateral epiglottic border resulting in the partial release of the stenotic lesion, the laser-safe tracheal tube was inserted through the opening. Until the time point at which the tracheal tube was inserted, the SpO_2 was maintained at greater than 90%. In another report on a male patient who was morbidly obese with a BMI 40 kg/m^2 and who had a neck circumference of 45 cm, mouth opening of 2 finger breaths, and Mallampati score of 4, HFNO at a flow rate of 60 L/min allowed for the performance of a 14-min long surgery without desaturation occurring [73].

HFNO may also be used in children, including in premature babies, who are undergoing airway surgeries. For example, a report describes the successful use of HFNO (at the flow rate of 2 L/kg/min) in more than 30 children (aged 6 days to 13 years) undergoing airway surgeries (e.g., aryepiglottoplasty, subglottic cyst excisions, tracheal dilatations, and endoscopic cricoid splints) [74]. The FiO_2 was titrated to maintain the SpO_2 at 95–99%, and spontaneous breathing was successfully preserved during surgery.

A study reported on a premature male baby who had a subglottic web after repeated tracheal intubations. He had severe inspiratory stridor that required laser resection and dilatation under general anesthesia [68]. Anesthesia was induced with sevoflurane and maintained with an infusion of propofol and remifentanil. Rocuronium was used to induce a full neuromuscular blockade, and an uncuffed tube was inserted. The surgeon placed the Parsons laryngoscope using the suspension apparatus. For the resection of the subglottic web, the trachea was extubated until the SpO_2 fell to 80%, following which it was re-intubated. The apnea time was 39 and 41 s; however, it could be increased to 95 and 160 s when HFNO with a flow rate of 4

Table 2. Characteristics of Clinical Studies on High-flow Nasal Oxygenation (HFNO) for Airway Surgery

Year, author, design	Number of patients	Inclusion	Apnea or spontaneous relaxation, neuromuscular relaxation	Oxygenation	Time of apnea or spontaneous respiration	SpO_2 and $EtCO_2$ or $PaCO_2$
Patel and Nouraei (2015), case series [59]	25	Adult Surgeries for laryngotracheal stenosis, vocal fold pathology and obstructive sleep apnea, and benign and malignant hypopharyngeal obstruction	Apnea. Rocuronium 0.5 mg/kg	Preoxygenation: HFNO at 70 L/min with FiO_2 of 1.0 for 10 min Peroxygenation: HFNO at 70 L/min with FiO_2 of 1.0	Median (IQR) [range]: 14 (9–19) [5–65] min	$SpO_2 \geq 90\%$ $EtCO_2$, mean (SD) [range]: 7.8 (2.4) [4.9–15.3] kPa.
Booth et al. (2017), case series [70]	30	Adult Elective microlaryngoscopic surgery	Spontaneous respiration No neuromuscular relaxation	Preoxygenation: HFNO at 30 L/min with FiO_2 of 1.0 for 1 min, then at 50 L/min for 2 min. Peroxygenation: HFNO at 70 L/min with FiO_2 of 1.0.	Median (IQR) [range]: 44 (40–49.5) [18–100] min	
Lyon and Callaghan (2017), case series [71]	28	Adult Laryngeal or tracheal surgeries	Apnea Rocuronium	Preoxygenation: HFNO at 80 L/min with FiO_2 of 1.0 for 3 min. Peroxygenation: HFNO at 80 L/min with FiO_2 of 1.0.	Median (IQR) [range]: 19 (15–24) [9–37] min	$SpO_2 \geq 85\%$ $EtCO_2$, median (IQR) [range]: 8.2 (7.2–9.4) [5.8–11.8] kPa.
Tam et al. (2017), case report [72]	1	Adult CO_2 laser release of supraglottic pharyngeal stenosis	Apnea Rocuronium and succinylcholine	Preoxygenation: HFNO at 35 L/min with FiO_2 of 1.0 for 3 min. Peroxygenation: HFNO at 70 L/min with FiO_2 of 1.0.	26 min	$SpO_2 \geq 90\%$
Lee and Quek (2018), case report [73]	1	Adult Morbid obesity Elective panendoscopy and biopsy of vocal cord lesion	Apnea Rocuronium 0.3 mg/kg	Preoxygenation: HFNO at 20 L/min, then at 60 L/min with FiO_2 of 1.0 for 15 min. Peroxygenation: HFNO at 60 L/min with FiO_2 of 1.0	14 min	$SpO_2 \geq 98\%$ $PaCO_2$: 60 mmHg
McCormack et al. (2017), case series [74]	> 30	Children	Spontaneous respiration No neuromuscular relaxation	Preoxygenation and peroxygenation: HFNO at 2 L/kg/min.	30–40 min	$tcCO_2$ 6.5–7 kPa
Riva et al. (2016), case report [68]	1	Premature baby boy weighed 4 kg with a corrected age between 43 and 46 weeks Laser resection and dilatation of subglottic web	Apnea Rocuronium	Peroxygenation: HFNO at 4 L/kg/min with FiO_2 of 0.3 or 1.0.	Range: (FiO_2 0.3) 95–160 s (FiO_2 1.0) 70–234 s	$SpO_2 \geq 80\%$ $EtCO_2$: 48–66 mmHg
Yang et al. (2018), case series [75]	23	Adult Elective laryngomicrosurgeries for vocal cord polyp, cyst, and laryngeal tumor biopsy.	Apnea. Succinylcholine 1.5 mg/kg	Preoxygenation: HFNO at 20 L/min with FiO_2 of 1.0 for 5 min. Peroxygenation: HFNO at 50 L/min with FiO_2 of 1.0.	Mean (SD): 24.1 (6.4) min	SpO_2, minimum and median: 72% and 100%
Humphreys et al. (2017), case series [76]	20	Children, age 5 days to 15 years Upper airway surgery or dynamic airway assessment	Spontaneous respiration No neuromuscular relaxation	Preoxygenation and peroxygenation: HFNO (0–12 kg) at 2 L/kg/min (13–15 kg) at 30 L/min (15–30 kg) at 35 L/min (30–50 kg) at 40 L/min (> 50 kg) at 50 L/min	Median [range]: 32 [3–61] min	SpO_2, minimum and mean: 77% and 96%

Table 2. Continued

Year, author, design	Number of patients	Inclusion	Apnea or spontaneous relaxation, neuromuscular relaxation	Oxygenation	Time of apnea or spontaneous respiration	SpO_2 and $EtCO_2$ or $PaCO_2$
Desai and Fowler (2017), case report [77]	1	Adult Emergent surgical tracheostomy due to parapharyngeal abscess	Spontaneous respiration No neuromuscular relaxation	Preoxygenation: HFNO at 30 L/min with FiO_2 of 1.0 for 15 min. Peroxygenation: HFNO at 30 L/min with FiO_2 of 1.0.	40 min	$SpO_2 \geq 89\%$
Ebeling and Riccio (2018), case series [78]	3	Adult (1) Microdebridement of bilateral true vocal cord polyps and Reinke's edema (2) Tracheal balloon dilation of subglottis stenosis (3) Biopsy of vocal cord lesion	Apnea Rocuronium	Preoxygenation: HFNO at 60 L/min with FiO_2 of 1.0 for 5 min. Peroxygenation: HFNO at 60 L/min with FiO_2 of 1.0.	(1) 15 min (2) 15 min (3) 40 min	$SpO_2 \geq 97\%$ (1) $tcCO_2$ 70 mmHg (2) $tcCO_2$ 70 mmHg (3) $tcCO_2$ 89.4 mmHg
Gustafsson et al. (2017), case series [79]	31	Adult Elective short laryngeal procedures, such as microlaryngoscopy	Apnea Rocuronium 0.6 mg/kg	Preoxygenation: HFNO at 40 L/min with FiO_2 of 1.0 for 3 min. Peroxygenation: HFNO at 70 L/min with FiO_2 of 1.0.	Mean (SD): 22.5 (4.5) min	$SpO_2 > 91\%$

$EtCO_2$: end-tidal CO_2, FiO_2: fraction of inspired oxygen, HFNO: high flow nasal oxygenation, IQR: interquartile range, PaO_2: partial pressure of arterial oxygen, SpO_2: peripheral capillary oxygen saturation, SD: Standard deviation, $tcCO_2$: transcutaneous CO_2.

L/kg/min and an FiO_2 of 0.3 was applied. When HFNO with an FiO_2 of 1.0 was used, the apnea time extended to over 4 min. Following 2–4 min of apnea during HFNO, the $EtCO_2$ was measured as 48–66 mmHg. This case report indicates that HFNO is efficient in extending the safe apnea time in an infant undergoing laryngeal repair even with a low FiO_2 of 0.3.

Complications

Several complications associated with the use of HFNO during airway surgery have been reported.

Hypoxemia

One of the major complications associated with the use of HFNO during airway surgeries is the failure to maintain oxygenation. For example, in a report on the use of HFNO at a flow rate of 50 L/min during laryngomicrosurgery [75], the SpO_2 decreased to 72% in 1 of the 23 studied patients, and tracheal intubation was temporarily required. In this case, HFNO was restarted, and the surgery could be completed without further complications.

In 20 infants and children (aged between 5 days to 15 years) who were undergoing upper airway surgeries or dynamic airway assessments lasting between 3–61 min, oxygenation was maintained via HFNO, but 1 of the neonates required rescue tracheal intubation at 3 min following apnea due to desaturation of 77% [76]. In a 35-year-old man with a parapharyngeal mass and a narrowing of the trachea to 4 mm, an emergency surgical tracheostomy was performed under sedation while HFNO at a flow rate of 30 L/min was applied with the patient in a 40° head-up position [77]. When the sedation level was deepened, the respiratory rate decreased, and complete airway obstruction occurred. The SpO_2 rapidly decreased to 89%, and an immediate tracheostomy was required. This case indicates that if the airway is obstructed, HFNO could delay but not prevent the onset of hypoxemia.

Excessive hypercapnea

Hypercapnea is another major complication that occurs during airway surgeries because unlike short periods of apneic oxygenation before tracheal intubation, apneic oxygenation during airway surgery could last for as long as 40–60 min. There have been some reports on excessive hypercapnea requiring tracheal intubation or jet ventilation [78]. For example, in a case series on 30 non-obese patients who underwent elective short laryngeal procedures, HFNO at a flow rate of 70 L/min was applied while the patients were under apnea during surgery, and the surgeon inserted a rigid tubular laryngoscope [79]. In 1 of the patients, HFNO had to be stopped, and supraglottic jet ventilation was required because the $PaCO_2$ exceeded a predetermined threshold of 11 kPa.

Compared with low-flow oxygenation, HFNO enables a greater clearance of carbon dioxide [71]. When HFNO (70–80 L/min) is used in adults for apneic oxygenation, the $EtCO_2$ increases at a rate of 0.12–0.17 kPa/min [59,71,79]. By maintaining spontaneous breathing, the increase in $EtCO_2$ can be reduced further (e.g., 0.03 kPa/min) [70].

The increase in $EtCO_2$ progresses much faster in children than in adults. For example, in children weighing 10–20 kg, the mean rate of increase in $tcCO_2$ was 0.55 kPa/min [47]. Younger children exhibited a more rapid carbon dioxide increase [47]. In a case report on infants weighing 4 kg, the $EtCO_2$ increased from 35 mmHg to 51–52 mmHg after 250–251 s of apnea with HFNO at a rate of 4 L/kg/min [68].

One feature of the increase in carbon dioxide during apnea is that for an initial 1–2 min, the amount of carbon dioxide increases rapidly and then slows down [80]. For example, in a study [80], apnea increased the $PaCO_2$ at a rate of 12 mmHg/min in the first minute, followed by a slow rise to 3.4 mmHg/min.

The exact mechanism of carbon dioxide clearance during HFNO is unclear although cardiogenic oscillations, dead space gas mixing, and micro-ventilation induced by pharyngeal pressure variations appear to be important factors [81].

Airway fire

Airway fire is a well-known complication that can occur during head and neck surgeries using lasers. Ignition sources, such as diathermy or laser rays, may come into accidental contact with inflammable items, such as tracheal tubes or surgical drapes, in an oxygen rich environment, and surgical fire can occur [82]. If HFNO is used during laser airway surgeries, a high concentration of oxygen flows through the surgical field of the airway, making it easier to ignite when the electrosurgical devices come into contact with this fuel. A case report on a 65-year-old female patient has been presented [83]. She was scheduled to receive a palatal biopsy. She had titanium dental implants in order to attach a palatal obturator following a previous surgery. HFNO at a rate of 30 L/min and an FiO_2 of 1.0 was used while she was spontaneously breathing following the administration of propofol and fentanyl. A burn occurred on the diathermy shaft when the surgeon used a diathermy device to achieve hemostasis at the biopsy site. Fortunately, the tissue of the patient was not harmed. It is recommended that during the use of HFNO, the FiO_2 should be lowered to the minimum level [71]. One possible method is to titrate the FiO_2 to 0.3 using a gas blender [70]. It is recommended that clinicians be constantly vigilant concerning the risk of airway fires during laser or diathermy procedures.

Settings of HFNO during surgery

When it is planned that HFNO is going to be employed for oxygenation during airway surgeries, special care needs to be taken with regard to the anesthesia method, airway patency, breathing mode, oxygen concentration, flow rate, and topicalization of the airway in order to maximize the margin of safety.

Anesthesia needs to be maintained with intravenous anesthesia techniques, such as the TCI of propofol [44,70,72,73,75,79] or its continuous infusion [59,68,71,76,78], because inhalational anesthetic agents cannot be administered via the HFNO system as they would be washed out with the high flow of gases, thereby not facilitating the adequate depth of anesthesia [84].

The reported flow rates of HFNO vary from 50 L/min [75] to 80 L/min [44,59,70–73,78,79] in adults, and a flow rate ≥ 50 L/min appears to be adequate. In children, the flow rate should be adjusted based on the body weight [68,76]. The FiO_2 may be adjusted, but it would be safer to start with 1.0.

When performing apneic oxygenation, it is necessary to make sure that the airway is not obstructed during airway surgeries. The jaw thrust method may frequently be required to maintain airway patency [59,70,71,78,79]. In the case of microlaryngeal surgery, the surgeon usually inserts a suspension laryngoscope around the glottis, and this device may help to maintain airway patency during surgery [68,70–72]. It may be useful for surgeons to insert a tubular laryngoscope to ensure that the dorsal part of the laryngeal inlet is open in order to allow oxygen flow [79]. It should be kept in mind, however, that suspension laryngoscopy is accompanied with an opened mouth, and this may limit the ability of HFNO to generate positive airway pressure [71].

HFNO may be used both in patients who are apneic [59,68,71–73,75,78,79] and in those who are breathing spontaneously [44,70,74,76,77]. The preservation of spontaneous breathing may permit a better control on the increase in carbon dioxide, airway patency, and oxygenation [44]. Additionally, spontaneous breathing may aid surgeons in locating the glottis by facilitating the confirmation of bubbling or the movement of the vocal cords even in the presence of severe laryngeal edema obscuring the anatomy. Spontaneous breathing could reduce the risk of neuromuscular blockade-induced complete airway obstruction.

To maintain spontaneous breathing, adequate titration of the sedative or anesthetic agents to maintain deep sedation and adequate topicalization of the upper airway are required; this makes sure that the patient can tolerate a surgery in the airway [70,74,76]. One method is to perform laryngoscopy and to spray a local anesthetic in the airway before performing the airway surgery [70]. The risk of airway reactivity increases when the neuromuscular blockade is not sufficient, topicalization of the airway is not adequate, and repeated attempts at the insertion of surgical instruments are required. In a case report on an infant undergoing laryngeal repair, it was outlined that the surgical procedure may require multiple attempts at intubation and extubation alongside a full neuromuscular blockade [68]. In addition, surgical stimulation varies constantly during a surgery, and sedative agents have to be titrated continuously in response to patient and surgical conditions; this may result in the sedation being too deep, which is associated with accidental and sudden apnea [70].

Acute respiratory acidosis due to an increase in carbon dioxide during apnea does not act as a significant risk [79]. In addition, moderate carbon dioxide accumulation of up to 100 mmHg is not associated with cardiac arrhythmia or sympathetic stimulation [59,85] whereas severe carbon dioxide retention of more than 100 mmHg is associated with delayed recovery, ICU admission, and complications, such as postoperative congestive heart failure [85]. Patients who are at a risk of carbon dioxide increase, such as those suffering from pulmonary hypertension, obstructive airway diseases, raised intracranial pressure, and cardiac dysrhythmia, may be excluded from the use of HFNO. As there is a strong correlation between the $tcCO_2$ and arterial $PaCO_2$, monitoring the $tcCO_2$ should be useful to detect hypercapnea [78,79].

Backup plan

Clinicians should be aware of the possibility that desaturation could occur during surgery and must have a backup plan to perform other oxygenation techniques. One of the plans is the use of jet ventilation. In a report on a patient who had tracheobronchomalacia with a BMI of 34 kg/m^2 and on another patient who had spasmodic dysphonia with a BMI of 52 kg/m^2, desaturation occurred during surgery, but jet ventilation was successfully established to increase the saturation [59]. In another report [73], infraglottic jet insufflation via cannula cricothyroidotomy was considered in order to reverse desaturation as this method does not interfere with the ongoing surgery.

In emergencies such as acute epiglottitis [44] or supraglottic-pharyngeal stenosis [72], clinicians should always keep in mind the possibility of a failure of HFNO and *a priori* prepare for emergency tracheostomy. The front of the neck should be evaluated thoroughly preoperatively, and the surgeon should be immediately available in the event of complete airway obstruction. In a case series [78], tracheal intubation with a smaller tube or supraglottic jet ventilation was planned before apneic oxygenation and was performed when the $tcCO_2$ reached 70 mmHg.

Summary of the Efficacy of HFNO

HFNO for the induction of anesthesia

It seems reasonable to conclude that HFNO is a superior technique to conventional oxygenation techniques in adults and children who require tracheal intubation in the operating room (Fig. 3). Regarding specific populations, such as those who are obese, pregnant, or in need of rapid-sequence induction of anesthesia, HFNO may be a feasible technique for delaying the onset of hypoxemia. In contrast, the efficacy of the use of HFNO in the case of critically ill patients remains unclear. Because the number of reported clinical trials is still insufficient and because of conflicting results, the most adequate protocol and indications for the use of HFNO should be explored and standardized via larger clinical trials.

When the first attempt at tracheal intubation fails, an immediate decision should be made as to whether and when bag-mask ventilation should be commenced. If a facemask is used during preoxygenation and if a nasal cannula is used only during the apneic periods in the case of a laryngoscopy until the tracheal tube insertion is completed, the nasal cannula may impair efficient preoxygenation via the facemask by introducing

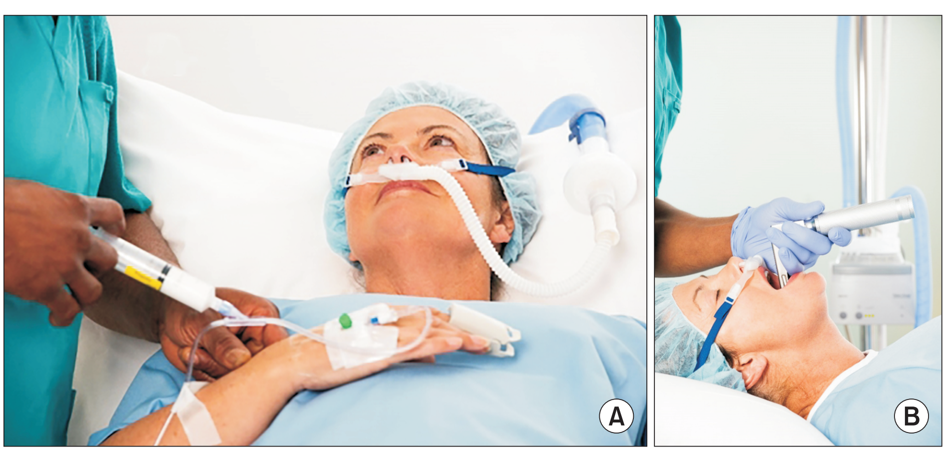

Fig. 3. High-flow nasal oxygenation for tracheal intubation in the operating room. (A) Preoxygenation. (B) Apneic oxygenation (© Fisher & Paykel Healthcare 2018. Used with permission).

oxygen leaks and the entrainment of room air [86]. When a nasal cannula is used together with a facemask, oxygen insufflation at a flow rate of 10 L/min or greater is recommended [86].

HFNO may be the most relevant in patients who are going to undergo rapid-sequence induction of anesthesia, which involves a relatively short apneic period (i.e., 1 min), compared to in those who are scheduled to undergo a conventional technique for the induction of anesthesia in which bag-mask ventilation can be avoided [36,39]. If it takes more than 3–4 min to secure the airway and if bag-mask ventilation is appropriate, then it may be less useful to employ HFNO because the oxygen saturation may decrease further in response to passive apneic oxygenation compared to with active bag-mask ventilation [10]. Nevertheless, the majority of cases involving difficult oxygenation after the induction of anesthesia cannot be predicted preoperatively [87], and thus, some researchers suggest that HFNO should be carried out in all the patients who receive anesthesia [22]. At the same time, clinicians should be aware that HFNO is not an adequate approach for recovering the SpO_2 when significant desaturation occurs. Therefore, before the induction of anesthesia, preoperative airway assessments should be performed meticulously, and an airway strategy should be developed with a backup plan.

It should be considered that the use of HFNO should be added to the difficult airway guidelines and that its areas of application should be expanded to special populations such as to those with reduced cardiopulmonary reserve, to children, and to obese and pregnant patients [88].

HFNO for airway surgery

Adequate communication, understanding, and teamwork are essential in order to establish intraoperative oxygenation using HFNO during airway surgeries. HFNO should not preclude the use of an alternate oxygenation plan, which should be made preoperatively, to resolve significant desaturation, hypercarbia, and acidosis. Therefore, sufficient planning and preparation should be carried out prior to preoxygenation. For short-duration surgeries, an increase in carbon dioxide and not the oxygenation technique may be the factor that determines the duration of apnea. $TcCO_2$ monitoring is recommended for long procedures that last for more than 30 min [89].

Conclusions

HFNO is a promising new technique that keeps patients safer during anesthesia. Despite the mounting evidence supporting its use, more research and clinical trials are needed in order to establish the ideal use of this technique in various populations. We hope that this review will help readers to understand the relevant techniques involved in the use of HFNO and to facilitate the introduction of its use into the Airway Management Guidelines in the future.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Hyun Joo Kim (Conceptualization; Data curation; Methodology; Project administration; Writing–original draft; Writing–review & editing)
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