Review Article

Role of High Flow Nasal Cannula (HFNC) for Pre-Oxygenation Among Pregnant Patients: Current Evidence and Review of Literature

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Abstract

With an increasing understanding of respiratory physiology and pathology, many new oxygen delivery devices have been introduced lately. Among them, high flow nasal cannula (HFNC) seems a promising modality that can deliver heated and humidified flows higher than the peak inspiratory flow at high FiO_2 (fractional inspired oxygen), hence decreasing the work of breathing without causing discomfort to the patient. Applications of HFNC have escalated for use in multiple areas besides perioperative period over the last decade. The use of HFNC in obstetric population is particularly intriguing as this population is at risk of adverse airway related events. Hence, this narrative review focuses upon the role of HFNC for pre-oxyenation of pregnant patients in peripartum and in intensive care units. We have reviewed the current state of knowledge and the future prospects of HFNC use in obstetric setting.

Keywords: *Apneic oxygenation, high flow nasal cannula (HFNC), Optiflow, pre-oxygenation, parturient, pregnancy*

Introduction

General anaesthesia may be required for obstetric or non-obstetric procedures in a pregnant patient. Pre-oxygenation is recommended for all patients during induction as well as extubation for the safe practice of general anaesthesia.[1] Airway management in obstetrics is deemed difficult due to not only maternal physiological and anatomical changes but also contextual factors like time, pressure and human factors.[2] Adequate pre-oxygenation prolongs safe apnea time and increases the margin of safety following induction of anaesthesia and securing the definitive airway.[3]

In parturients, the safe apnea time may be low, and pre-oxygenation with conventional techniques may be suboptimal.[4] This may lead to fatal complications like hypoxic brain injury, hemodynamic instability, cardiac arrest, and fetal and maternal death.

Latest obstetrics airway management guidelines recommend to achieve an EtO2 >90% within 3 min for adequate pre-oxygenation.[5] However, this target is frequently not achievable with the traditional method of pre-oxygenation via a tight fitting mask for 3 min.[6]

In order to increase the safe apnea time, the guidelines state that the newer methods of pre-oxygenation and apneic oxygenation via nasal Cannula or (heated humidified nasal cannula) HFNC (heated humidified nasal cannula) should be applied. Adequate hands free pre-oxygenation and apneic oxygenation achieved by HFNC may provide longer and safer apnea time in the pregnant population.

The use of HFNC for pre-oxygenation and apneic oxygenation has shown promising results in non-pregnant patients and critically ill patients.[5] However, the evidence of its use in the obstetric population is either incomplete or conflicting. In this literature review, we discuss the physiology of pre-oxygenation, efficacy and efficiency of HFNC in pre-oxygenation, and the latest evidence of its use in the obstetric population.

Methods

The electronic search strategies included databases PubMed, Embase, Medline, and Google Scholar. The search strategy was built on topics of high flow nasal Cannula

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AND obstetrics AND pre-oxygenation. The search included a combination of the following keywords: high flow nasal cannula, high flow nasal oxygen, HFNO, HFNC, Optiflow, THRIVE, transnasal humidified rapid insufflation ventilatory exchange, pre-oxygenation, apneic/apnoeic oxygenation, perioperative, intraoperative, post-operative, post-extubation, induction, obstetric, parturient, caesarean section, pregnant, pregnancy.

Physiology of pre-oxygenation and apneic oxygenation

Oxygen reserves in the body are primarily stored as functional residual capacity (FRC) in the lungs, which is defined as the volume of the lung at the end of the normal tidal breath. FRC of a normal adult measures 2500-3000 ml. On breathing room air, the alveolar oxygen content is 16%(~400 ml) and 75% nitrogen. During apnea, oxygen is consumed from alveoli at the rate of 250 ml/min.[7] Further on breathing room air, @ 250 ml/min of oxygen consumption and baseline reserve of 400 ml, the duration of apnea is between 1 and 2 min. The aim of pre-oxygenation is to 'denitrogenate' the lungs and increases the oxygen content to nearly 90% of the FRC (~2300 ml). Hence, following pre-oxygenation, assuming the reserve to be 2300 ml, the duration of apnea is grossly increased to 8-10 min. The safe apnea time of duration of apnea without desaturation (DAWD) is defined as the interval between onset of apnea and the time oxygen saturation reaches a value of less than 90% (PaO_2~60 mmHg).[8]

The efficacy of pre-oxygenation is most commonly defined in terms of EtO2 (end-tidal oxygen concentration) or arterial pressure of oxygen (PaO2).[7] EtO2 of more than 90% is considered as the target endpoint.[7] This efficacy can be increased by head-up positioning and giving PEEP which increases FRC.[9] The efficiency of pre-oxygenation is measured in terms of maximum safe apnea time.[7]

The concept of Apneic oxygenation has been known for long, but clinical implications have been realized lately. If there is patent air passage between lungs and oropharyngeal spaces, the oxygen will move by mass flow even during apnea.[10] This is possible due to the negative pressure gradient created by continuous oxygen removal from alveoli at 250 ml/min. Apneic oxygenation can be used as an adjunct with pre-oxygenation to increase the safe apnea time. Since carbon dioxide is not removed during apneic oxygenation, the safe time limit of apneic oxygenation is 15 min (rate of rising of CO_2~3-4 mmHg/min), taking into consideration the decreased pH due to hypercapnia.[11] Peroxygenation is the term given to combined techniques of pre-oxygenation (before induction of anaesthesia) and apneic oxygenation (after induction of anesthesia to securing the airway) to increase the safe apnea time.

Current techniques of pre-oxygenation

The various techniques of pre-oxygenation are compared in terms of efficacy and efficiency. The standard procedure of pre-oxygenation consists of Tidal volume breathing (TVB) of 100% oxygen for 3 min in head-up position via a leak-proof face mask for elective procedures ('slow' technique) and eight vital capacity breaths for 60 seconds or four vital capacity breaths for 30 seconds ('fast' techniques) for emergency intubations.[12] The addition of PEEP by closing the adjustable pressure liming valve (APL) valve improves the efficacy of pre-oxygenation by increasing FRC. Another technique utilising NIV has been studied for pre-oxygenation in hypoxemic patients, especially in intensive care units.[13]

High Flow Nasal Cannula and THRIVE

After the description of apneic oxygenation for increasing safe apnea time, various techniques were used in different studies to provide apneic oxygenation during intubation, like a nasopharyngeal catheter, standard nasal cannula with both low and high flows up to 15 litres.[14] The oxygen delivered by these techniques was cold, dry, and caused sinus pain, epistaxis and therefore, intolerable to the patient. Moreover, flow could not be increased for more than15 litres, limiting the efficacy of apneic oxygenation.

High frequency nasal Cannula is a novel device for delivering a high flow of oxygen up to 70 l/min, heated and humidified up to 37 degrees Celsius through nasal Cannula using an air oxygen blender.[15] FiO_2 of up to 1.0 can be delivered via HFNC. High flow reduces the room air entrainment. The use of HFNC for apneic oxygenation is called Transnasal Humidified Rapid Insufflation Ventilatory Exchange (THRIVE).[16]

The various benefits of THRIVE over conventional pre-oxygenation techniques are as follows:[17]

- Heated and humidified oxygen improves mucociliary clearance, protects airway mucosa, decreases the incidence of mucus plug formation and hence reduces the incidence of atelectasis
- High flows matching with peak inspiratory flow can be provided with HFNC, which reduces the work of breathing
- It can deliver high and fixed FiO_2 accurately, which reduces the air entrapment and hence increases the efficacy of pre-oxygenation
- Washout of anatomical dead space reduces the rebreathing of CO_2
- Flows up to 50 l/min can easily be tolerated by patients
- Generation of PEEP prevents atelectasis.
- Improved CO_2 washout during apnea as compared to other techniques
- It can be used for pre-oxygenation and apneic oxygenation. Since it is a nasal cannula, it need not be removed during laryngoscopy, and there is a smooth transition from pre-oxygenation to apneic oxygenation
- THRIVE is tolerated better than tight-fitting face mask in claustrophobic patients.

THRIVE is a promising oxygenation technique for intubation in intensive care units, operation theatres, and emergency areas. Its use has been vastly studied in critically ill and obese patients.

Maternal physiology and airway management

The incidence of difficult airway and respiratory complications are higher in pregnant patients.[18] The upper airway oedema, increase in breast size, and pregnancy weight gain makes the maternal airway anatomically difficult and challenging. The general anaesthesia induction for emergency caesarean sections is time-sensitive and stressful, which contributes to an increased incidence of failed endotracheal intubations. The increased risk of gastroesophageal reflux and aspiration mandates the practice of modified rapid sequence induction, contributing further to challenging airway management.

The increased abdominal girth pushes the diaphragm upwards, leading to decreased FRC. The oxygen consumption and minute ventilation are higher in a parturient.[19,20] Decreased FRC with increased oxygen consumption contributes to the reduction of both efficacy and efficiency of pre-oxygenation. During emergency caesarean section, the time for pre-oxygenation is limited, leading to higher incidences of inadequate pre-oxygenation. While a method of 8 VC breaths over 60 seconds may be sufficient for EtO2 to be more than 90%, the safe apnea time achieved in a pregnant patient may not be enough for managing a difficult airway. To increase the duration of safe apnea time, a combination of pre-oxygenation, and apneic oxygenation may be more advantageous.

Current guidelines and evidence of HFNC use in the pregnant population

The current guidelines recommend the use of nasal Cannula or HFNC for apneic oxygenation during airway instrumentation of pregnant patients.[5] This recommendation was based on results extrapolated from non-pregnant patients. Although the evidence of the use of HFNC for pre-oxygenation and apneic oxygenation in the pregnant population was scarce while the recommendations were formed, some studies were done post guidelines with conflicting results. Tan *et al*.[21] suggested that pre-oxygenation with HFNO is inadequate as an EtO2 of 90% cannot be achieved after 3 min. They anticipated longer time requirements for adequate results with HFNO.

Au K *et al*.[22] concluded in a biased coin up down allocation trial that EtO2 of more than 90% cannot be achieved even after 8 min of pre-oxygenation by HFNC. They also reconfirmed that 3 min is inadequate time for pre-oxygenation even with a face mask in a pregnant patient. Air entrapment is the main contributing factor for inadequacy. S. Al Sulttan *et al*.[23] demonstrated a similar lack of efficacy even with up to 20 vital capacity breaths with HFNO, and only 70% of term patients achieved the target of EtO2 >90% with traditional face mask pre-oxygenation.

Et02 >90% may not be an achievable target for a term women undergoing caesarean delivery. Though these studies concluded HFNO as an inadequate technique of pre-oxygenation due to non-achievable end target oxygen of 90%, more recent studies consider time to desaturation as a more desirable target.

Pillai A *et al*.[24] predicted that HFNO significantly prolongs safe apnea time in pregnant patients using computational modeling (Nottingham physiology simulator).

Using the ICSM simulation suite based on the physiology simulator, D. Stolady *et al*.[25] predicted that HFNO provides longer safe apnea time in pregnant subjects despite generating low EtO2. Even after achieving Eto2 of 60%, the safe apnea time was prolonged for more than 60 minutes in a non-obese patient. The apnea time was superior compared with face mask pre-oxygenation in all models. The HFNO was used for both pre-oxygenation and apneic oxygenation.

Zhou *et al*.[26] evaluated the efficacy of HFNO for both pre-oxygenation and apneic oxygenation at 50 l/min during RSI for cesarean section compared to facemask and concluded that ETo2 after intubation was higher in the HFNO group as compared to facemask ventilation. So after taking into consideration the combined effect of both pre-oxygenation and apneic oxygenation, the safe apnea time achieved by HFNO may be superior to the traditional face mask technique. However, these results were not applicable for pregnant women with higher BMI (>50). The flow rates used in various studies are different. 50 l/min flows are recommended by the manufacturer and are better tolerated by the patients as compared to 70 l/min.[27] The various studies are summarized in Table 1.

HFNC for critically ill obstetric patients

During pregnancy or peripartum period, 2% of the pregnant population may require admission to intensive care unit.[28] The critically ill patient may also present for emergency caesarean section or other life-saving procedures. The various causes of respiratory failure can be pulmonary oedema due to pre-eclampsia, eclampsia and tocolytics, cardiogenic pulmonary oedema, amniotic fluid embolism, massive transfusion complications, peripartum cardiomyopathy, regional anaesthesia complications, coronavirus disease 2019 (COVID-19), and pneumonia. Intubation of a critically ill pregnant patient is a major challenge. The use of NIV in the pregnant population can increase the risk of aspiration, while conventional oxygen therapy may be inadequate.[29] HFNC has been used for peri intubation, apneic oxygenation, and pre-oxygenation in the non-pregnant population. A metaanalysis by Jhou *et al*.[30] has analyzed seven studies in which HFNC was used for apneic and pre-oxygenation for intubating critically ill

Table 1: Summary of clinical studies related to use of HFNC for pre-oxygenation in pregnant patients

Year author	Number of patients	Intervention	Comparator	Outcome, results, intervention
Tan *et al*.[21] (2018) Prospective observational study	Seventy three term participants	3 min HFNO pre-oxygenation (30 l/min for 30 sec, 50 l/min for 50 s)	-	1) who achieved Et02 >90% after first expired breath- 60% (95%CI – 54-66%) 2) who achieved ET02 >80% was 84%(95% CI: 80-88%)
Au k *et al*.[22] (2020) Biased up down sequential allocation trial	Eighty healthy parturients	(n=40) HFNO pre-oxygenation With 50 L/min flow and closed mouth breathing	Face mask pre-oxygenation	The effective time interval for 90% of parturients to achieve end-tidal oxygen ≥90% for standard flow rate facemask was estimated to be 3.6 min, but could not be estimated for high-flow nasal oxygen groups even after 8 min.
S. Al-Sulttan *et al*.[23] (2020) Prospective, up-down sequential allocation study	Twenty women at term	Successful pre-oxygenation occurred in 4 (20%), 3 (15%) and 14 (70%) women with HFNO mouth closed, HFNO mouth open, and via face mask, respectively	-	2) At up to 20 vital capacity breaths, face mask pre-oxygenation was more successful at achieving EN90 compared with both HFNO with a closed (P=0.006) or open (P=0.001) mouth. Closed mouth HFNO did not outperform open-mouth pre-oxygenation.
D. Stolady *et al*.[25] (2021) A modelling investigation	Ten virtual subjects with BMI of 24 kg m^2 (BMI24), 35 kg m^2 (BMI35), 40 kg m2 (BMI40), 45 kg m^2 (BMI45), and 50 kg m^2 (BMI50), in active labor and not in labor (in the Interdisciplinary Collaboration in Systems Medicine (ICSM) simulation suite based on the Nottingham Physiology Simulator)	Varying FEO_2 values (60%, 70%, 80%, and 90%) with HFNC technique	Varying FE02 values with facemask technique	1.HFNO provided longer safe apnoeic times in all models, with all $FE0O_2$ values. 2.Labor and increased BMI reduced this effect, in particular a BMI of 50 kg m^2 reduced the improvement in apnoea time to 1.8-8.5 min (depending on the $FE0O_2$), compared with an improvement of more than 60 min in the subject with BMI 24 kg m^2. 3) extension of safe apnea time is limited in patients with BMI >50 kgm^2
Zhou *et al*.[26] (2021) prospective RCT	Thirty-four healthy parturients undergoing C section			1) PaO_2 immediately after intubation in HFNO group was higher than that in SFM group (441.41±46.73 mmHg versus 328.71±72.80 mmHg, P<0.0001) 2) EtO_2 concentration on commencing ventilation in HFNO group was significantly higher than that in SFM group (86.71±4.12%) versus (76.94±7.74%) P<0.0001)

patients. They concluded that HFNC reduced the incidence of severe hypoxemia during intubation in patients with mild hypoxemia (pf ratio >200 mmHg) and decreased the length of ICU stay by 1.8 days. The latest guidelines recommend that in perioperative or periprocedural hypoxemic patients, use of noninvasive respiratory support technique (NIV/CPAP) than conventional oxygen therapy to improve oxygenation, reduce atelectasis, pulmonary complications, and mortality.[31] If there is low tolerance to NIV/CPAP, then HFNC should be used. The recommendations are for abdominal surgeries, cardiac surgeries, and lung resection. Further research requires a specific obstetric population, but since the cesarean section is an open abdominal surgery, results can be extrapolated in obstetric practice.

HFNC settings for induction of anaesthesia in pregnant patients

HFNC is usually well tolerated by patients who are awake even at high flows, except for some patients, it may cause moderate discomfort.[32] HFNC may be started at low flows of 30-40 L/min initially and then increased to high flows of 50-70 L/Min when the patient loses consciousness. Since obstetric patients undergo rapid sequence induction, the FiO_2 should be between 0.9 and 1 from the beginning. The patient is asked to do deep breathing from the nose

with mouth shut. When the patient loses consciousness, the airway patency is maintained by head tilt, jaw thrust, chin lift, or oropharyngeal airway.

Uses of HFNC in various domains

HFNC was initially investigated in the neonatal population for managing acute respiratory failure. Near the 2000s use of HFNC became popular in critically ill patients.[33] HFNC is used as an alternative to NIV masks and CPAP in ICU. Anesthesiologists started using HFNC preoperatively for pre-oxygenation in critically ill patients and in operation theatres for elective procedures. HFNC is shown to be useful during induction of anesthesia and extubation in obese patients.[34] The use of HFNC has also been studied in the immediate postoperative period to avoid intubation and pulmonary complications.[35] Various studies have compared conventional oxygen therapy with HFNC and NIV in terms of different outcomes.

In various studies, it has been established HFNC is non-inferior to NIV and superior to conventional oxygen therapy.[31] HFNC has been extensively used in the COVID pandemic as a method of high flow and FiO_2 oxygen therapy.[36]

Complications

There are no absolute contraindications for the use of HFNC. One of the complications includes epistaxis, which may be a concern in pregnant patients due to engorged nasal mucosa.[32] There is a theoretical risk of gastric insufflation due to the generation of positive pressure. The positive pressure generated is less than 10 mmHg only if the mouth is closed and there is no evidence of increased aspiration risk due to HFNC.[37] The administration of 100% oxygen may lead to absorption atelectasis. Intraoperative PEEP and intermittent recruitment manoeuvres can be used to prevent atelectasis. Since there is limited washout out of C CO_2 leading to hypercapnia and inadequate monitoring of $ETCO_2$, it is recommended to use transcutaneous CO_2 monitors whenever HFNC is used for a prolonged time.[38] HFNC can be avoided in patients who are at risk due to hypercapnia like pulmonary hypertension, raised intracranial pressure, and obstructive airway diseases.

Conclusion

The role of HFNC for noninvasive ventilation amid the current pandemic has been enormous. criteria which can help in deciding HFNC over face mask are, early achievement of ET02, increased apnea time, and greater comfort to the patient.[39] Prolonging safe apnea time is the most important aim of pre-oxygenation. HFNO, when used for both pre-oxygenation and apneic oxygenation together, may increase the safe apnea time more than just traditional "pre-oxygenation only" techniques in spite of not achieving standard EtO2 values of 90%. This impresses upon the importance of apneic oxygenation. However, the combination of face mask technique for pre-oxygenation and HFNO for apneic oxygenation, its use in critically ill, high risk, and obese pregnant females and adequate flow rates are still areas of research to be explored. During time-critical caesarean sections, the use of HFNO may be less relevant considering the amount of time taken to set it up. HFNO can be used as a promising oxygenation technique during induction as well as extubation of general anaesthesia in pregnant patients undergoing elective or semi-urgent caesarean section to prolong time to desaturation.

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Conflicts of interest

There are no conflicts of interest.

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