PERIODICUM BIOLOGORUM
VOL. 127, No 1–2, 65–69, 2025
DOI: 10.18054/pb.v127i1-2.35816

UDC 57:61
CODEN PDBIAD
ISSN 0031-5362

Review article

Perioperative impact of high-flow nasal oxygenation in obstetric general anesthesia

ANA VUZDAR TRAJKOVSKI[1]*
VESNA GRGIĆ[1]
MARINA KATALINIĆ NOVAK[1]
KREŠIMIR REINER[1,2]
IVAN ŠKLEBAR[1,3,4]

[1] University Department for Anesthesiology, Resuscitation, Intensive Care and Pain Therapy, Zagreb University Hospital Center, Zagreb, Croatia

[2] School of Medicine, University of Zagreb, Zagreb, Croatia

[3] School of Medicine, Catholic University of Croatia, Zagreb, Croatia

[4] Bjelovar University of Applied Sciences, Bjelovar, Croatia

***Correspondence:**
Ana Vuzdar Trajkovski
E- mail address: ireland514@yahoo.com

Keywords: cesarean section; airway management; oxygen therapy; obstetrics

Abbreviations

ASA	– American Society of Anesthesiologists
BMI	– body mass index
CPAP	– continuous positive airway pressure
FetO2	– end-tidal oxygen fraction
FiO2	– inspired oxygen fraction
FM	– face mask
HFNO	– high – flow nasal oxygenation
NIV/CPAP	– non invasive ventilation/ continuous positive airway pressure
PaO_2	– partial pressure of oxygen in arterial blood
PF ratio	– PaO2/FiO2 ratio
THRIVE	– transnasal humidified rapid insufflation ventilatory exchange

Received March 31, 2025
Revised June 29, 2025
Accepted July 7, 2025

Abstract

Background and purpose: *High-flow nasal oxygenation (HFNO) is gaining attention in anesthesia for cesarean sections under general anesthesia due to its potential to reduce hypoxemia - a major cause of maternal morbidity and mortality. Pregnant patients face increased risk from anatomical and physiological changes, including airway edema, reduced functional residual capacity, and increased aspiration risk. Traditional preoxygenation with 100% oxygen via a face mask may not provide adequate oxygen reserves, prompting exploration of HFNO as an alternative. This paper reviews current evidence on the use of HFNO preoxygenation during anesthesia induction for cesarean sections.*

Materials and methods*: An extensive literature search was performed to evaluate existing research on HFNO as a preoxygenation technique in obstetric general anesthesia.*

Results: *Eight studies were identified that assess HFNO in this context. While some report inferior performance in achieving optimal end-tidal oxygen fraction compared to face mask methods, others highlight benefits. A 2021 randomized trial found HFNO yielded higher arterial oxygen tension and end tidal oxygen fraction post-intubation. Additionally, a recent multicenter pilot study reported no desaturation events among pregnant patients, supporting HFNO's safety and potential efficacy.*

Conclusion: *HFNO offers advantages such as prolonged safe apnea time and ease of application. However, its effectiveness in the obstetric population remains insufficiently validated. More robust clinical trials are required before HFNO can be integrated into standard anesthetic protocols for cesarean sections.*

INTRODUCTION

Hypoxemia during induction of anesthesia is one of the leading causes of anesthesia-related morbidity and mortality, and the incidence of failed airway establishment in pregnant women is thought to be approximately 10 times higher than in the general surgical population *(1,2)*. Airway establishment in pregnant women is challenging due to the anatomical and physiological changes that occur during pregnancy. Pregnant women often have significant airway and tongue edema, an increased risk of aspiration of gastric contents due to delayed gastric emptying, and reduced functional residual capacity, making them susceptible to more rapid onset of hypoxemia in the event of prolonged intubation *(3)*. The increasing use of regional anesthesia for obstetric procedures has also led to a decrease in the number of general anesthe-

sia procedures performed, and, consequently, to a decrease in the opportunity to gain extensive clinical experience in airway establishment in this vulnerable population.

Preoxygenation delays hypoxemia by increasing the alveolar oxygen reserve, thereby increasing the time of safe apnea. The time of safe apnea is the time from the cessation of breathing or ventilation to the moment when arterial blood saturation drops to 90%, after which the saturation continues to drop precipitously. Hypoxemia is a dangerous condition, and, with further progression, it can lead to dysrhythmias, hemodynamic instability, hypoxic brain injury, and ultimately death. The usual method of preoxygenation in pregnant women is to inhale 100% oxygen through an oronasal mask that fits well on the face for 3 minutes or until end - tidal oxygen fraction (FetO2) ≥ 0.9 is reached, and this method is included in most guidelines for intubation of pregnant women *(4).* However, there are studies that show that the preoxygenation performed in this way is often inadequate, and it seems that there is room for improvement when it comes to preoxygenation in the pregnant population. However, the procedure performed should be safe and have a better effect than the current one *(5).* The question arises whether high-flow nasal oxygenation (HFNO) could fulfill the mentioned criteria.

HFNO is a method by which humidified and heated oxygen is delivered to the patient's respiratory system through a nasal cannula at a high flow rate, up to 70 L/min. The device can titrate inspired oxygen fraction (FiO2) up to 100%, and an oxygen reserve is created in the nasal cavity, which keeps FiO2 constant because it eliminates the anatomical dead space and reduces rebreathing of carbon dioxide. Also, HFNO ensures a low continuous positive airway pressure (CPAP), in the range of 2.7 to 7.4 cmH2O, thereby reducing the work of breathing *(6).* It is mainly used in intensive care units, and it is increasingly being used as a method for oxygenation in apnea during the induction of general anesthesia. It certainly has the advantage of not interfering with balloon ventilation through the mask or attempts at laryngoscopy for intubation.

MATERIALS AND METHODS

In order to review the results of studies in which HFNO was used during the induction of general anesthesia for cesarean section, the available literature was searched, all of it published in English in the last 20 years (from 2004 to 2024). The databases searched were Scopus, Medline, Embase, Web of Science, and Cochrane Library. The search was conducted according to these key words: cesarean section; airway management; oxygen therapy; obstetrics. The primary focus is on the selection and analysis of those studies in which HFNO was used as an alternative to classical preoxygenation during the induction of general anesthesia for the cesarean section, and especially for emergency cesarean section.

RESULTS

Although a many numerous of studies on the use of HFNO in various clinical scenarios have been published in the given period, only a few papers were found that address the topic of HFNO use during the induction of general anesthesia. The key characteristics of the articles mentioned are listed in Table 1.

DISCUSSION

A number of studies have examined the role of HFNO in preoxygenation and apneic oxygenation during the induction of general anesthesia in recent years. Most of these have been conducted in a general, non-obstetric population. The THRIVE study in 25 patients with a difficult airway demonstrated that HFNO successfully prolonged the time of apnea without desaturation *(6).* In another study, which specifically selected patients at increased risk of hypoxia during intubation, HFNO was used for preoxygenation and oxygenation during apnea, and the incidence of clinically significant desaturation was shown to be only 7% *(7).* Since there was no evidence for the use of HFNO in pregnant women, one study was done on a computer model using a simulator that modeled the respiratory and cardiovascular system with the changes that occur during pregnancy. It was shown that apneic oxygenation with FiO2 of 100% can prolong the desaturation time to more than 50 min in average pregnant women and to more than 40 min in morbidly obese pregnant women (BMI 50kg/m^2) *(8).* A small pilot study was then conducted on 4 pregnant women who agreed to the research. First, HFNO 30 L/min was applied for 30 seconds and then 50 L/min for a further 150 seconds. At the end of the 3-minute period, gas concentrations at the end of expiration were measured using the mask. It was shown that at the end of the preoxygenation period, all 4 patients reached an arterial blood saturation of 100%, but only one reached the recommended FetO2 of ≥0.9 *(9).* Several studies followed that compared standard preoxygenation using a mask and using HFNO in pregnant women. In one study, mean FetO2 ≥90% was not reliably achieved with the use of HFNO, and in another it was shown that FetO2 ≥90% is achieved in about 60% of pregnant women. Therefore, the conclusion is that HFNO is inferior to standard preoxygenation via a well-fitting mask *(10, 11).* Also, the biased-coin up–down sequential allocation trial in 2020 showed similar results. The effective time interval for 90% of parturients to achieve an 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 eight minutes *(12).* In 2021, a randomized study was conducted in pregnant women and

Table 1. *List of papers dedicated to the study of high - flow nasal preoxygenation for cesarean section under general anesthesia.*

Author and year of publication	Type of research	Key findings	Comparison with classic preoxygenation
Tan PCF. et al. 2016 *(9)*	A pilot study of four women at term. HFNO (first 30 s at 30 l.min^{-1}, then next 150 s at 50 l.min^{-1}) was applied	Only one of the four women achieved the recommended pre-oxygenation induction of anesthesia trigger threshold of FetO2 ≥ 90% after 3 min HFNO preoxygenation	The need for a larger study is emphasized.
Shippam W. et al. 2019 *(10)*	40 healthy parturients were randomly allocated to compare pre-oxygenation using high-flow nasal oxygen (30-70 l.min-1 oxygen flow) via nasal prongs with standard 15 l.min-1 oxygen breathing via a tight-fitting face mask	With 3-min tidal volume breathing, the respective estimated marginal means for high-flow nasal oxygen and standard flow rate facemask pre-oxygenation were 87.4% (95% CI 85.5-89.2%) and 91.0% (95% CI 89.3-92.7%), p = 0.02	High-flow nasal oxygen pre-oxygenation performed worse than standard flow rate facemask pre-oxygenation in healthy term parturient.
Tan PCF. et al. 2019 *(11)*	A prospective observational study.73 term participants underwent a 3 min HFNO protocol (30 L min-1 for 30 s and then 50 L min-1 for 150 s).	The proportion with the first expired breath FetO2 ≥ 90% was 60% [95% confidence interval (CI): 54-66%] and FetO2 ≥ 80% was 84% (95% CI: 80-88%).	HFNO using this protocol is inadequate to preoxygenate term pregnant women.
Au K. et al. 2020 *(12)*	80 healthy parturient were randomly assigned to standard facemask (n = 40) or high flow nasal oxygen (n = 40) groups to determine the effective time interval in 90% of healthy parturient to achieve a target endpoint end-tidal oxygen of ≥ 90%	Under the conditions of our study, the effective time interval for 90% of parturient to achieve an 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 eight minutes	Standard facemask preoxygenation is superior to HFNO preoxygenation
Zhou S. et al. 2021 *(13)*	Prospective randomized, controlled study on 34 healthy parturient undergoing general anesthesia for caesarean section	PaO2 in the HFNO group was significantly higher than that in the SFM group (441.41 ± 46.73 mmHg versus 328.71 ± 72.80 mmHg, P < 0.0001). The FetO2 concentration in the HFNO group was higher than that in the SFM group (86.71 ± 4.12% versus 76.94 ± 7.74%, P < 0.0001)	HFNO better
Osman YM. et al. 2021 *(15)*	Randomized study on 100 ASA II pregnant women scheduled for elective caesarean section under general anesthesia	The safe apnea time was significantly longer in HFNO group with median of 7 min compared to facemask ventilation with 4 min.	HFNO better
Sjöblom A. et al. 2023 *(14)*	Prospective, non-randomized, multi-center study on 34 pregnant women with a gestational age ≥30 weeks undergoing caesarean section under general anesthesia	There was no difference detected in end-tidal oxygen concentration after tracheal intubation, 87% (6) in the high-flow nasal oxygen group vs. 80%	HFNO equal or better
Tan PCF, et al. 2024 *(16)*	Randomized study on 70 healthy participants of gestational age ≥ 37 weeks in a simulated environment	First FetO2 after HFNO pre-oxygenation was greater than after FM pre-oxygenation	Pre-oxygenation with HFNO was not inferior to FM pre-oxygenation.

Abbreviations: ASA –American Society od Anesthesiologists; FetO2 – end-tidal oxygen fraction; FM – face mask, HFNO – High-flow nasal oxygenation; PaO_2 – partial pressure of oxygen in arterial blood, SFM – standard face mask

showed that HFNO is a safe method in which partial arterial oxygen pressure and FetO2 are higher immediately after intubation compared to standard mask preoxygenation *(13).*

Among the more recent research is a pilot study from 2023 in which it was observed how many pregnant women will experience a drop in arterial blood saturation below 93%. It was a multicenter study in which 34 pregnant women were included, 25 of whom agreed to preoxygenation using HFNO, while 9 were preoxygenated by the standard method using an oronasal mask. None of the involved pregnant women had a desaturation below 93%, and the lowest saturation in both groups was 97% (14).

A study of 100 pregnant women examined the efficacy of HFNO using the THRIVE protocol versus a traditional face mask for preoxygenation during the induction of general anesthesia for cesarean section. THRIVE (transnasal humidified rapid insufflation ventilatory exchange) is a protocol that uses high flow rates of warmed and humidified oxygen (e.g., 50–70 L/min) via a nasal cannula and maintains continuous oxygenation during apnea, thereby prolonging safe ventilation-free time. Results have shown that THRIVE significantly prolongs safe apnea time (7 min vs. 4 min) and improves oxygenation (PaO_2 355 mmHg vs. 101 mmHg), thereby reducing the risk of desaturation and improving patient safety *(15).*

A more recent randomized controlled crossover trial examined the no inferiority of high-flow humidified nasal oxygen (HFNO) to face mask (FM) preoxygenation in pregnant women at term. It found HFNO no inferior to FM, with 71% of subjects achieving a targeted FetO2 ≥ 90% with HFNO compared to 44% with FM. The results suggest that HFNO may be a suitable alternative for preoxygenation in pregnant women, as standard FM methods often fail to achieve recommended oxygenation levels *(16)*. A recent study has been published about investigating the efficacy of high-flow nasal oxygen (HFNO) compared with traditional face mask (FM) ventilation in preoxygenation of pregnant women prior to general anesthesia. HFNO has been shown to be beneficial because it allows hands-free preoxygenation in emergency situations, improves patient comfort, and potentially facilitates emergency procedures if general anesthesia is required for cesarean section *(17)*.

During pregnancy or the peripartum period, 2% of the pregnant population may require admission to an intensive care unit *(18)*. The critically ill patient may also present for emergency caesarean section or other life-saving procedures. A metaanalysis by Jhou et al. *(19)* has analyzed seven studies in which HFNO was used for apneic and pre-oxygenation for intubating critically ill patients. They concluded that HFNO 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. If there is low tolerance to NIV/CPAP, then HFNO should be used. It is recommended 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 *(20)*.

It is also worth mentioning the published protocol of a study that plans to investigate the effect of high-flow nasal oxygen (HFNO), compared to room air, on fetal acidemia during planned cesarean section, using umbilical artery blood gas analysis. Since fetal acidemia is more common during cesarean section than during vaginal delivery, the aim of the study is to determine whether HFNO can improve fetal oxygenation and reduce the risk of metabolic acidosis. The study will involve 120 pregnant women divided into two groups - one will receive HFNO at a flow rate of 40 L/min, and the other room air at a flow rate of 2 L/min. The primary outcome of the study is umbilical artery lactate levels, while secondary outcomes include pH, partial pressures of oxygen and carbon dioxide, Apgar scores, and neonatal complications. This study is the first to plan to investigate the effect of HFNO on fetal acid-base balance during cesarean section. Therefore, it could have important clinical implications for optimizing intrauterine resuscitation and improving neonatal outcomes *(21)*.

CONCLUSION

The results so far point to the possible advantages of using HFNO in the induction of general anesthesia for cesarean section, especially in the case of emergency cesarean section and potentially difficult intubation. More extensive research is needed before the HFNO preoxygenation method in the induction of general anesthesia for cesarean section is accepted as a standard.

REFERENCES

1. MCDONNELL NJ, PAECH MJ, CLAVISI OM, SCOTT KL 2008 Difficult and failed intubation in obstetric anaesthesia: an observational study of airway management and complications associated with general anaesthesia for caesarean section. Int J Obstet Anesth 17:292-297. https://doi.org/10.1016/j.ijoa.2008.01.017
2. TAO W, EDWARDS JT, TU F, XIE Y, SHARMA SK 2012 Incidence of unanticipated difficult airway in obstetric patients in a teaching institution. J Anesth 3:339-345. https://doi.org/10.1007/s00540-012-1338-1
3. KODALI B-S, CHANDRASEKHAR S, BULICH LN, TOPULOS GP, DATTA S 2008 Airway changes during labor and delivery. Anesthesiology 108:357-362. https://doi.org/10.1097/ALN.0b013e31816452d3
4. MACHLIN HA, MYLES PS, BERRY CB, BUTLER PJ, STORY DA, HEATH BJ 1993 End-tidal oxygen measurement compared with patient factor assessment for determining preoxygenation time. Anaesth Intensive Care 21:409-413. https://doi.org/10.1177/0310057X9302100406
5. PORTER R, WRENCH IJ, FREEMAN R 2011 Preoxygenation for general anaesthesia in pregnancy: is it adequate? Int J Obstet Anesth 20:363-365. https://doi.org/10.1016/j.ijoa.2011.07.007
6. PATEL A, NOURAEI SAR 2015 Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE): a physiological method of increasing apnoea time in patients with difficult airways. Anaesthesia 70:323-329. https://doi.org/10.1111/anae.12923
7. DOYLE AJ, STOLADY D, MARIYASELVAM M, WIJEWARDENA G, GENT E, BLUNT M, YOUNG P 2016 Preoxygenation and apneic oxygenation using Transnasal Humidified Rapid-Insufflation Ventilatory Exchange for emergency intubation. J Crit Care 36:8-12. https://doi.org/10.1016/j.jcrc.2016.06.011
8. PILLAI A, CHIKHANI M, HARDMAN JG 2016 Apnoeic oxygenation in pregnancy: a modelling investigation. Anaesthesia 71:1077-1080. https://doi.org/10.1111/anae.13563
9. TAN PCF, DENNIS AT 2016 High flow humidified nasal preoxygenation in pregnant women. Anaesthesia 71:851-852. https://doi.org/10.1111/anae.13533
10. SHIPPAM W, PRESTON R, DOUGLAS J. TAYLOR J, ALBERT A. CHAU A 2019 High-flow nasal oxygen vs. standard flow-rate facemask pre-oxygenation in pregnant patients: a randomised physiological study. Anaesthesia 74:450-456. https://doi.org/10.1111/anae.14567
11. TAN PCF, O'MILLAY OJ, LEETON L, DENNIS AT 2019 High-flow humidified nasal preoxygenation in pregnant women: a prospective observational study. Br J Anaesth 122:86–91. https://doi.org/10.1016/j.bja.2018.08.015
12. AU K, SHIPPAM W, TAYLOR J, ALBERT A, CHAU A 2020 Determining the effective pre-oxygenation interval in obstetric patients using high-flow nasal oxygen and standard flow rate facemask: a biased-coin up-down sequential allocation trial. Anaesthesia 75(5):609-616. https://doi.org/10.1111/anae.14995

13. ZHOU S, ZHOU Y, CAO X, NI X, DU W, XU Z, LIU Z 2021 The efficacy of high flow nasal oxygenation for maintaining maternal oxygenation during rapid sequence induction in pregnancy: A prospective randomised clinical trial. Eur J Anaesthesiol 38(10): 1052-1058. https://doi.org/10.1097/EJA.0000000000001395
14. SJÖBLOM A, HEDBERG M, JOHANSSON S, HENNINGSSON R, SOUMPASIS I, LAFRENZ H, TÖRNBERG D, LODENIUS Å, FAGERLUND MJ 2023 Pre-oxygenation using high-flow nasal oxygen in parturients undergoing caesarean section in general anaesthesia: A prospective, multi-centre, pilot study. Acta Anaesthesiol Scand 67(8): 1028-1036. https://doi.org/10.1111/aas.14264
15. OSMAN YM, REHAB ABD EL-RAOF R 2021 High flow nasal cannula oxygen preventing deoxygenation during induction of general anaesthesia in caesarean section: A randomized controlled trial. Trends Anaesth Crit Care 40: 23-27. https://doi.org/10.1016/j.tacc.2021.06.006
16. TAN PCF, PEYTON PJ, DEANE A, UNTERSCHEIDER J, DENNIS AT 2024 Pre-oxygenation using high flow humidified nasal oxygen or face mask oxygen in pregnant people - a prospective randomised controlled crossover non-inferiority study (The HINOP2 study). Int J Obstet Anesth 60:104236. https://doi.org/10.1016/j.ijoa.2024.104236
17. REALE SC, FARBER MK 2024 High flow nasal cannula: A new tool for obstetric pre-oxygenation. Int J Obstet Anest 61: 104282. https://doi.org/10.1016/j.ijoa.2024.104282
18. POLLOCK W, ROSE L, DENNIS C-L 2010 Pregnant and postpartum admissions to the intensive care unit: A systematic review. Intensive Care Med 2010;36:1465-74. https://doi.org/10.1007/s00134-010-1951-0
19. JHOU HJ, CHEN PH, LIN C, YANG LY, LEE CH, PENG CK 2020 High-flow nasal cannula therapy as apneic oxygenation during endotracheal intubation in critically ill patients in the intensive care unit: A systematic review and metaanalysis. Sci Rep 2020;10:3541. https://doi.org/10.1038/s41598-020-60636-9
20. SINGH, AJAY; DHIR, ANKITA; JAIN, KAJAL; TRIKHA, ANJAN 2022 Role of High Flow Nasal Cannula (HFNC) for Pre-Oxygenation Among Pregnant Patients J Obstet Anaesth Crit Care 12(2):99-104. https://doi.org/10.4103/JOACC.JOACC_18_22
21. LI YH, LEI GY, GUO J, YI M, FU YJ, WANG GY 2024 Effect of maternal oxygen supplementation for parturient undergoing elective cesarean section by high-flow nasal oxygen compared with room air on fetal acidemia: study protocol for a randomized controlled trial. Trials 22;25(1):73. https://doi.org/10.1186/s13063-024-07927-y