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Research Article

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Comparison of the Effectiveness of High-Flow Nasal Oxygen vs. Standard Facemask Oxygenation for pre- and apneic oxygenation during Anesthesia Induction: A Systematic Review and Meta-analysis

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Abstract

Background

In recent years, high flow nasal oxygen(HFNO) has been widely used in clinic, especially in perioperative period. Many studies have discussed the role of HFNO in pre- and apneic oxygenation, but their results are controversial. Our study aimed to examine the effectiveness of HFNO in pre- and apneic oxygenation by a meta-analysis of RCTs.

Methods

EMBASE, PUBMED, and COCHRANE LIBRARY databases were searched from inception to July 2021 for relevant randomized controlled trails(RCTs) on the effectiveness of HFNO versus standard facemask ventilation(FMV) in pre- and apenic oxygenation. Studies involving one of the following six indicators: (1)Arterial oxygen partial pressure(PaO₂), (2)End expiratory oxygen concentration(EtO₂), (3)Safe apnoea time, (4)Minimum pulse oxygen saturation(SpO_{2min}), (5)Oxygenation(O₂) desaturation, (6)End expiratory carbon dioxide(EtCO₂) or Arterial carbon dioxide partial pressure(PaCO₂) were included. We select random effect model or fixed effect model for analysis according to the heterogeneity of the article, and express it as the mean difference(MD) or risk ratio(RR) with a confidence interval of 95%(95%CI). We conducted a risk assessment of bias for eligible studies and assessed the overall quality of evidence for each outcome.

Results

14 RCTs and 1012 participants were finally included. We found the PaO_2 was higher in HFNO group than FMV group with a MD(95% CI) of 57.38 mmHg(25.65 to 89.10; *p*=0.0004) after preoxygenation and the safe apnoea time was significantly longer with a MD(95% CI) of 86.93 seconds(44.35 to 129.51; *p*<0.0001) during anesthesia induction. There were no significant statistical difference in the minimum O_2 saturation, CO_2 accumulation, end expiratory oxygen concentration and O_2 desaturation rate during anesthesia induction between the two groups.

Conclusions

This systematic review and meta-analysis suggests that HFNO should be considered as an airway management tool for patients with high-risk hypoxemia or difficult airway during anesthesia induction. Compared with FMV, continuous use of HFNO during anesthesia induction can significantly improve oxygenation and prolong safe apnoea time in surgical patients.

Keywords

High flow nasal oxygen, facemask ventilation, preoxygenation, anesthesia induction, airway management

Introduction

Hypoxemia during anesthesia induction is still a problem that anesthesiologists need to pay attention to, especially for patients with high risk of hypoxemia and potentially difficult airway, which is one of the leading causes of anesthesia-related morbidity and mortality.^[1] According to Audrey et al's research, cardiac arrest can occur in 2-3% of intubation procedure in intensive care unit(ICU), and is strongly related to hypoxemia or absence of preoxygenaion before intubation.^[2] Preoxygenation before anesthesia induction can increase alveolar oxygen reserve of patients by denitrogenation, so as to increase safe apnoea time and reduce the incidence of hypoxemia and subsequent complications during endotracheal intubation. Consequently, the Difficult Airway Society guidelines recommended that all patients should be preoxygenated before induction of general anesthesia.^[3] The standard method of preoxygenation is performed using a facemask with an adequate seal between the patient and the circuit for 3 minutes with a fresh gas flow of 10 liter·min^{-1,[4]} In addition, apneic oxygenation can also prolong safe apnoea time and reduces the incidence of arterial oxygen desaturation during intubation.^[5]. Preoxygenation and apneic oxygenation are especially important in patients whereby bag-mask ventilation after the induction of anesthesia is to be avoided and in patients at higher risk of hypoxemia.^[5,6]

HFNO is composed of an air/oxygen blender, an active humidifier, a single heated circuit and a nasal cannula, which can provide constant inhaled oxygen concentration of 0.21-1.0 and oxygen flow rate of 1-60 liter·min⁻¹ or even higher.^[7] It has been proposed that the use of HFNO can generate continuous positive airway pressure, reduce anatomical dead space, improve mucociliary clearance and reduce the work of breathing.^[8,9,10,11] Since Patel first used HFNO for preoxygenation and apneic oxygen in patients with predicted difficult airway in 2015, and proposed that HFNO can significantly prolong the safe apnoea time of patients under general anesthesia.^[6] Many clinical anesthesiologists has carried out extensive and in-depth research on the application of HFNO in perioperative period, especially in the pre- and apneic oxygenation efficacy of HFNO during anesthesia induction. However, many studies have reached controversial results. There was a systematic review and meta-analysis have indicated the use of HFNO in the intraoperative setting can reduce the risk of O₂ desaturation, increase safe apnoea time and SpO_{2min} in patients at higher risk of hypoxemia.^[12] However, it was based on small-sampled studies and did not restrict the control group to standard face mask ventilation. In addition, recent published RCTs can be included in our systematic and meta-analysis.^[13-19]

Therefore, we conducted a systematic review and meta-analysis to update the existing evidence and gain further insight into the effectiveness of HFNO compared with FMV for pre- and apneic oxygenation during anesthesia induction.

Methods

Search strategy

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis(PRISMA) guidelines.^[20] The PRIAMA Checklist is provided in Additional file 1. English databases including PUBMED, EMBASE, and COCHRANE LIBRARY were searched from inception to July 2021 to find RCTs exploring the effectiveness of HFNO compared with FMV for pre- and apneic oxygenation in adult patients(>18 years old). According to the PICOS approach, the following terms were selected: "High flow

nasal oxygen," "HFNO," "High flow nasal cannula," "HFNC," "Transnasal humidified rapid-insufflation ventilatory exchange," "THRIVE," "Facemask," "Facemask ventilation," "Preoxygenation," "Intubation," "Anesthesia induction," "Randomised controlled trial," "RCT," "randomized," "controlled,". We also searched Google Scholar and clinical trail registry to identify grey literature and checked the reference list of all included studies to identify additional studies missed from the original electronic search.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: 1)comparing the effects of HFNO and FMV during anesthesia induction; 2)involving one of the following six indicators: (1)PaO₂, (2)EtO₂, (3)safe apnoea time, (4)SpO_{2min}, (5)O₂ desaturation, (6)EtCO₂ or PaCO₂, at anesthesia induction period for pre- or apenic oxygenation ; 3) randomized controlled trials. We excluded studies if they 1) were intensive care unit and pediatric patients; 2)were non mask controlled experiments, including bite block or nasal cannula ventilation; 3)were not able to extract data; 4) were not available for full text.

Articles selection and data extraction

Titles and abstracts were independently screened by 2 authors (Song, Sun). Following selection of abstracts, full text of articles identified for possible inclusion were obtained and assessed for inclusion independently by the 2 reviewers (Song, Sun). Disagreements were resolved by consensus or by consulting the senior author(Su). Study characteristics were extracted independently by 2 authors (Shi, Liu) using a standard data collection form in an Excel worksheet. The following information was extracted from each study: author, year of publication, type of surgery, number of patients, intervention characteristics and inclusion indicators. The 6 indicators extracted were PaO₂, EtO₂, safe apnea time, SpO_{2min}, O₂ desaturation and EtCO₂ or PaCO₂. The data were extracted independently by two authors (Shi, Liu) and then reviewed by the senior author(Su). When there is missing data, contact the relevant author to obtain the missing data.

Risk of bias assessment

Two reviewers(Song, Sun) independently assessed risk of bias in included studies using the Cochrane Collaboration risk-of-bias tool.^[21] Studies were categorized into high, low, or unclear risk of bias according to the following predefined criteria: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment(detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other potential sources of bias. Each study was compared for consistency, with any disagreement resolved by discussion between the two reviewers (Song, Sun) or mediated by a third reviewer(Su).

Statistical analysis

Meta-analysis was performed using Review Manager (RevMan version 5.4.1, The Nordic Cochrane Centre, Copenhagen, Denmark). Categorical and continuous variable summary data from each individual study were entered into Review Manager. The statistical method used for categorical outcome (O₂ desaturation) was Mantel-Haenszel and the effect measure was risk ratio (RR). The statistical method used for continuous outcome (PaO₂, EtO₂, safe apnoea time, SpO_{2min}, EtCO₂ or PaCO₂) was inverse variance and the effect measure was mean

difference. The analysis model was selected according to the heterogeneity. When l^2 is greater than 50%, the random effect analysis model was used, on the contrary, the fixed effect analysis model was used. Subgroup analysis and sensitivity analysis excluding literature one by one were used to explore the causes of high heterogeneity. Forest plots, RR (95% confidence interval [CI]), mean difference (95% CI), and heterogeneity (χ^2 and l^2) were generated for the 6 outcomes. For studies that showed results in median and range or interquartile range, the methodology of Wan et al^[22] was used to convert them into mean and standard deviation.

Results

The initial electronic search retrieved 1965 citations, and the grey literature search identified additional 408 studies. This process identified 121 potentially eligible studies for full-text review. After duplicate and ineligible studies were removed, 14 RCTs with a total of 1012 participants were finally included in our systematic review and meta-analysis(Fig. 1).^[13-19,23-29] The characteristics of included studies are presented in Table 1. The methodological quality of the involved trails is shown in Fig. 2. Two studies were multi-center RCT^[15,17] and the reminder were single-center RCTs. All 14 studies included one or more of the following outcomes: (1)PaO₂, (2)EtO₂, (3)safe apnoea time, (4)SpO_{2min}, (5)O₂ desaturation, (6)EtCO₂ or PaCO₂, at anesthesia induction period for pre- or apenic oxygenation.

PaO_2

Eight RCTs compared the PaO₂ after preoxygenation between HFNO and FMV group. HFNO was administered at flow rates between 30 and 70 liter·min⁻¹ while the flow rate of FMV group was 6-15 liter·min⁻¹ during preoxygenation. Meta-analysis based on the eight studies showed a statistically significant higher PaO₂ after preoxygenation in the HFNO group than FMV group with a MD(95% Cl) of 67.82 mmHg(29.25 to 106.40; p=0.0006). Due to high heterogeneity, we performed the sensitivity analysis by excluding the eight studies one by one, and found that by excluding Yasser MO et al's article could significantly reduce heterogeneity. And still statistically significant with a MD(95% Cl) of 57.38 mmHg(25.65 to 89.10; p=0.0004; Fig. 3). Subgroup analysis showed no significant difference in PaO2 between after preoxygenation and after intubation(p=0.70; Fig. 3). Funnel plot analysis suggested visually no significant asymmetry, suggesting a low chance of publication bias(Additional file 2, S1).

EtO₂

Five studies compared the EtO₂ between HFNO and FMV group. Three studies^[16,23,28] compared the EtO₂ after preoxygenation and two studies^[15,19] compared the EtO₂ after intubation. Meta-analysis based on the five studies showed that EtO₂ was similar in the HFNO group versus FMV group with a MD(95% CI) of -3.34%(-8.83 to 2.14; p=0.23; Fig. 4). Due to high heterogeneity, we performed the sensitivity analysis by excluding the five studies one by one, but there was no significant change in heterogeneity. Subgroup analysis showed that there was no significant difference in EtO₂ between after preoxygenation and intubation(MD -5.82; 95%CI -11.96 to 0.33; p=0.06 and MD 0.71; 95%CI -16.90 to 18.32; p=0.94; Fig. 4).

Safe apnea time

Four RCTs compared safe apnoea time during the peri-intubation period between HFNO and FMV. The definition of safe apnoea time was different in four articles. Two defined from the cessation of spontaneous breathing until the SpO₂ decreased to 90% or the apnoea time reached 6 minutes or 10 minutes,^[13,14] one defined the apnoea time from the onset of cessation of breathing until the SpO₂ decreased to 95% or the apnoea time reached 6 minutes^[29] and one defined from the cessation of spontaneous breathing until the SpO₂ decreased to 92%.^[18] In all four RCTs, facemask assisted ventilation was not implemented in control groups during apneic oxygenation. Airway patency was carefully maintained using a chin left or jaw thrust in all subjects.

From meta-analysis of the four RCTs, safe apnoea time was significantly longer in HFNO compared with FMV group by a MD(95% CI) of 110.36 seconds(50.56 to 170.16; p=0.0003). Due to the high heterogeneity, we excluded the literature one by one for sensitivity analysis. We found that when excluding Yasser MO et al's research can significantly reduce heterogeneity, and there were still statistical differences with a MD(95% CI) of 86.93 seconds(44.35 to 129.51; p<0.0001; Fig. 5A).

Minimum O₂ Saturation(SpO_{2min})

Three RCTs compared the $\text{SpO}_{2\text{min}}$ during the peri-intubation period between HFNO and FMV. Meta-analysis showed that the $\text{SpO}_{2\text{min}}$ was similar in HFNO and FMV subjects with a MD(95% CI) of 3.17% (-1.37 to 7.70; *p*=0.17; Fig. 5B). Due to the high heterogeneity, we excluded the studies one by one for sensitivity analysis. After excluding Sjöblom A et al's study, the heterogeneity decreased slightly, but there was a significant statistical difference in HFNO verses FMV with a MD(95% CI) of 4.91% (1.49 to 8.32; *p*=0.005).

O₂ desaturation

Five RCTs compared the rate of O_2 desaturation during intubation period between HFNO and FMV group. Desaturation was defined as $SpO_2 \leq 90\%$ in two studies, $^{[26-27]} SpO_2 \leq 93\%$ in two studies $^{[15,25]}$ and $SpO_2 \leq 92\%$ in one study. ^[18] Meta-analysis showed that the rate of peri-intubation O_2 desaturation was similar in HFNO group versus FMV group with a RR(95% CI) of 0.59(0.24 to 1.48; p=0.26; Fig. 5C).

PaCO₂ or End-tidal CO₂

Nine RCTs compared the EtCO₂ or PaCO₂ between HFNO group and FMV group during intubation period. Since both EtCO₂ and PaCO₂ can reflect the accumulation of CO₂ in the body, we analyzed EtCO₂ and PaCO₂ together. Meta-analysis showed that the CO₂ accumulation was similar in HFNO group versus FMV group with a MD(95% Cl) of 0.56 mmHg(-0.81 to 1.93; p=0.43; Fig. 6). We also performed subgroup analysis with EtCO₂ and PaCO₂, and found no significant statistical difference(p=0.09) between the EtCO₂ group(MD -0.18; 95% Cl -1.25 to 0.89; p=0.75) and the PaCO₂ group(MD 2.59; 95% Cl -0.38 to 5.57; p=0.09; Fig. 6). Funnel plot analysis suggested visually no significant asymmetry, suggesting a low chance of publication bias(S2).

Discussion

This systematic review and meta-analysis shows that compared with FMV, HFNO can significantly improve oxygenation and prolong safe apnoea time during anesthesia induction, but there is no significant statistical difference in the rate of O_2 desaturation, preoxygenation efficacy, minimum O_2 saturation and CO_2 level.

Airway management is of paramount importance in anesthesia induction period. Given the potential benefits of HFNO, including continuous positive airway pressure, reduce anatomical dead space, continuous apneic oxygenation reduce discomfort during endotracheal intubation,^[6,8,9,30] it has been widely used in intensive care unit(ICU), emergency department and operating room.^[2,5,6] Previous studies have shown that the use of HFNO during endotracheal intubation can reduce the incidence of hypoxemia, prolong the safe apnoea time and increase the minimum O₂ saturation in ICU patients.^[9,31-32] However, unlike critically ill patients in ICU, most surgical patients have well compensated cardiopulmonary function. The use of HFNO in anesthesia induction may draw different conclusions from ICU.

Meta-analysis showed that compared with FMV group, PaO₂ in HFNO group was higher during anesthesia induction(*p*=0.0004) and subgroup analysis showed that there was no significant difference(*p*=0.70) in PaO₂ between after preoxygenation and after intubation. This finding shows that compared with FMV, the use of HFNO during anesthesia induction can significantly improve the oxygenation of patients, which has been confirmed by previous studies. Badigar and colleagues^[33] investigated the oxygenation efficacy of HFNO in awake fibre-optic intubation in difficult airway patients, and found that HFNO can significantly improve oxygenation and prolong the safe apnoea time. The research of Corley A et al and Mauri T et al have shown that the mechanisms of HFNO improving oxygenation in patients may lie in increasing end expiratory lung volume and tidal volume by producing flow dependent positive airway pressure.^[9,11]

However, many studies have questioned the efficiency of HFNO in preoxygenation, especially in pregnant women. The studies of Au K et al and AI Sulttan S et al Showed that compared with FMV, the preoxygenation efficiency of HFNO in pregnant women was lower than that in FMV group, and Tan PCF et al's study showed that after 3 minutes preoxygenation of HFNO in pregnant women, the proportion of EtO_2 reaching 90% was only 60%, which was lower than that of FMV in previous studies.^[34-36] However, a modelling investigation by Stolady et al showed that despite generating lower EtO_2 , continuous application of HFNO could provide longer safe apnoea time in pregnant subjects in labour.^[37] In our study, meta analysis showed that there was no significant difference(p=0.23) in EtO_2 during anesthesia induction between FMV group and HFNO group and subgroup analysis also showed no significant difference(p=0.49) in EtO_2 between after preoxygenation and after intubation. However, due to the high heterogeneity of these results, we should treat these conclusions with caution. More studies are still needed to compare the EtO_2 changes after preoxygenation of HFNO and FMV.

Meta-analysis showed that safe apnoea time during anesthesia induction was longer in HFNO group than FMV group(*p*<0.0001). This finding is in line with the previous research conclusions in both ICU and operating room.^[5,38-39] Patel A et al first introduced HFNO for anesthesia induction preoxygenation and apneic oxygenation during surgery in patients with predictable difficult airway, and found that it can significantly prolong the safe apnoea time, with a median apnoea time of 14 minutes and a maximum of 65 minutes.^[6] HFNO can provide continuous supply for patients with apnoea through the effect of apneic oxygenation during intubation period, so as long to prolong safe apnoea time.^[6,9] Taking advantage of the fact that HFNO can significantly prolong the safe apnoea time, many medical institutions have successfully carried out tubeless anesthesia, especially in short operations with shared airway such as subglottic stenosis and upper airway surgeries.^[40-41] However, studies recently published by Piosik ZM et al and Booth AWG et al indicates that although the apneic oxygenation of HFNO can ensure the oxygenation of patients and maintain long-term tubeless anesthesia, it is easy to result in CO₂ accumulation and respiratory acidosis when the apnoea time is greater than 30 minutes.^[32,42] This extends previous knowledge and has implications for the safe application of HFNO during prolonged procedures.

Meta-analysis showed that there was no significant difference in the rate of O_2 desaturation(p=0.26) and the SpO_{2min} (p=0.17) between HFNO and FMV subjects during intubation period. These findings are not exactly consistent with the studies on HFNO in ICU. Doyle AJ et al's observational study showed that the use of HFNO during emergency intubation can reduce the incidence of desaturation in patients with high risk hypoxemia.^[43] Many studies have also shown that the use of HFNO can reduce the rate of O₂ desaturation of critically ill patients in ICU^[31,38,44], but Vourc'h M et al's study shown no difference.^[45] In addition, according to Guitton C, Vourc'h M and Simon M et al's studies, compared with FMV, the use of HFNO preoxygenation in ICU did not improve the SpO_{2min} during intubation in critically ill patients.^[31,45-46] A systematic review and meta-analysis examined the benefits of high-flow nasal cannula in the peri-intubation period of patients in ICU, and found that there was no difference in severe O₂ desaturation, serious complications and oxygenation compared with conventional oxygen therapy.^[47]

Meta-analysis showed no statistically significant difference(p=0.43) in EtCO₂ and PaCO₂ between HFNO group and FMV group. And subgroup analysis also showed no significant difference(p=0.09) in the EtCO₂ versus PaCO₂. Many studies have shown that HFNO can enhance CO₂ clearance by an interaction between highly turbulent supraglottic flow vortices and cardiogenic oscillation^[48], but the human body will still increase CO₂ accumulation at the rate of 0.9 to 1.8 mmHg·min^{-1[6,49]}. Although many studies have shown that there is no significant difference in CO₂ accumulation during anesthesia induction between HFNO group with conventional oxygen therapy group^[12,46], it is necessary to monitor CO₂ when using HFNO for a long time, and the monitoring of PaCO₂ has higher sensitivity than EtCO₂.

Several potential limitations are also present in this meta-analysis. First, we included 14 RCTs and observed six indicators, and there were relatively few articles included in each index, even though this is the largest number of RCTs that can be searched. Second, in this article, we included different populations into the meta-analysis. Due to the limited number of articles included in each observation index, we did not conduct subgroup analysis for different populations. Third, in this meta-analysis, although we reduced the heterogeneity through sensitivity analysis, each observation index still has a certain heterogeneity. Several important variables may be the source of heterogeneity, including the definition of each observation index, the use method of HFNO, the type of surgery and the subject population. Finally, due to the limited articles included in each indicator, we only evaluated the publication bias of PaO₂ and CO₂ indicators.

Conclusion

This systematic review and meta-analysis comprehensively evaluated the effectiveness of HFNO verses FMV for pre- and apneic oxygenation during anesthesia induction. After including 14 RCTs and 1012 participants, we found that compared with FMV, HFNO can significantly improve oxygenation and prolong safe apnoea time during anesthesia induction, and there was no significant statistical difference in the rate of O_2 desaturation, minimum O_2 saturation, EtO₂ and CO₂ level. We suggest that HFNO should be considered as an airway management tool for patients with high-risk hypoxemia or difficult airway during anesthesia induction. Its continuous application during anesthesia induction can significantly improve oxygenation, prolong safe apnoea time. Further well-powered RCTs should focus on comparing the effectiveness of HFNO verses FMV in special surgical populations, such as patients with hypoxemia, patients with difficult airway and pediatric patients.

List of abbreviations

HFNO: High flow nasal oxygen; RCTs: Randomized controlled trails; FMV: Facemask ventilation; PaO₂: Arterial oxygen partial pressure; EtO₂: End expiratory oxygen concentration; SpO_{2min}: Minimum pulse oxygen saturation; EtCO₂: End expiratory carbon dioxide; PaCO₂: Arterial carbon dioxide partial pressure; MD: Mean difference; RR: Risk ratio; 95%CI: Confidence interval of 95%; ICU: Intensive care unit.

Declarations

Ethics approval and consent to participate

No patients or members of public were involved in the present study. No patients were asked to advise on the interpretation or writing up of results.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files]. All data are from EMBASE, PubMed and Cochrane library databases (https://www.elsevier.com/solutions/embase-biomedical-research; https://pubmed.ncbi.nlm.nih.gov/advanced/; https://www.cochranelibrary.com/)

Competing interests

The authors declare that they have no competing interests.

Founding

Not applicable.

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Contributions

Jian-li Song made substantial contributions conception and design of the study; Jian-li Song and Yan Sun searched and screened literature; Yu-bo Shi, Xiao-yin Liu and Zhen-bo Su extracted data from the collected literature and analyzed the data; Jian-li Song and Yan Sun wrote the manuscript; Yu-bo Shi, Xiao-yin Liu and Zhen-bo Su revised the manuscript; all the authors approved the final version of manuscript. Jian-li Song and Yan Sun contributed equally to this work.

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Additional information

Additional file 1. PRISMA checklist.docx Additional file 2. S1: Funnel plot of PaO₂ S2: Funnel plot of CO₂ accumulation

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Figure 1

Studyflow diagram oftrial selection.



Risk of bias assessment. A Risk of bias summary. B Risk of bias graph. The plus sign indicates low risk, the sinus sign indicates high risk, and the question sign mark uncertain risk.

	1	HENO			FMV			Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	N, Random, 95% Cl			
Heinrich S 2014	404.67	66.67	11	338.67	76.98	11	12.2%	66.00 [5.82, 126.18]				
Jacob R 2021	493.5	48	20	482.25	48.75	18	18.0%	11.25 [-19.57, 42.07]				
Lyons C 2021	399.38	73.13	25	352.5	76.88	26	15.9%	46.88 [5.71, 88.05]				
Mir F 2017	327.75	114	20	314.25	121.5	20	10.1%	13.50 (-59.52, 86.52)				
Ng 2018	419.25	91.25	24	361.75	91.75	24	13.8%	57.50 [5.73, 109.27]				
Yasser MO 2021	427.75	47.83	50	299.25	51.83	50	0.0%	128.50 [108.95, 148.05]				
Zhen H 2020	378.87	110.7	30	292.5	84.14	28	14.0%	86.37 [35.97, 136.77]				
Zhou S 2020	444.41	46,73	17	328.71	72.8	17	15.9%	115.70 [74.58, 156.82]				
Total (95% CI)			147			144	100.0%	57.38 [25.65, 89.10]	+			
Heterogeneity: Tau ^a :	= 1204.94	; Chi*=	19.08,	df = 6 (P :	= 0.004); I [≠] = 69	9%		the the transferred			
Test for overall effect	Z = 3.54	(P = 0.0)	004)	241 0121 (8)	Contraction of the second	ACCURCES!			-200 -100 0 100 200			
		0 <u>0</u>	22						Pavours [experimental] Pavours [control]			
	Expe	eriment	al	с	ontrol			Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl			
9.1.1 PaQ. (After pre	eoxygena	tion)		10000								
Heinrich S 2014	404.67	66.67	11	338.67	76.98	11	12.2%	66.00 (5.82, 126, 18)				
Hua Z 2020	378.87	110.7	30	292.5	84.14	28	14.0%	86.37 [35.97, 136.77]				
Jacob R 2021	493.5	48	20	482.25	48.75	18	18.0%	11.25 - 19.57, 42.07				
Lyons C 2021	399.38	73.13	25	352.5	76.88	26	15.9%	46.88 (5.71, 88,05)				
Ng 2018	419.25	91.25	24	361.75	91.75	24	13.8%	57,50 (5,73, 109,27)				
Yasser MO 2021	427.75	47.83	50	299.25	51.83	50	0.0%	128.50 [108.95, 148.05]				
Subtotal (95% CI)			110			107	74.0%	48.61 [20.37, 76.86]				
Heterogeneity: Tau* =	= 494.63;	Chi ² = 7	81, df	= 4 (P = 0	1.10); P =	= 49%						
Test for overall effect	: Z = 3.37	(P = 0.0	007)	11								
9.1.2 PaO, (After int)	ubation)											
Mir F 2017	327.75	114	20	314.25	121.5	20	10.1%	13.50 [-59.52, 86.52]	*			
Zhou S 2020	444.41	46.73	17	328.71	72.8	17	15.9%	115.70 [74.58, 156.82]				
Subtotal (95% CI)			37			37	26.0%	69.24 [-30.50, 168.98]				
Heterogeneity: Tau ^a = Test for overall effect	= 4308.36 : Z = 1.36	; Chi ^a = (P = 0.1	5.71, d 7)	f=1 (P=	0.02); P	e = 82%						
Total (95% CI)			147			144	100.0%	57.38 [25.65, 89.10]	-			
Heterogeneity: Tau*:	1204.94	; Chi*=	19.08,	df = 6 (P :	= 0.004); i ² = 69	9%					
Test for overall effect	: Z = 3.54	(P = 0.0)	004)			12.0			-100 -50 0 50 100			
Test for subarous dif	ferences:	Chi#=0	0.15. df	= 1 (P =)	0.70). P	= 0%			Lavorus lextremmental Lavorus [compol			

Forest plots of Pa02 in HFNO versus FMV after pLmger-i and after intubation. Subgroup analysis shows the Pa02 after p'riation versus after intubation. Cl indicates confidence interval; gb degrees of freedom; HFNO, high-flow nasal oxygen; FMV, facemask ventilation; IV, inverse variance; 02, oxygen; SD, standard deviation.

	1	FNO			FMV			Mean Difference	Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	_	IV,	Random, 95	5% CI	
Hanouz JL 2019	77	12	50	89	2	50	19.8%	-12.00 [-15.37, -8.63]			-		
Jacob R 2021	91	2	20	93	2	18	21.2%	-2.00 [-3.27, -0.73]			•		
Shippam W 2019	85.75	6.25	17	89.5	5.5	20	19.4%	-3.75 [-7.58, 0.08]					
Sjöblom A 2021	76.7	16.1	174	84.9	7.7	175	20.4%	-8.20 [-10.85, -5.55]					
Zhou S 2020	86.71	4.12	17	76.94	7.74	17	19.1%	9.77 [5.60, 13.94]			*		
Total (95% CI)			278			280	100.0%	-3.34 [-8.83, 2.14]			٠		
Heterogeneity: Tau ² = Test for overall effect	= 36.55; (: Z = 1.19	Chi≇=) (P = 0	80.52,).23)	df = 4 (F	• < 10.0	0001);	r≊= 95%		-100	-50	O HENO EMV	50	100

	1	HFNO			FMV			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
8.1.1 EtO, (After pre	oxygena	tion)							
Hanouz JL 2019	77	12	50	89	2	50	19.8%	-12.00 [-15.37, -8.63]	+
Jacob R 2021	91	2	20	93	2	18	21.2%	-2.00 [-3.27, -0.73]	-
Shippam W 2019	85.75	6.25	17	89.5	5.5	20	19.4%	-3.75 [-7.58, 0.08]	*
Subtotal (95% CI)			87			88	60.5%	-5.82 [-11.96, 0.33]	•
Heterogeneity: Tau ² :	= 27.15;	Chi ^a =	29.63,	df = 2 (F	× 0.0	0001);	² = 93%		
Test for overall effect	: Z = 1.86	6 (P = (0.06)						
8.1.2 EtO, (After intu	ubation)								
Sjöblom Å 2021	76.7	16.1	174	84.9	7.7	175	20.4%	-8.20 [-10.85, -5.55]	
Zhou S 2020	86.71	4.12	17	76.94	7.74	17	19.1%	9.77 [5.60, 13.94]	-
Subtotal (95% CI)			191			192	39.5%	0.71 [-16.90, 18.32]	-
Heterogeneity: Tau ² :	= 158.28	; Chi ^e =	= 50.85	, df = 1 i	P < 0.	00001)	; P = 98%		
Test for overall effect	t Z = 0.08	8 (P = (94)						
Total (95% CI)			278			280	100.0%	-3.34 [-8.83, 2.14]	•
Heterogeneity: Tau*:	= 36.55;	Chi≇=	80.52,	df = 4 (F	< 0.0	0001);	l° = 95%		
Test for overall effect	Z = 1.19	$\Theta(\mathbb{P}=0)$) 23)						-100 -30 0 50 100
Test for subaroup dif	fferences	: Chi*	= 0.47.	df = 1 (i	P = 0.4	19), j #=	0%		ravous lexhermenail Lavous (counoi)

Forest plots of EtO2 in HFNO versus FMV after pmageraatM and intubation. Subgroup analysis shows the EtO2 after armagg,r_lation versus after intubation. Cl indicates confidence interval; fib degrees of freedom; 1-IFNO, high-flow nasal oxygen; FMV, facemask ventilation; IV, inverse variance; 02, oxygen; SD, standard deviation.



A. Forest plots of safe apnoea time in HFNO versus FMV after preoxyjenation. B. Forest plots of Sp02,mn in HFNO versus FMV during intubation. C. Forest plots of the rate of 02 desaturation in HFNO versus FMV during intubation. Cl indicates confidence interval; MD, mean difference; RR, risk ratio. a degrees of freedom; HFNO, high-flow nasal oxygen; FMV, facemask ventilation; IV, inverse variance; 02, oxygen; SD, standard deviation.

	E	IFNO			FMV			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Ci	IV, Random, 95% Cl
Hua Z 2020	72	9.23	30	69.54	12.26	28	4.9%	2.46 [-3.16, 8.08]	
Jacob R 2021	37.43	5.48	20	38.4	8.48	18	6.6%	-0.97 [-5.57, 3.63]	
Lodenius A 2018	37.5	6	40	39.75	7.5	39	11.6%	-2.25 [-5.25, 0.75]	
Mir F 2017	43.5	8.25	20	42	7.5	20	6.1%	1.50 [-3.39, 6.39]	
Ng1 2018	52.25	6.25	24	46	7	24	8.8%	6.25 [2.50, 10.00]	
Sjöblom A 2021	34.8	6	174	34.2	6	175	21.4%	0.60 [-0.66, 1.86]	
Tremey B 2020	39.98	6.82	30	38.75	5.68	31	11.0%	1.23 [-1.92, 4.38]	
Wong DT 2019	37.9	3	20	38.8	2.5	20	18.6%	-0.90 [-2.61, 0.81]	
Zhou S 2020	38.28	3.18	17	38.05	5.76	17	11.1%	0.23 [-2.90, 3.36]	
Total (95% CI)			375			372	100.0%	0.56 [-0.81, 1.93]	*
Heterodeneity, Tau* :	= 1.88; C	$hf^2 = 1$	5.95. d	(= 8 (P	= 0.04);	F= 50	%		
Test for overall effect	Z = 0.80) (P = (0.43)		Section Period				-10 -5 0 5 10 Favours [experimental] Favours [control]

	F	IFNO			FMV			Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl			
7.1.1 EtCO.,												
Jacob R 2021	37.43	5.48	20	38.4	8.48	18	6.6%	-0.97 [-5.57, 3.83]	+			
Lodenius A 2018	37.5	6	40	39.75	7.5	39	11.6%	-2.25 [-5.25, 0.75]	•			
Sjöblom A 2021	34.8	6	174	34.2	6	175	21.4%	0.60 [-0.66, 1.86]	•			
Tremey B 2020	39.98	6.82	30	38.75	5.68	31	11.0%	1.23 [-1.92, 4.38]	1 7			
Wong DT 2019	37.9	3	20	38.8	2.5	20	18.6%	-0.90 [-2.61, 0.81]	i •			
Subtotal (95% CI)			284			283	69.2%	-0.18 [-1.25, 0.89]	i I			
Heterogeneity: Tau ² =	= 0.27; C	$hi^2 = 4$.82, df	= 4 (P =	0.31); P	² = 17%						
Test for overall effect	Z = 0.32	? (P = (0.75)	1								
7.1.2 PaCO												
Hua Z 2020	72	9.23	30	69.54	12.26	28	4.9%	2.46 [-3.16, 8.08]				
Mir F 2017	43.5	8.25	20	42	7.5	20	6.1%	1.50 [-3.39, 6.39]	+			
Ng1 2018	52.25	6.25	24	46	7	24	8.8%	6.25 [2.50, 10.00]	-			
Zhou S 2020	38.28	3.18	17	38.05	5.76	17	11.1%	0.23 [-2.90, 3.36]	i +			
Subtotal (95% CI)			91			89	30.8%	2.59 [-0.38, 5.57]	•			
Heterogeneity: Tau ² =	= 4.54; C	hi²= 6	02, df	= 3 (P =	0.11); P	°= 50%	5					
Test for overall effect	Z=1.71	(P = (0.09)	1870 A.C. 18	ste militar							
Total (95% CI)			375			372	100.0%	0.56 [-0.81, 1.93]				
Heterogeneity Tau ² =	= 1.98; C	$hi^2 = 1$	5.95. d	f= 8 (P =	= 0.04);	$ ^2 = 50^{\circ}$	96		1. 1. J.			
Test for overall effect	Z = 0.80	(P = 0)	0.43)	A. A.			2.57		-100 -50 0 50	100		
Test for subornup dif	Terences	Chi	= 2.95	df = 1.6	P = 0.09	0 17 = 8	6 1 %		HENO EMV			

Forest plots of EtCO2 or PaCO2 in HFNO versus FMV after intubation . Subgroup analysis shows the EtCO2 versus PaCO7 after latubsuat Cl indicates confidence interval; 41. degrees of freedom; HFNO, high-flow nasal oxygen; FMV, facemask ventilation; IV, inverse variance; 02, oxygen; SD, standard deviation.

Supplementary Files

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