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 trials (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 (SpO₂min), (5) Oxygenation (O₂) desaturation, (6) End expiratory carbon dioxide (EtCO₂) or Arterial carbon dioxide partial pressure (PaCO₂) were included. Due to the source of clinical heterogeneity in the observed indicators in this study, we adopt random-effects model for analysis, 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: Fourteen RCTs and 1012 participants were finally included. We found the PaO₂ 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 s (44.35 to 129.51; p < 0.0001) during anesthesia induction. There were no significant statistical difference in the minimum SpO₂, CO₂ accumulation, EtO₂ and O₂ desaturation rate during anesthesia induction between the two groups.

Conclusions: This systematic review and meta-analysis suggests that HFNO should be considered as an oxygenation tool for patients 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.

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Introduction
Oxygenation is fundamental to safe anaesthetic practice and anaesthesiologists need to be skilled in oxygenation techniques. Hypoxemia during anesthesia induction is one of the leading causes of anesthesia-related morbidity and mortality [1], and anaesthesiologists should take it seriously and avoid its occurrence. It has been reported that cardiac arrests can occur in 2–3% of intubation procedure in intensive care unit (ICU), and is strongly related to hypoxemia or absence of preoxygenation 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 min with a fresh gas flow of 10 L·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 L·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 [8–11]. In 2015, HFNO was first used for preoxygenation and apneic oxygen in patients with predicted difficult airway, and was 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 SpO₂min 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. We selected 6 indicators to compare the use of HFNO and FMV during anesthesia induction. Among them, PaO₂ and EtO₂ can represent the efficacy of pre-oxygenation, safe apnoea time, SpO₂min and O₂ desaturation can represent the efficiency of pre-oxygenation, and EtCO₂ or PaCO₂ can be used to observe the effect of apneic oxygenation on patient ventilation [4].

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 PRISMA Checklist is provided in Additional file 1. English databases including PUBMED, EMBASE, and COCHRANE LIBRARY were searched from inception to December 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 PICO 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 trial registry to identify grey literature and checked the reference list of all included studies to identify additional studies missed from the original electronic search. This study does not contain any conference abstracts.

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) SpO₂min, (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 bile 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 PaO$_2$, EtO$_2$, safe apnoea time, SpO$_2$min, O$_2$ desaturation and EtCO$_2$ or PaCO$_2$. 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.

When comparing the safe apnoea time, the included articles have different definitions. Two defined from the cessation of spontaneous breathing until the SpO$_2$ decreased to 90% or the apnoea time reached 6 min or 10 min [13, 14], one defined the apnoea time from the onset of cessation of breathing until the SpO$_2$ decreased to 95% or the apnoea time reached 6 min [21] and one defined from the cessation of spontaneous breathing until the SpO$_2$ decreased to 92% [18]. And there are also differences in the definition of deoxygenation, desaturation was defined as SpO$_2$$\leq$90% in two studies [22, 23], SpO$_2$$\leq$93% in two studies [15, 24] and SpO$_2$$\leq$92% in one study [18]. In our analysis, we directly compared this indicator without adopting a unified definition.

**Risk of bias assessment**

Two reviewers (Song, Sun) independently assessed risk of bias in included studies using the Cochrane Collaboration risk-of-bias tool [25]. 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 (O$_2$ desaturation) was Mantel–Haenszel and the effect measure was risk ratio (RR). The statistical method used for continuous outcome (PaO$_2$, EtO$_2$, safe apnoea time, SpO$_2$min, EtCO$_2$ or PaCO$_2$) was inverse variance and the effect measure was mean difference. Due to the source of clinical heterogeneity in the observed indicators in this study, we adopt random-effects model for analysis. 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 ($\chi^2$ and $I^2$) were generated for the 6 outcomes. For studies that showed results in median and range or interquartile range, the methodology of Wan et al. [26] 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, 21–24, 27–29]. The characteristics of included studies are presented in Table 1. The methodological quality of the involved trials 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) PaO$_2$, (2) EtO$_2$, (3) safe apnoea time, (4) SpO$_2$min, (5) O$_2$ desaturation, (6) EtCO$_2$ or PaCO$_2$, at anesthesia induction period for pre- or apenic oxygenation.

**PaO$_2$**

Eight RCTs compared the PaO$_2$ after preoxygenation between HFNO and FMV group, including a total of 391 patients. HFNO was administered at flow rates between 30 and 70 L-min$^{-1}$ while the flow rate of FMV group was 6–15 L-min$^{-1}$ during preoxygenation. Meta-analysis based on the eight studies showed a statistically significant higher PaO$_2$ after preoxygenation in the HFNO group than FMV group with a MD (95% CI) 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% CI) of 57.38 mmHg (25.65 to 89.10; \( p = 0.0004 \); Fig. 3). The seven RCTs included a total of 291 patients. The source of heterogeneity may come from different patient populations, different pre-oxygenation time and different ways to use HFNO in the included articles. 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 and S1).

EtO2

Five studies compared the EtO2 between HFNO and FMV group. 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. The source of heterogeneity may come from different patient populations, different pre-oxygenation time and different ways to use HFNO in the included articles. Three studies [16, 27, 29] compared the EtO2 after preoxygenation and two studies [15, 19] compared the EtO2 after intubation. 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). 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 s (44.35 to 129.51; \( p < 0.0001 \); Fig. 5A). The source of heterogeneity may come from different patient populations, different pre-oxygenation time, different ways to use HFNO and the different definitions of the safe apnoea time in the included articles.

Safe apnoea time
Four RCTs compared safe apnoea time during the peri-intubation period between HFNO and FMV. 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 s (50.56 to 170.16; \( p = 0.0003 \)).

Minimum O2 saturation(\( \text{SpO}_{2\text{min}} \))
Three RCTs compared the \( \text{SpO}_{2\text{min}} \) during the peri-intubation period between HFNO and FMV.
Meta-analysis showed that the SpO2min 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; \( p = 0.005 \)). The source of heterogeneity may come from different patient populations, different pre-oxygenation time and different ways to use HFNO in the included articles.

### Table 1 Main characteristics of included studies.

| Authors (years) | Country | Type of study | Type of surgery | Number of patients | Intervention characteristics | Inclusion indicators |
|-----------------|---------|---------------|-----------------|--------------------|-----------------------------|---------------------|
| Yasser 2021     | Egypt   | RCT           | GA in caesarean section | 100 | 30-50L/min, n=50 | 6L/min, n=50 | 1, 3 |
| Loddenius 2018  | Sweden  | RCT           | Emergency surgery | 79 | 40-70L/min, n=40 | 10L/min, n=39 | 4, 5, 6 |
| Mir F 2017      | British | RCT           | Emergency surgery | 40 | 30-70L/min, n=20 | 12L/min, n=20 | 1, 5, 6 |
| Hua Z 2020      | China   | RCT           | GA in elderly     | 58 | 30-70L/min, n=30 | 10L/min, n=28 | 1, 3, 6 |
| Ng I 2018       | Australia | RCT           | GA in neurosurgical patients | 48 | 30-50L/min, n=24 | 10L/min, n=24 | 1, 5, 6 |
| Hanouz 2019     | France  | RCT           | Physiological study | 50 | 60L/min, n=50 | 12L/min, n=50 | 2 |
| Wong 2019       | Canada  | RCT           | GA in morbidly obese patients | 40 | 40-60L/min, n=20 | 15L/min, n=20 | 3, 4, 6 |
| Heinrich 2014   | Germany | RCT           | GA in morbidly obese patients | 22 | 50L/min, n=11 | 12L/min, n=11 | 1 |
| Sjöblom 2021    | Sweden  | RCT           | Emergency surgery | 349 | 30-70L/min, n=174 | 10L/min, n=175 | 2, 4, 5 |
| Shippam 2019    | British | RCT           | Physiological study | 37 | 30-70L/min, n=17 | 15L/min, n=20 | 2 |
| Rosén 2021      | Sweden  | RCT           | GA in obese patients | 38 | 70L/min, n=20 | 8L/min, n=18 | 1, 2, 6 |
| Tremey B 2020   | France  | RCT           | GA                | 61 | 30-60L/min, n=30 | 10L/min, n=31 | 3, 6 |
| Lyons C 2021    | Ireland | RCT           | GA                | 51 | 50L/min, n=25 | 15L/min, n=26 | 1, 3 |
| Zhou S 2020     | China   | RCT           | GA in caesarean section | 34 | 50L/min, n=17 | 10L/min, n=17 | 1, 2, 6 |

RCT=randomized controlled trial, GA=general anesthesia, HFNO=high flow nasal oxygen, FMV=face mask ventilation. 1) PaO2, 2) EtO2, 3) Safe apnoea time, 4) Minimum O2 saturation, 5) O2 desaturation, 6) EtCO2 or PaCO2.
O₂ desaturation

Five RCTs compared the rate of O₂ desaturation during intubation period between HFNO and FMV group. Meta-analysis showed that the rate of peri-intubation O₂ desaturation was similar in HFNO group versus FMV group with a RR (95% CI) of 0.66 (0.14 to 3.12; \( p = 0.60 \); Fig. 5C). The source of heterogeneity may come from different patient populations, different definition of desaturation, different pre-oxygenation time and different ways to use HFNO in the included articles.

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% CI) 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% CI -1.25 to 0.89; \( p = 0.75 \)) and the PaCO₂ group (MD 2.59; 95% CI -0.38 to 5.57; \( p = 0.09 \); Fig. 6). The source of heterogeneity may come from the difference between EtCO₂ and PaCO₂, the different pre-oxygenation time and the different apneic oxygenation time in the included articles. 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 intubation. Studies have shown that this can improve outcomes for patients undergoing intubation. However, the incidence of O₂ desaturation during intubation is still high in both groups, indicating the need for ongoing research into the optimal methods of oxygenation during this critical period.
anesthesia induction, but there is no significant statistical difference in the rate of O2 desaturation, EtO2, minimum SpO2 and CO2 level.

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. The oxygenation efficacy of HFNO in awake fibreoptic intubation in patients with difficult airways has been studied and found that HFNO can significantly improve oxygenation and prolong the safe apnoea time [30]. Previous studies have shown that HFNO can provide a stable inspired oxygen concentration, the distal positive airway pressure generated by high flow gas can increase end-expiratory lung volume, alveolar oxygen partial pressure and reduce intrapulmonary shunt, and the less dead space ventilation than FMV due to the washout effect of THRIVE [9, 19, 23, 28]. This may be a potential mechanism for HFNO to increase the PaO2 compared with FMV during pre-oxygenation.

In addition, we found 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, 31, 32]. It has been reported that HFNO can significantly prolong safe apnoea time when used for preoxygenation and apneic oxygenation during surgery in patients with predictable difficult airway, with a median apnoea time of 14 min and a maximum of 65 min [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

**Fig. 4** Forest plots of ETO2 in HFNO versus FMV after preoxygenation and intubation. Subgroup analysis shows the ETO2 after preoxygenation versus after intubation. CI indicates confidence interval; df, degrees of freedom; HFNO, high flow nasal oxygen; FMV, facemask ventilation; IV, inverse variance; o2 oxygen; SD, standard deviation
airway surgeries [33, 34]. However, studies recently published 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 min [35, 36]. This extends previous knowledge and has implications for the safe application of HFNO during prolonged procedures.

However, there are still some differences compared with previous studies. In our findings, there was no significant difference in the rate of O₂ desaturation (p = 0.60) and the SpO₂min (p = 0.17) between HFNO and FMV subjects during intubation period. These findings are not exactly consistent with the studies on HFNO in the ICU. Previous studies have shown that the use of HFNO during endotracheal intubation can reduce the incidence of hypoxemia and increase the minimum O₂ saturation in ICU patients [9, 35, 37]. But, an observational study showed that the use of HFNO during emergency intubation can reduce the incidence of desaturation in patients with high risk hypoxemia [38]. And there were also studies showing no differences [39–41]. The reason for this difference may be that, unlike ICU patients, surgical patients have well compensated cardiopulmonary function.

According to our findings, we can recognize that HFNO is an effective oxygenation tool in general anesthesia surgery. Oxygenation is of paramount importance in anesthesia induction period, especially in patients with difficult airways and high-risk hypoxemia patients. Previous studies have demonstrated the effectiveness of HFNO use in these specific populations [6, 9, 37]. However, in this paper, we did not compare the use of HFNO and FMV in these special populations, and therefore cannot suggest that HFNO is superior to FMV when used in these populations.

The strengths of this review include a comprehensive search strategy using major biomedical databases for...
published data and grey literature, and a focus on clinically relevant outcomes. Secondly, we followed a rigorous methodology. The review of eligibility criteria, data extraction, and outcome methodology assessment were all performed in duplicate with a high degree of inter-rater agreement. Thirdly, this review contained the largest number of RCTs published on this topic, which allowed outcomes to meet the optimal information size and allowed us to make more reliable inferences.

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 heterogeneity. 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 versus FMV for pre- and apneic oxygenation during anesthesia...
induction. According to our findings, compared with FMV, HFNO can improve oxygenation of patients during pre-oxygenation, and its continuous application during induction of anesthesia can significantly prolong the safe apnoea time. We suggest that HFNO should be considered as an oxygenation tool during anesthesia induction in patients undergoing general anesthesia surgery. Further well-powered RCTs should focus on comparing the effectiveness of HFNO versus FMV in special surgical populations, such as patients with hypoxemia, patients with difficult airway and pediatric patients.

Abbreviations
HFNO: High flow nasal oxygen; RCTs: Randomized controlled trails; FMV: Facemask ventilation; PaO₂: Arterial oxygen partial pressure; EtCO₂: End expiratory oxygen concentration; SpO₂min: 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.

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s12871-022-01615-7.

Acknowledgements
Not applicable.

Authors' 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.

Funding
This research was funded by the Key R&D Project of Jilin Province Science and Technology Development Program (No. 20202040165YY).

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/).

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.

Competing interests
The authors declare that they have no competing interests.

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