Comparison of Preoxygenation Strategies for Intubation of Critically Ill Patients

TAKE-HOME MESSAGE

When compared with facemask oxygenation, noninvasive positive pressure ventilation and high-flow nasal cannula reduce the risk of hypoxemia during tracheal intubation among critically ill adults.

METHODS

DATA SOURCES

MEDLINE, Embase, Web of Science, Scopus, and the Cochrane Central Register of Controlled Trials were searched from inception to October 31, 2024, without language restrictions. Reference lists of previous systematic reviews and included studies were manually screened for additional trials.

STUDY SELECTION

The authors included randomized trials comparing preoxygenation strategies (noninvasive positive pressure ventilation [NIPPV], high-flow nasal cannula, standard oxygen therapy, or a combination) in critically ill adults (more than or equal to 18 years) undergoing intubation in the emergency department (ED), intensive care unit (ICU), or surgical setting. Studies conducted exclusively in pediatric populations or among mixed populations in which more than 20% were pediatric patients were excluded. Two reviewers independently screened studies, resolving disagreements by consensus or third-party adjudication.

EBEM Commentators
Michael Gottlieb, MD
Robert Alexander, DO
Alexis K. Love, MD
Department of Emergency Medicine, Rush University Medical Center, Chicago, IL

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Results

Table. Comparison of the risk of hypoxemia between preoxygenation strategies in critically ill patients undergoing tracheal intubation.

Comparison	No. of Studies* (No. of Participants)	Direct Estimate RR (95% CI)	Network Estimate RR (95% CI)	Heterogeneity (I^2)*	Certainty
High-flow nasal cannula versus Facemask	8 (1,316)	0.74 (0.55-0.98)	0.69 (0.54-0.88)	0%	High
NIPPV versus Facemask	3 (1,555)	0.47 (0.35-0.63)	0.51 (0.39-0.65)	15%	High
High-flow nasal cannula versus NIPPV	1 (313)	1.18 (0.80-1.75)	1.38 (1.04-1.82)	N/A	Moderate
NIPPV versus NIPPV plus High-flow nasal cannula	1 (49)	Not reported	5.21 (0.65-41.43)	N/A	Very low

CI, Confidence interval; *N/A*, not applicable; *NIPPV*, non-invasive positive pressure ventilation; *RR*, relative risk.
*For direct estimate only.

The search yielded 4,153 unique reports, of which 15 randomized controlled trials (n=3,420) from 9 countries were included. The

DATA EXTRACTION AND SYNTHESIS

Two reviewers independently extracted data, resolving disagreements by consensus or third-party adjudication. Data were extracted using a standardized form and included study characteristics, patient demographics, intervention and comparator details, and outcomes. The primary outcome was the incidence of hypoxemia (less than 90%) during intubation. Secondary outcomes included severe hypoxemia (less than 80%), lowest oxygen saturation, mortality, and intubation-related complications. Risk of bias was assessed using the Cochrane Risk of Bias 2.0 tool.[1] Data were synthesized using a Bayesian network meta-analysis framework. Relative risk (RR) with 95% confidence intervals (CIs) were calculated for dichotomous outcomes, whereas absolute effects were presented as events per 100 patients using median risk across groups. Pairwise meta-analysis of direct estimates was performed using random-effects modeling. Statistical heterogeneity was assessed using the I^2 and chi-square testing, as well as visual inspection of forest plots. The authors assessed the strength of the evidence using the Grading of Recommendations Assessment, Development, and Evaluation criteria.

participants per study ranged from 38 to 1,301. The median age in the studies ranged from 40 to 78 years, and 40.2% (n=1375) of the total participants were women. Eight studies were performed in the ICU, 3 in the ED, 2 in elective surgery, and 2 in emergency surgery settings. Three studies compared non-invasive positive pressure ventilation (NIPPV) to facemask, 10 compared high-flow nasal cannula to facemask, one compared NIPPV to high-flow nasal cannula, and one compared NIPPV with high-flow nasal cannula to NIPPV. Hypoxemia was defined variably across the included studies, ranging from SpO_2 less than 80% to less than 93%. Five of the 15 studies were identified as having high risk of bias.

The authors found NIPPV reduced hypoxemia compared to facemask and high-flow nasal cannula (Table). High-flow nasal cannula also reduced hypoxemia versus facemask. NIPPV probably reduced serious adverse events compared to facemask (RR 0.30, 95% CI 0.12 to 0.77; moderate certainty evidence) and might have reduced the risk of adverse events compared to high-flow nasal cannula (RR 0.32, 95% CI 0.11 to 0.91; low certainty evidence). There was no significant effect of preoxygenation strategy on all-cause mortality (low to moderate certainty) or first attempt intubation success (low certainty) in any of the comparisons. There was no evidence of network-wide heterogeneity for the outcomes of interest. Subgroup and sensitivity analysis did not find any evidence of effect modification.

Commentary

Tracheal intubation is a common procedure, occurring in approximately 422,000 ED patients annually, which corresponds to 3 per 1,000 ED visits.[2] Despite this, it remains a high-risk procedure with international data reporting that 9.3% of patients experienced severe hypoxemia and 3.1% had cardiac arrest.[3] Preoxygenation is an important preparatory step among patients requiring endotracheal intubation, with the primary goal being to increase the body's reserve of oxygen, thereby extending the time until hypoxemia occurs during the intubation procedure.[4]

Multiple options exist for preoxygenation, including facemask, high-flow nasal cannula, and NIPPV. Although the traditional approach relied primarily on preoxygenation through facemask, more recent literature has challenged this using high-flow nasal cannula or NIPPV.[5] This systematic review and network meta-analysis of randomized control trials compared the different modalities and found high-flow nasal cannula and NIPPV were associated with reduced rates of peri-intubation hypoxemia. Among those, the most pronounced effect was seen in the group receiving NIPPV.

This study has several important limitations. First, many of the trials were small with a single large trial comprising over one-third of the data.[5] Additionally, there was inconsistent reporting of baseline characteristics, and multiple studies did not report measures of illness or severity of comorbidities (eg, chronic lung disease). The data also did not account for differences in concomitant interventions (eg, positioning strategies and sedation types) and intubator experience. Moreover, there was substantial clinical heterogeneity with respect to patient population, clinical setting, and outcome definitions. This was particularly important for hypoxemia, with thresholds varying from 80% to 93%. Although the majority of studies compared NIPPV or high-flow

nasal cannula to facemask, there were limited data comparing high-flow nasal cannula versus NIPPV. Further, this review did not report on how the devices were used, such as mask fit and flow rate. Finally, many of the outcomes had wide CIs and low or very low levels of certainty, limiting the strength of the recommendations.

Based on these findings, NIPPV or high-flow nasal cannula for pre-oxygenation may be preferred over facemask when feasible and available. Further studies should identify which populations experience the greatest benefit and the influence of peri-intubation apneic oxygenation on each approach.

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