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The Analysis Study of Comparison of High Flow Nasal Cannula versus Conventional Oxygen Therapy and Non Invasive Ventilation in Adults with Acute Hypoxemic Respiratory Failure: A Comprehensive Systematic Review

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ABSTRACT

Background: Acute respiratory failure (ARF) is a common and severe complication among hospitalized patients. This systematic review aims to compare high-flow nasal cannula, conventional oxygen therapy, and non-invasive ventilation in the management of acute hypoxemic respiratory failure by analyzing available studies of the last 10 years. **Methods:** The study adhered to PRISMA 2020 standards, examining English literature from 2014 to 2024. It excluded editorials, reviews from the same journal, and submissions without a DOI. PubMed, SagePub, SpringerLink, and Google Scholar were utilized as literature sources. **Result:** Initially retrieving 360 articles from online databases (PubMed, SagePub, SpringerLink and Google Scholar) eight relevant papers were selected after three rounds of screening for full-text analysis. **Conclusion:** HFNC shows notable benefits over COT and NIV for acute hypoxemic respiratory failure, improving oxygenation and patient comfort. It reduces intubation rates and may offer survival advantages. HFNC's effectiveness and tolerance make it a valuable option, though individual patient factors should guide therapy choices.

Keyword: acute respiratory failure, high flow nasal cannula, conventional oxygen therapy, noninvasive ventilation

INTRODUCTION

Acute respiratory failure (ARF) is a common and severe complication among hospitalized patients, frequently leading to intensive care unit (ICU) admissions. The condition is associated with an in-hospital mortality rate of

20.6% and accounted for an economic burden of $54.3 billion in the United States in 2009.[1] Among patients with ARF, approximately 42.1% require mechanical ventilation (MV), which is linked to prolonged hospital stays and elevated healthcare costs. ARF can be categorized into acute hypoxemic respiratory failure (AHRF) and acute hypercapnic respiratory failure. Treatment typically involves supplemental oxygen and addressing the underlying cause of respiratory distress.[2]

Conventional oxygen therapy (COT) is often the initial approach in managing AHRF, utilizing devices such as nasal cannulae (NC) or face masks (FM) to deliver oxygen at flow rates up to 15 L/min. However, COT may fall short in meeting patients' spontaneous inspiratory flow rates, resulting in inconsistent oxygen delivery and necessitating escalation to more advanced therapies such as non-invasive ventilation (NIV) or MV.[3,4]

High-flow nasal cannula (HFNC) oxygen therapy represents an emerging alternative that offers significant potential advantages over COT. HFNC systems can deliver heated and humidified oxygen at flow rates up to 60 L/min with a precise fraction of inspired oxygen (FiO2) ranging from 21% to 100%. This therapy generates a constant high flow, reducing oxygen dilution, washing out physiologic dead space, and producing positive end-expiratory pressure (PEEP) that can enhance ventilation. Additionally, the heated humidification promotes secretion clearance, reduces bronchospasm, and preserves mucosal integrity.[5,6]

While HFNC has been extensively studied in neonatal and pediatric populations, its application in adults with AHRF is less well understood. Current evidence from various trials suggests that HFNC may offer benefits in post-cardiac surgery and post-extubation settings, as well as during bronchoscopy.[7] However, the effectiveness of HFNC compared to COT and NIV in adults with AHRF in emergency and inpatient settings remains unclear.[8,9] This systematic review aims to compare high-flow nasal cannula, conventional oxygen therapy, and non-invasive ventilation in the management of acute hypoxemic respiratory failure by analyzing available studies of the last 10 years.

METHODS

Protocol

The author carefully followed the rules laid out in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. This was done to make sure the study met all its standards. The selection of this methodological approach was specifically aimed at ensuring the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic to compare high-flow nasal cannula, conventional oxygen therapy, and non-invasive ventilation in the management of acute hypoxemic respiratory failure based on literatures of the last 10 years. This study meticulously analyzed data on literatures to provide insights and enhance patient treatment strategies. The primary objective of this paper is to highlight the collective significance of the identified key points.

Inclusion criteria for this study entail: 1) Papers must be in English, and 2) Papers must have been published between 2014 and 2024. Exclusion criteria comprise: 1) Editorials; 2) Submissions without a DOI; 3) Previously published review articles; and 4) Duplicate entries in journals.

Search Strategy

The keywords used for this research are acute respiratory failure, high flow nasal cannula, conventional oxygen therapy, noninvasive ventilation. The Boolean MeSH keywords inputted on databases for this research are: *((("acute"[All Fields] OR "acutely"[All Fields] OR "acutes"[All Fields]) AND ("respiratory insufficiency"[MeSH Terms] OR ("respiratory"[All Fields] AND "insufficiency"[All Fields]) OR "respiratory insufficiency"[All Fields] OR ("respiratory"[All Fields] AND "failure"[All Fields]) OR "respiratory failure"[All Fields]) AND ("high"[All Fields] AND ("flow camb"[Journal] OR "flow"[All Fields]) AND ("cannula"[MeSH Terms] OR "cannula"[All Fields] OR ("nasal"[All Fields] AND "cannula"[All Fields]) OR "nasal cannula"[All Fields]))) OR (("conventional"[All Fields] OR "conventionals"[All Fields]) AND ("oxygen inhalation therapy"[MeSH Terms] OR ("oxygen"[All Fields] AND "inhalation"[All Fields] AND "therapy"[All Fields]) OR "oxygen inhalation*

therapy"[All Fields] OR ("oxygen"[All Fields] AND "therapy"[All Fields]) OR "oxygen therapy"[All Fields])) OR ("noninvasive ventilation"[MeSH Terms] OR ("noninvasive"[All Fields] AND "ventilation"[All Fields]) OR "noninvasive ventilation"[All Fields])) AND ((y_10[Filter]) AND (clinicaltrial[Filter])).

Data retrieval

The authors assessed the studies by reviewing their abstracts and titles to determine their eligibility, selecting relevant ones based on their adherence to the inclusion criteria, which aligned with the article's objectives. A consistent trend observed across multiple studies led to a conclusive result. The chosen submissions had to meet the eligibility criteria of being in English and a full-text.

This systematic review exclusively incorporated literature that met all predefined inclusion criteria and directly pertained to the investigated topic. Studies failing to meet these criteria were systematically excluded, and their findings were not considered. Subsequent analysis examined various details uncovered during the research process, including titles, authors, publication dates, locations, study methodologies, and parameters.

Quality Assessment and Data Synthesis

Each author independently evaluated the research presented in the title and abstract of the publication to determine which ones merited further exploration. The subsequent stage involved assessing all articles that met the predefined criteria for inclusion in the review. Decisions on including articles in the review were based on the findings uncovered during this evaluation process.

Table 1. Article Search Strategy

Database	**Strategi Pencarian**	***Hits***
Pubmed	*((("acute"[All Fields] OR "acutely"[All Fields] OR "acutes"[All Fields]) AND ("respiratory insufficiency"[MeSH Terms] OR ("respiratory"[All Fields] AND "insufficiency"[All Fields]) OR "respiratory insufficiency"[All Fields] OR ("respiratory"[All Fields] AND "failure"[All Fields]) OR "respiratory failure"[All Fields]) AND ("high"[All Fields] AND ("flow camb"[Journal] OR "flow"[All*	100

	Fields]) AND ("cannula"[MeSH Terms] OR "cannula"[All Fields] OR ("nasal"[All Fields] AND "cannula"[All Fields]) OR "nasal cannula"[All Fields]))) OR (("conventional"[All Fields] OR "conventionals"[All Fields]) AND ("oxygen inhalation therapy"[MeSH Terms] OR ("oxygen"[All Fields] AND "inhalation"[All Fields] AND "therapy"[All Fields]) OR "oxygen inhalation therapy"[All Fields] OR ("oxygen"[All Fields] AND "therapy"[All Fields]) OR "oxygen therapy"[All Fields])) OR ("noninvasive ventilation"[MeSH Terms] OR ("noninvasive"[All Fields] AND "ventilation"[All Fields]) OR "noninvasive ventilation"[All Fields])) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))Fields])) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))	
Science Direct	*(((acute respiratory failure) AND (high flow nasal cannula)) OR (conventional oxygen therapy)) OR (noninvasive ventilation)*	150
Sagepub	*(((acute respiratory failure) AND (high flow nasal cannula)) OR (conventional oxygen therapy)) OR (noninvasive ventilation)*	50
Google Scholar	*(((acute respiratory failure) AND (high flow nasal cannula)) OR (conventional oxygen therapy)) OR (noninvasive ventilation)*	160

Table 2. JBI *Critical appraisal of Study*

Parameters	Messika (2015)	Frat (2015)	Itagaki (2014)	Schwabbauer (2014)	Frat (2015)	Rittayamai (2015)	Bell (2015)	Nair (2021)
1. Bias related to temporal precedence Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation Was there a control group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Bias related to confounding factors Were participants included in any comparisons similar?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	No.	No.	No.	No.	No.	No.	No.	No.
5. Bias related to assessment, detection, and measurement of the outcome Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcomes of participants included in any comparisons measured in the same way?	No.	No.	No.	No.	No.	No.	No.	No.
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Statistical conclusion validity Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

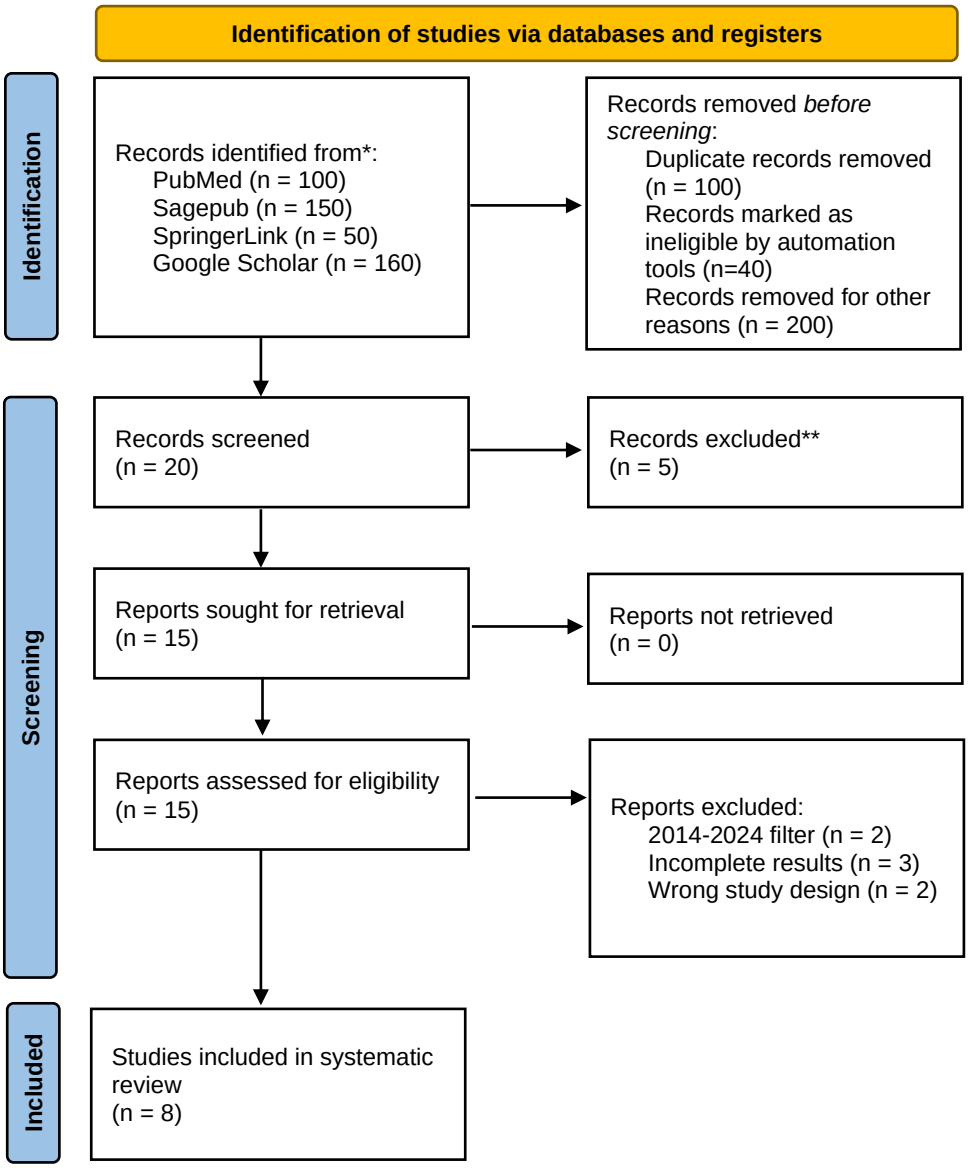

Figure 1. Article search flowchar

RESULT

The initial number of articles retrieved from online databases (PubMed, SagePub, SpringerLink, and Google Scholar) is 360 articles. After conducting three levels of screening, eight articles that directly relate to the current systematic review have been chosen for further assessment through full-text reading and analysis. Table 1 presents the selected literature included in this analysis.

Table 1. The literature included in this study

No.	Author	Origin	Method	Sample	Result
1.	Messika, et al.[4] (2015)	France	Prospective cohort study	607 patients	Out of 607 patients admitted, 560 required ventilatory or oxygen support, with 180 receiving non-invasive ventilatory support. High-flow nasal cannula (HFNC) was used in 87 patients, including 51 as a first-line treatment, 45 of whom had acute respiratory distress syndrome (ARDS). Pneumonia was the cause of ARDS in 82% of cases, and the intubation rate for these patients was 40%. HFNC failure was associated with higher Simplified Acute Physiology Score II (SAPS II), additional organ failure (primarily hemodynamic or neurological), and trends toward lower PaO2/FIO2 and higher breathing frequency.
2.	Frat, et al.[10] (2015)	France	Prospective cohort study	28 patients	In a study of 28 patients with acute hypoxemic respiratory failure (82% with acute respiratory distress syndrome, ARDS), high-flow nasal cannula (HFNC) significantly improved oxygenation and reduced breathing frequency compared to standard oxygen therapy. HFNC was better tolerated than non-invasive ventilation (NIV), with lower discomfort scores. Patients received HFNC for an average of 75 hours and NIV for 23 hours.

					Intubation was required in 36% of patients, with a breathing frequency of ≥30 breaths/min after HFNC initiation being an early predictor of intubation.
3.	Itagaki, et al.[11] (2014)	Japan	Retrospective cohort study	40 patients	In patients with mild to moderate respiratory failure, the use of high-flow nasal cannula (HFNC) significantly reduced breathing frequency from 25 to 21 breaths per minute. Additionally, measures of thoraco-abdominal synchrony, including MCA/VT and phase angle, showed significant improvement.
4.	Schwabbauer, et al.[12] (2014)	Germany	Retrospective cohort study	14 patients	In patients with hypoxic respiratory failure, non-invasive ventilation (NIV) achieved the highest PaO2 levels (129 mmHg) compared to high-flow nasal cannula (HFNC, 101 mmHg) and Venturi mask (VM, 85 mmHg). However, HFNC significantly reduced dyspnea and discomfort compared to NIV, with no significant difference between HFNC and VM in terms of dyspnea and discomfort. Patients rated HFNC as the most comfortable option, followed by VM and then NIV. For further treatment, most patients preferred HFNC.
5.	Frat, et al.[13] (2015)	France	Prospective cohort study	310 patients	In a study of 310 patients with non-hypercapnic acute hypoxemic respiratory failure, the intubation rates were not significantly

					different among the three treatment groups: 38% for high-flow oxygen, 47% for standard oxygen, and 50% for non-invasive ventilation (NIV). However, patients in the high-flow oxygen group had significantly more ventilator-free days (24 days) compared to those receiving standard oxygen (22 days) and NIV (19 days). High-flow oxygen also showed a significant survival benefit at 90 days, with lower mortality rates compared to standard oxygen and NIV.
6.	Rittayamai, et al.[14] (2015)	Thailand	Prospective cohort study	40 patients	In patients with acute dyspnea and hypoxemia, high-flow nasal cannula (HFNC) significantly improved both dyspnea and patient comfort compared to conventional oxygen therapy (COT). There was no significant difference in breathing frequency between the two groups by the end of the study. HFNC was well tolerated with no serious adverse events. Although the hospitalization rate was lower in the HFNC group compared to the COT group (50% vs. 65%), the difference was not statistically significant.
7.	Bell, et al.[15] (2015)	Australia	Randomised controlled trial	28 patients	In a trial involving 100 patients, the intervention group receiving high-flow nasal cannula (HFNC) oxygenation showed a significant improvement in respiratory status compared to standard oxygen therapy.

					Specifically, a higher proportion of patients in the HFNC group had a reduced respiratory rate at 2 hours (66.7% vs. 38.5%, P = 0.005) and a lower proportion required escalation in ventilation therapy (4.2% vs. 19%, P = 0.02).
8.	Nair, et al.[16] (2021)	France	Retrospective cohort study	99 patients	In this study, baseline characteristics and PaO_2/FiO_2 ratios were similar between the non-invasive ventilation (NIV) and high-flow nasal cannula (HFNC) groups. The intubation rate at 48 hours showed no significant difference (33% NIV vs. 20% HFNC, P = 0.12). However, by day 7, the intubation rate was significantly lower in the HFNC group (27.27%) compared to the NIV group (46.29%, P = 0.045). This difference remained significant after adjusting for chronic kidney disease and arterial pH (P = 0.03). Hospital mortality rates were not significantly different between the HFNC (29.1%) and NIV (46.2%) groups (P = 0.06).

Messika, et al.[4] (2015) concluded that HFNC was successful in a significant portion of severe ARDS cases and could be considered as a first-line therapy for acute respiratory failure, including ARDS patients.

Frat, et al.[10] (2015) suggested that HFNC can effectively improve oxygenation and be used between NIV sessions to prevent oxygenation decline.

Itagaki, et al.[11] (2014) concluded that HFNC enhances thoraco-abdominal synchrony in adult patients with respiratory failure.

Schwabbauer, et al.[12] (2014) concluded that HFNC provides a good balance between oxygenation and comfort and is well tolerated by patients.

Frat, et al.[13] (2015) concludes that while intubation rates were similar, high-flow oxygen provided a mortality advantage.

Rittayamai, et al.[14] (2015) concludes that HFNC may benefit patients requiring oxygen therapy in the emergency department.

Bell, et al.[15] (2015) concludes that HFNC oxygenation improves respiratory outcomes in patients presenting to the emergency department with acute undifferentiated shortness of breath.

Nair, et al.[16] (2021) showed no significant improvement in oxygenation or intubation rates at 48 hours was demonstrated between NIV and HFNC.

DISCUSSION

The comparison of High Flow Nasal Cannula (HFNC), Conventional Oxygen Therapy (COT), and Non-Invasive Ventilation (NIV) in managing adults with acute hypoxemic respiratory failure reveals several insights from the studies reviewed. HFNC has demonstrated notable advantages in improving oxygenation and patient comfort. Specifically, HFNC significantly enhanced oxygenation compared to standard oxygen therapy and was better tolerated than NIV. This is consistent with findings from Messika et al. (2015) and Frat et al. (2015), who highlighted HFNC's efficacy in improving oxygenation, particularly in patients with acute respiratory distress syndrome (ARDS).[4,13]

Despite these benefits, the impact of HFNC on intubation rates compared to NIV is mixed. While Frat et al. (2015) observed no significant difference in intubation rates at 48 hours between HFNC and other treatments, HFNC was associated with a lower intubation rate at 7 days compared to NIV, as reported by Nair et al. (2021). This suggests that HFNC might be linked to a reduced need for intubation over the longer term.[10,16] Additionally, Bell et al. (2015) found that HFNC reduced the need for escalation in ventilation therapy compared to standard

oxygen therapy, highlighting its potential in preventing the need for more invasive interventions.[15]

HFNC's better tolerance and comfort compared to NIV are also noteworthy. Studies by Schwabbauer et al. (2014) and Rittayamai et al. (2015) reported that patients experienced less discomfort and improved comfort scores with HFNC. This improved tolerance likely contributes to its effectiveness and patient satisfaction.[12,14]

Regarding mortality and ventilator-free days, HFNC showed a survival advantage over standard oxygen and NIV in some studies, such as Frat et al. (2015), who noted a significant mortality benefit at 90 days. Furthermore, HFNC was associated with more ventilator-free days compared to standard oxygen and NIV, suggesting it may offer additional benefits in managing acute respiratory failure.[13]

Overall, HFNC appears to be a valuable option for managing acute hypoxemic respiratory failure, offering improvements in comfort, dyspnea, and potentially survival. However, the choice between HFNC, COT, and NIV should be tailored to individual patient needs, taking into account factors such as the severity of respiratory failure, comorbid conditions, and patient comfort. Further research is needed to confirm these findings and better define HFNC's role in different patient populations.[11]

CONCLUSION

HFNC shows notable benefits over COT and NIV for acute hypoxemic respiratory failure, improving oxygenation and patient comfort. It reduces intubation rates and may offer survival advantages. HFNC’s effectiveness and tolerance make it a valuable option, though individual patient factors should guide therapy choices.

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