

LA EFECTIVIDAD DEL OXÍGENO DE ALTO FLUJO NASAL EN LA INSUFICIENCIA RESPIRATORIA: REVISIÓN SISTEMÁTICA

A efetividade do oxigénio nasal de alto fluxo na insuficiência respiratória: revisão sistemática

The effectiveness of high-flow nasal oxygen in respiratory insufficiency: systematic review

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ABSTRACT

Background: respiratory insufficiency is a syndrome with a great impact on hospital admissions, morbidity and mortality. The applicability of High-flow nasal oxygen has been the subject of interest in critically ill patients. **Objective:** to know the effectiveness of High-flow nasal oxygen as a treatment for respiratory insufficiency in adult patients admitted to the intensive care units. **Methods:** systematic reviews of effectiveness using the PICO strategy and recommendations from the Joanna Briggs Institute. The survey was carried out in august 2021 using the PubMed and EBSCOhost access platforms. **Results:** 583 results were identified. Six randomized clinical trials were analyzed. The selection was made after elimination of duplicates; title reading, abstract reading and full text reading according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram. **Conclusion:** high-flow nasal oxygen proved to be comfortable, tolerable and effective in the treatment of hypoxemic and hypercapnic respiratory insufficiency. It was effective when compared with conventional oxygen therapy in the post-extubation of hypoxemic patients and in reducing partial pressure of carbon dioxide when compared with Non-Invasive Ventilation in hypercapnic patients.

Keywords: respiratory insufficiency; critical care; systematic review

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RESUMO

Enquadramento: a insuficiência respiratória é uma síndrome com grande impacto nos internamentos, na morbilidade e mortalidade. A aplicabilidade do oxigénio nasal de alto fluxo tem sido alvo de interesse no doente crítico. **Objetivo:** conhecer a efetividade do oxigénio nasal de alto fluxo no tratamento da insuficiência respiratória no adulto em unidades de cuidados intensivos.

Métodos: revisão sistemática de efetividade que utiliza a estratégia PICO e recomendações do Joanna Briggs Institute. A pesquisa foi realizada em agosto de 2021 com recurso às plataformas de acesso PubMed e EBSCOhost. **Resultados:** identificaram-se 583 resultados. Foram analisados seis ensaios clínicos randomizados. A seleção foi feita após eliminação de duplicados; leitura do título, resumos e textos integrais de acordo com o diagrama Preferred Reporting Items for Systematic Reviews and Meta-Analyses. **Conclusão:** o oxigénio nasal de alto fluxo revelou-se confortável, tolerável e eficaz no tratamento da insuficiência respiratória hipoxémica e hipercápnica. Foi eficaz quando comparado com oxigenoterapia convencional na pós-extubação de doentes hipoxémicos e na redução da pressão parcial de dióxido de carbono quando comparado com a Ventilação Não Invasiva nos doentes hipercápnicos.

Palavra-chave: insuficiência respiratória; cuidados críticos; revisão sistemática

RESUMEN

Marco contextual: la insuficiencia respiratoria es un síndrome que tiene un gran impacto en los ingresos hospitalarios, la morbilidad y mortalidad. La aplicabilidad del oxígeno nasal de alto flujo ha sido objeto de interés en pacientes críticos. **Objetivo:** conocer la efectividad del oxígeno nasal de alto flujo en el tratamiento de la insuficiencia respiratoria en adultos en unidades de cuidados intensivos. **Métodos:** revision sistemática de efectividad utilizando la estrategia PICO y recomendaciones del Instituto Joanna Briggs. La búsqueda se llevó a cabo en agosto de 2021 utilizando las plataformas de acceso PubMed y EBSCOhost. **Resultados:** se identificaron 583 resultados. Se analizaron seis ensayos clínicos aleatorios. La selección se realizó después de la eliminación de duplicados; lectura de títulos, de resúmenes y de texto completo siguiendo el diagrama Preferred Reporting Items for Systematic Reviews and Meta-Analyses. **Conclusión:** el Oxígeno nasal de alto flujo demostró ser cómodo, tolerable y eficaz en el tratamiento de la insuficiencia respiratoria hipoxémica e hipercápnica. Fue eficaz en comparación con la oxigenoterapia convencional en la postextubación de pacientes hipoxémicos y en la reducción de la presión parcial de dióxido de carbono en comparación con la Ventilación No Invasiva en pacientes hipercápnicos.

Palabra Clave: insuficiencia respiratoria; cuidado crítico; revisión sistemática

INTRODUCTION

In Portugal, according to data from the national observatory of respiratory diseases, pneumonia and Respiratory Insufficiency (RI) were the respiratory pathologies that had the greatest impact on the number of hospitalizations between 2007 and 2016 (Santos, 2018). The episodes of hospitalization due to RI have been increasing in people of both genders, with increases reaching a percentage of 56% between 2007 and 2016. When analyzed by age, it was found that these increases are particularly relevant in people over 79 years old, with an increase of 120% and a high mortality rate of around 25% (Santos, 2018). RI represents a complex clinical presentation, resulting from multiple diseases that can affect the different components of the respiratory system, defined by the presence of a set of signs and symptoms (syndrome), and physiological changes that reflect the respiratory system's inability to adequately remove the CO₂ produced in the body and/or adequately oxygenate arterial blood (Martins, 2019). This is classified as hypoxemic (type I), also known as alveolar-capillary, which is characterized by a decrease in PaO₂ (PaO₂ < 60 mmHg in room air, or PaO₂/FiO₂ ratio ≤ 300 mmHg in patients under oxygen or ventilation therapy) and normal or reduced PaCO₂ levels. Alternatively, it can be classified as hypercapnic (type II), in which there is an increase in PaCO₂ (PaCO₂ > 45 mmHg), often accompanied by hypoxemia (Gomes & Sotto-Mayor, 2001; Martins, 2019; Pádua et al., 2003; Roussos & Koutsoukou, 2003). In this context, the approach to RI may require a therapeutic escalation strategy based on the application of a wide range of non-ventilatory interventions (conventional oxygen therapy and high-flow oxygen) and ventilatory interventions (Non-

Invasive Ventilation [NIV], Mechanical Ventilation, and Extra Corporeal Membrane Oxygenation) (Scala & Heunks, 2018). The reason for applying these artificial supports is essentially to gain time for etiological therapy to reverse the cause of acute respiratory system decompensation (Scala & Heunks, 2018). In these patients, where the probability of in-hospital death is high, and even higher the longer recognition and adequate treatment of RI is delayed, the therapeutic escalation strategy is of extreme importance (Bellani et al., 2016; Virani et al., 2019). Recently, there has been a growing interest in an alternative to conventional oxygen therapy in this therapeutic escalation: High-Flow Nasal Oxygen (HFNO) (Scala & Heunks, 2018). The use of this therapy in pediatrics and neonatology since the 1950s has led to the development of systems adapted for adults, which reliably provide heated and humidified oxygen at high flows through nasal cannulas, leading to its use in critically ill adults (Spoletini et al., 2015; Wilkinson et al., 2016). HFNO is a therapeutic modality based on four essential components: a high-flow oxygen source with air mixer, which allows for the definition of FiO₂ up to 1, at a flow rate ranging from 5 to 60 L/min; a humidifier; a heated inspiratory circuit between 31° and 37°C; and specific nasal cannulas with a wider diameter compared to conventional nasal cannulas that, together, provide heated and humidified oxygen at flows much higher than those of conventional oxygen therapy (Nishimura, 2015). The physiological effects associated with HFNO include: clearing of the dead space in the pharynx, reduction of nasopharyngeal resistance, the effect of Positive End-Expiratory Pressure (PEEP), alveolar recruitment, increased humidification, better control of FiO₂, and

mucociliary clearance (Gotera et al., 2013). In patients with RI of various etiologies, HFNO has been shown to result in greater comfort and oxygenation than conventional oxygen therapy provided via a face mask. In the “High Flow Nasal Oxygen in the Resuscitation of patients with Acute Lung Injury” (FLORALI) study, the largest multicenter randomized study to date, treatment with HFNO compared to conventional oxygen therapy or NIV did not result in significantly different intubation rates at 28 days, but did show a statistically significant difference in favor of HFNO in 90-day mortality and reduction of intubation rates in the $\text{PaO}_2/\text{FiO}_2 < 200$ mmHg subgroup (Frat et al., 2015). Therefore, experience in the use of HFNO in adults is limited, and there are no established guidelines or decision-making pathways to guide the use of HFNO for adults (Dres & Demoule, 2017; Ischaki et al., 2017). Thus, in this systematic literature review, we aim to assess the effectiveness of HFNO in the treatment of RI in adult patients admitted to the Intensive Care Unit (ICU).

METHOD

Protocol Registration

The protocol for this study was published and registered in the International Prospective Register of Systematic Reviews, known as PROSPERO, with the identification code CRD42021271482, and no changes were made to the initially defined protocol (Aramid Gomes et al., 2021).

Study type

Systematic literature reviews aim to provide a comprehensive and unbiased synthesis of relevant studies in a single document, using rigorous and transparent methods. They seek evidence that meets

pre-specified eligibility criteria in order to answer a specific research question (Aromataris & Munn, 2020a; Cumpston et al., 2019). The methodology used for the present article consists of a systematic review of effectiveness as described in the Joanna Briggs Institute (JBI) systematic review manual and was configured as a narrative synthesis of results. This methodology aims to determine to what extent an intervention, when used appropriately, achieves the intended effect (Tufanaru et al., 2020).

Research question and aim

We used the PICO (Population, Intervention, Comparison, and Outcome) mnemonic to construct the following research question: "What is the effectiveness of HFNO in the treatment of RI in adult patients admitted to the ICU?" In this sense, the (P)opulation is adult patients admitted to the ICU with RI; the (I)ntervention is HFNO; the (C)omparison is any treatment; the (O)utcome is the treatment of RI. The purpose of this review is to know the effectiveness of HFNO as a treatment for RI in adult patients admitted to the ICU (Tufanaru et al., 2020).

Inclusion and exclusion criteria

The inclusion criteria are: articles written in Portuguese, English, and Spanish; articles that address the research question; articles published in the last five years (2016-2021); experimental studies; adult patients admitted to ICU, and experimental studies found in secondary bibliographic references. The exclusion criteria are: articles that are duplicated in the database; articles outside the scope of the PICO question; articles without full text, and studies that meet only 6 out of the 13 conditions provided in the methodological quality assessment tool.

Review Strategy

In August 2021, a literature search was conducted using Medical subject Headings (MeSH) browser to identify the descriptors and keywords that guided our bibliographic research, resulting in the descriptors "critical care," "intensive care," "respiratory insufficiency," "child," "pediatrics," and the keywords "high flow." These identified terms allowed us to structure a Boolean phrase, using the AND, OR, and NOT operators with additional instruments, including parentheses, quotation marks, and asterisks. These operators enabled the definition of relationships between the search terms, resulting in the phrase: ("RESPIRATORY INSUFFICIENCY") AND ("HIGH FLOW") AND ("CRITICAL CARE" OR "INTENSIVE CARE") NOT (CHILD* OR PEDIAT*). The search for articles was conducted on the PubMed and EBSCOhost search engines, including all associated databases: CINAHL®Complete; MEDLINE Complete; Nursing & Allied Health: Comprehensive Edition; Cochrane Controlled Trials Register; Cochrane Database of Systematic Reviews; Cochrane Methodology Register; Library, Information Science & Technology Abstracts; MedicLatina; Cochrane Clinical Answers.

Study screening and selection

Article selection was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). Two reviewers conducted the article selection process, taking into consideration the research question, the objective of the review, and the pre-specified inclusion criteria. In cases where there was no consensus between the reviewers, a third reviewer was consulted to break the tie. All reviewers evaluated the studies

independently for inclusion in the review, and consensus was reached in all domains.

Critical Appraisal

The methodological quality of the studies included in the review was independently assessed by two reviewers using the critical appraisal tools standardized by JBI (Aromataris & Munn, 2020b). A third reviewer was added to break the tie in cases of disagreement. For the studies included in this review, the checklist for randomized controlled trials was used, which includes 13 questions that verify the necessary conditions for the study's methodological design, allowing for the identification of systematic errors in design, conduct, and analysis that can compromise the validity of its inferences (Tufanaru et al., 2020).

Methodology for analysis of study results

All relevant data to be extracted for the review were analyzed independently by two reviewers. A table was used for the systematic recording of the study content, as proposed in the JBI manual, which included the following data: study authors, title, year, study location, study level of evidence, evaluation of the study's methodological quality, objective of the study under analysis, and recording of the study intervention and results (Aromataris & Munn, 2020b).

RESULTS

EndNote was the software used for managing the results that emerged from the search. The process of article inclusion involved the following stages: identification, selection, eligibility, and inclusion, using the PRISMA diagram (Moher et al., 2009). Analysis of Figure 1 reveals 583 results. Eighty-five duplicate articles were eliminated, leaving 498 articles. Out of these, 401 were excluded after reading the titles,

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leaving 97. Analysis of the abstracts led to the exclusion of 76 articles. Out of the 21 articles selected after reading the abstracts, 10 were excluded for not meeting the eligibility criteria. Out of the 11 articles

evaluated for full-text reading, 5 were excluded due to low methodological quality (<50%) after applying the tool for analysis of methodological quality, and 6 were considered for inclusion in this review.

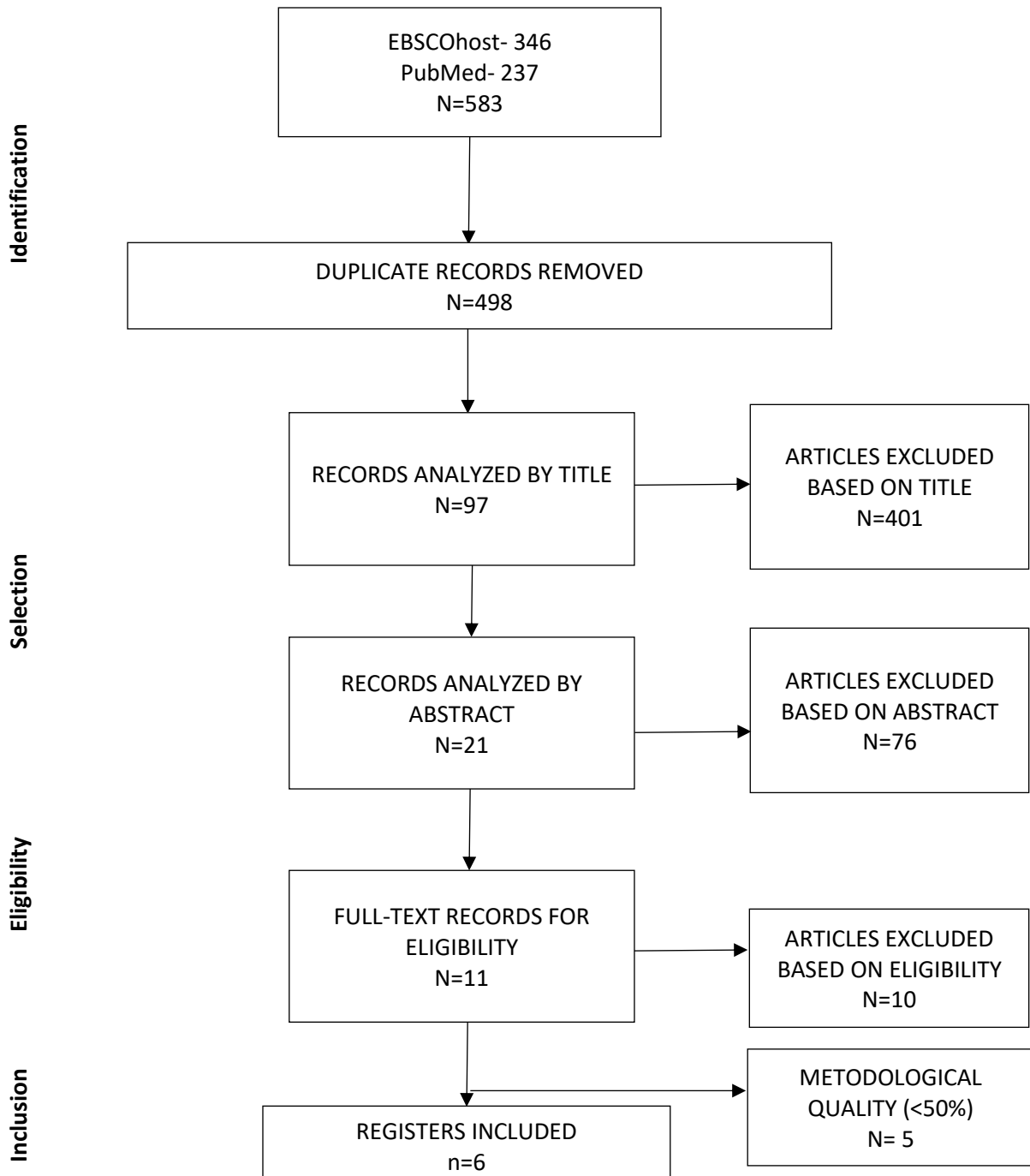


Figure 1: PRISMA (Moher et al., 2009)

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The analysis of table 1 provides information on the summary of the main characteristics of the articles and their results. All selected articles for analysis are randomized clinical trials, with a level of evidence 1c according to JBI classification (2013).

Table 1

Results extracted from studies included in the systematic literature review

AUTHORS	Simon et al. (2016)		
TITLE	High flow nasal cannula oxygen versus bag-valve-mask for Preoxygenation before intubation in patients with hypoxemic respiratory failure- a randomized controlled trial		
YEAR/LOCATION	2016, Germany		
JBI LEVEL OF EVIDENCE (2013)	Randomized (1c)	METHODOLOGICAL QUALITY EVALUATION (Tufanaru et al., 2020)	7/13 54%
SAMPLE	n= 40 (n= 20 for HFNO mean age 63, n= 20 for bag valve mask, 55% men mean age 54; PaO ₂ /FiO ₂ >200 ≤300 mmHg)		
AIM OF THE STUDY			
Compare the use of HFNO with the bag valve mask in pre-oxygenation during intubation in patients with hypoxemic RI			
INTERVENTION			
Pre-oxygenation with bag valve mask versus HFNO			
RESULTS			
1) PaO ₂ /FiO ₂ , PaCO ₂ , SpO ₂ , RR, HR, mean arterial pressure and degree of intubation difficulty, with no statistically significant differences between groups at baseline; 2) after pre-oxygenation, SpO ₂ increased in the bag valve mask group to 94% and in the HFNO group to 98% (p= 0.004); 2) the lowest mean SpO ₂ during intubation was 89% in the HFNO group and 86% in the bag valve mask group (p=0.45); 3) at the end of intubation, there were no statistically significant differences in SpO ₂ , PaO ₂ /FiO ₂ , PaCO ₂ ; 4) the results cannot be inferred for other populations.			
AUTHORS	Song et al. (2017)		
TITLE	The value of high-flow nasal cannula oxygen therapy after extubation in patients with acute respiratory failure		
YEAR/LOCATION	2017, China		
JBI LEVEL OF EVIDENCE (2013)	Randomized (1c)	METHODOLOGICAL QUALITY EVALUATION (Tufanaru et al., 2020)	8/13 62%
SAMPLE	n= 60 (n= 30 for HFNO mean age 66, 53.3% men; n= 30 for conventional oxygen therapy mean age 71, 60% men; PaO ₂ /FiO ₂ ≥150 and <300mmHg)		
AIM OF THE STUDY			
Comparing HFNO with conventional oxygen therapy in the post extubation in a patient with hypoxemic RI			
INTERVENTION			
Conventional oxygen therapy versus HFNO in the post extubation			
RESULTS			
1) PaO ₂ , PaCO ₂ , SpO ₂ , HR and mean arterial pressure without statistically significant differences at baseline between groups; 2) the success rate with HFNO was 90% compared to conventional oxygen therapy 63.3% (p=0.012); 3) after 24h of extubation, PaO ₂ and SpO ₂ had a statistically significant increase in the HFNO group (p=0.016 and p=0.011 respectively); 4) RR was lower for the group with HFNO (p=0.003) 5) in HR and mean arterial pressure, no statistically significant differences were observed between the two groups (p=0.598 and p=0.824 respectively); 6) interface discomfort and symptoms of dryness of the airways were lower in the HFNO group (p=0.001); 7) the results cannot be inferred for other populations.			

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AUTHORS	Azoulay et al. (2018)		
TITLE	Effect of high-flow nasal oxygen vs standard oxygen on 28-day mortality in immunocompromised patients with acute respiratory failure: the HIGH randomized clinical trial		
YEAR/LOCATION	2018, France		
JBI LEVEL OF EVIDENCE (2013)	Randomized (1c)	METHODOLOGICAL QUALITY EVALUATION (Tufanaru et al., 2020)	9/13 69%
SAMPLE	n= 778 (n= 388 for HFNO median age 64, 69.6% men; n= 388 for conventional oxygen therapy median age 63, 63.6% men; PaO ₂ > 100 ≤ 300mmHg)		

AIM OF THE STUDY

To compare HFNO with conventional oxygen therapy in reducing the mortality rate in immunocompromised patients with hypoxemic RI

INTERVENTION

Conventional oxygen therapy versus HFNO in the treatment of RI

RESULTS

1) the difference in the mortality rate (at the 28th and 90th day) and the IMV rate was not statistically significant between the groups (p=0.94 and p=0.17 respectively); 2) PaO₂ /FiO₂, RR, HR, comfort, dyspnea and healthcare-associated infections without significant differences between the groups, with a trend towards better results in the HFNO group; 3) results cannot be inferred for other populations.

AUTHORS	Spoletini et al. (2018)		
TITLE	High-flow nasal therapy vs standard oxygen during breaks off noninvasive ventilation for acute respiratory failure: a pilot randomized controlled trial		
YEAR/LOCATION	2018, United States of America		
JBI LEVEL OF EVIDENCE (2013)	Randomized (1c)	METHODOLOGICAL QUALITY EVALUATION (Tufanaru et al., 2020)	7/13 54%
SAMPLE	n= 47 (n= 23 for HFNO mean age 68, 65.2% women; n= 24 for conventional oxygen therapy mean age 63, 58.3% women; PaO ₂ > 100 and ≤300mmHg)		

AIM OF THE STUDY

To compare HFNO with conventional oxygen therapy as an adjunct to NIV in the treatment of patients with hypoxemic RI

INTERVENTION

Conventional oxygen therapy versus HFNO in the treatment of IR combined with NIV

RESULTS

1) PaO₂ /FiO₂, PaCO₂, SpO₂, RR, mean arterial pressure, PH, and NIV settings, with no statistically significant differences at baseline between groups; 2) between the groups, the duration of NIV (tendency to be lower in the HFNO group) and dyspnea (tendency to be higher in the conventional oxygen therapy group) did not obtain statistically significant differences (p>0.05); 3) comfort with HFNO was greater and statistically significant when compared with NIV and conventional oxygen therapy (p<0.05); 4) HFNO caused less ocular irritation when compared to NIV and greater comfort during meals when compared to conventional oxygen therapy (p<0.05); 5) RR at NIV intervals increased in both groups, being statistically significant in the group with conventional oxygen therapy (p<0.05); 5) SpO₂ was similar between NIV, conventional oxygen therapy and HFNO (tending > NIV > conventional oxygen therapy > HFNO) (p<0.05).

AUTHORS	Frat et al. (2019)		
TITLE	Non-invasive ventilation versus high-flow nasal cannula oxygen therapy with apnoeic oxygenation for preoxygenation before intubation of patients with acute hypoxaemic respiratory failure: a randomized, multicentre, open-label trial		
YEAR/LOCATION	2019, France		

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JBIR LEVEL OF EVIDENCE (2013)	Randomized (1c)	METHODOLOGICAL QUALITY EVALUATION (Tufanaru et al., 2020)	9/13 69%
SAMPLE	n= 313 (n= 142 for NIV mean age 64, 71% men; n= 171 for HFNO mean age 64, 65% men; PaO ₂ ≤ 300mmHg)		

AIM OF THE STUDY

Compares HFNO with NIV for intubation pre-oxygenation in hypoxemic RI

INTERVENTION

Pre-oxygenation with NIV versus HFNO

RESULTS

1) PaO₂ /FiO₂ , RR, SpO₂ and degree of intubation difficulty without statistically significant differences between groups at baseline; 2) for the risk rate of severe hypoxemia (SpO₂ < 80%) of 25% the groups did not show statistically significant differences 3) during intubation the rate of severe hypoxemia was lower in the group with pre-oxygenation with NIV (23% with NIV and 27% with HFNO); 4) mean SpO₂ during intubation in patients with PaO₂ /FiO₂ ≤ 200mmHg were higher in the NIV group (p=0.02); 5) mean SpO₂ during intubation in patients with PaO₂ /FiO₂ > 200mmHg were similar between groups (p=0.31); 6) SpO₂ is higher at the end of preoxygenation in the NIV group in patients with PaO₂ /FiO₂ ≤ 200mmHg (p=0.02); 7) the results can be generalized to all patients with hypoxemic RI during pre-oxygenation in the ICU.

AUTHORS	Papachatzakis et al. (2020)		
TITLE	High-flow oxygen through nasal cannula vs. Non-invasive ventilation in hypercapnic respiratory failure: a randomized clinical trial		
YEAR/LOCATION	2020, Greece		
JBIR LEVEL OF EVIDENCE (2013)	Randomized (1c)	METHODOLOGICAL QUALITY EVALUATION (Tufanaru et al., 2020)	7/13 54%
SAMPLE	n= 40 (n= 20 for NIV mean age 78, 55% women; n= 20 for HFNO mean age 76, 50% women;		

AIM OF THE STUDY

Comparing HFNO with NIV in hypercapnic RI

INTERVENTION

NIV versus HFNO in the treatment of hypercapnic RI

RESULTS

1) PaCO₂, PaO₂, pH, SpO₂, HR, and HCO₃⁻ without statistically significant differences between groups at baseline; 2) length of hospital stay did not differ statistically significantly between the two groups with an average of 11.5 days (p=0.655); 3) the mortality rate was the same between the two groups (15%); 4) the decrease in HR between baseline and hospital discharge was statistically significant only in the NIV group (p=0.0452); 5) PaCO₂ in the HFNO group was lower than in the NIV group (50.8 mmHg versus 59.6 mmHg , p=0.024); 5) no need for intubation in both groups; 6) 15% of patients in the NIV group switched to HFNO due to nasal ulcer discomfort and intolerance; 7) the results cannot be inferred for other populations.

List of acronyms: HR- Heart Rate; FiO₂- Fraction of inspired oxygen; RR- Respiratory Rate; HCO₃⁻- Bicarbonate; mmHg - millimeters of mercury; n- sample; O₂- Oxygen; HFNO- High Flow Nasal Oxygen; Pearson's p- p (< 0.05); PaCO₂- Partial pressure of

carbon dioxide in arterial blood; PaO₂- Partial pressure of oxygen in arterial blood; Ph- Hydrogenionic potential; SpO₂- Peripheral oxygen saturation; IMV- Invasive Mechanical Ventilation; NIV - Non-Invasive Ventilation

DISCUSSION

The articles included in this review are mostly from Europe, with one from China and one from the United States, and were published between 2016 and 2020. In the selected studies, homogeneity was observed in all samples and between the analyzed groups. Methodological quality varied between 54% and 69% after applying the tool for assessing methodological quality. This low methodological quality represents a greater likelihood of producing less reliable results, making replication difficult due to low internal and external validity. All of these studies focused on investigating the effectiveness of HFNO in the treatment of patients with hypoxemic and/or hypercapnic RI, comparing HFNO with bag valve mask and NIV in pre-oxygenation for intubation, HFNO with conventional oxygen therapy in three distinct situations: in immunocompromised patients; post-extubation; as an adjuvant to NIV, and the last study comparing HFNO with NIV in patients with hypercapnic RI. The studies by Simon et al. (2016) and Frat et al. (2019) focused on the applicability of HFNO in pre-oxygenation prior to intubation, as compared to bag valve mask and NIV. Pre-oxygenation using HFNO for intubation is viable and safe as compared to bag valve mask in patients with hypoxemic RI with $\text{PaO}_2/\text{FiO}_2 > 200 \leq 300$ mmHg, proven by statistically significant evidence in SpO_2 . However, these values are not sufficiently robust to favor the choice of HFNO over bag valve mask, since there were no statistically significant differences in the mean values of SpO_2 , $\text{PaO}_2/\text{FiO}_2$, and PaCO_2 at the end of intubation (Simon et al., 2016). The safety and feasibility of HFNO in pre-oxygenation of hypoxemic patients with $\text{PaO}_2/\text{FiO}_2 > 200 \leq 300$ mmHg is also supported by the work of Frat

et al. (2019), which showed that SpO_2 means did not reveal statistically significant differences when compared to the VNI group in pre-oxygenation. However, in this study, VNI was found to be better at preventing severe hypoxemia than HFNO. This advantage was only statistically significant in patients with $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 200 mmHg (Frat et al., 2019). After extubation of patients with RI, the use of HFNO achieved statistically significant success compared to conventional oxygen therapy (Song et al., 2017). The use of HFNO resulted in an improvement in oxygenation (PaO_2 and SpO_2) and a reduction in respiratory rate and discomfort associated with the interface and dryness of the airways (Song et al., 2017). However, the study by Azoulay et al. (2018) safeguarded that there were no statistically significant differences in the survival rate of immunocompromised patients with hypoxemic RI when treated with HFNO compared to conventional oxygen therapy. Immunocompromised patients tend to have more severe hypoxemia (Frat et al., 2016), and as expected, as perceived by the work of Song et al. (2017), HFNO was expected to lead to better oxygenation, which was not proven for these patients with the work of Azoulay et al. (2018). However, a trend towards better results with HFNO was observed in $\text{PaO}_2/\text{FiO}_2$, respiratory rate, heart rate, comfort, dyspnea, and healthcare-associated infections (Azoulay et al., 2018). In this sense, in the approach to hypoxemic IR in immunocompromised patients, this oxygenation method may not be the most effective way to improve survival rate (Azoulay et al., 2018). Regarding the comparison between HFNO and conventional oxygen therapy, the study by Spoletini et al. (2018) showed that there were no statistically

significant differences when used during intervals of IR treatment with NIV. However, as in previous studies, there was a trend towards better results when using HFNO during NIV intervals, compared to conventional oxygen therapy, as evidenced by respiratory rate and comfort. The HFNO causes less eye irritation and facilitates feeding when compared to conventional oxygen therapy (Spoletini et al., 2018). These results may be associated with the mechanisms of action of HFNO, which allow for greater comfort and lower energy expenditure for the patient by meeting the increased inspiratory flow demand and providing greater oxygen efficiency (Mauri et al., 2017). Additionally, these mechanisms also increase functional residual capacity, CO₂ washout in dead space, and improve compliance with treatment. On the other hand, for hypercapnic RI, the first-line treatment is NIV (Nicolini et al., 2014). However, the study by Papachatzakis et al. (2020), which compared NIV with HFNO, showed controversial results. This work showed that hospital stay and mortality rates did not differ significantly between the two groups and only statistically significant differences were observed in heart rate (better in the NIV group) and PaCO₂ (better in the HFNO group). Moreover, it was also possible to perceive that HFNO was an alternative for patients (15%) who did not tolerate NIV. The main reasons related to NIV intolerance (skin lesions and eye irritation) are consistent with what was described in the Nicolini et al. (2014) study. Thus, HFNO may be an alternative treatment for hypercapnic RI, especially when NIV is not well tolerated (Papachatzakis et al., 2020).

CONCLUSION

In the studies included in this review, it was not possible to determine the effectiveness of HFNO in the treatment of RI due to the low methodological quality of the studies, which compromised the generalization of the presented results. Additionally, the impossibility of comparing results through quantitative synthesis, due to the non-inclusion of studies with comparable control groups, prevented the measurement of the intervention's effect size. However, it was possible to know the efficacy of HFNO. It was found to be efficacious when compared to conventional oxygen therapy, bag valve mask, and NIV in the treatment of hypoxemic and hypercapnic RI. This efficacy had significant evidence when HFNO was compared to conventional oxygen therapy in post-extubation of hypoxemic patients and in reducing PaCO₂ when compared to NIV in hypercapnic patients. In the pre-oxygenation of patients with hypoxemic IR with PaO₂/FiO₂ > 200 ≤ 300, it is possible to use NIV, HFNO, and bag valve mask effectively. However, when we refer to patients with hypoxemia with PaO₂/FiO₂ ≤ 200mmHg, evidence points to the efficacy of NIV over HFNO. Additionally, HFNO, probably due to its mechanisms of action, showed better rates of comfort and reduction of adverse effects resulting from the use of NIV or conventional oxygen therapy, indicating HFNO as an efficacious alternative in the treatment of RI. As recommendations for clinical practice, the use of HFNO can be considered as an efficacious strategy in the treatment of hypoxemic and hypercapnic RI, in the context of pre-oxygenation, post-extubation, and as an adjunct to NIV. For patients, HFNO presents itself as a more comfortable and tolerable alternative. As recommendations for research, it should focus on

randomized studies that present and add results that can be quantitatively generalized and compared to each other, allowing the creation of guidelines for the application of HFNO.

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