



VENTILAÇÃO NÃO INVASIVA EM PACIENTES IMUNOCOMPROMETIDOS COM INSUFICIÊNCIA RESPIRATÓRIA HIPOXÊMICA AGUDA: REVISÃO INTEGRATIVA

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ABSTRACT

Objective: Respiratory insufficiency is the main cause of admission to intensive care units and the noninvasive ventilation (NIV) is an alternative for ventilatory support indicated for the treatment of respiratory distress in the intra-hospital services and home care. When considering the different employment possibilities of noninvasive ventilation and its complications, in this study, we aim to answer the question: What is the outcome of using NIV in immunocompromised patients? **Method:** This is an integrative review which consulted the databases LILACS, SCIELO, PUBMED and BIREME in the period from 2013 to 2017. The used keywords were: noninvasive ventilation, respiratory insufficiency, physiotherapy, immunocompromised host. **Result:** Nine articles were selected, five studies demonstrated a favorable outcome for the use of NIV, being most studies with HIV patients. The most used interface was a facial mask followed by the or onasal and nasal mask and in different ventilatory modes. **Conclusion:** Based on this integrative review, the evidence suggests that the NIV may be associated with a lower risk of mortality and intubation, considering this alternative viable in the treatment of immunocompromised patients with acute hypoxemic respiratory failure.

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INTRODUCTION

Respiratory insufficiency is a condition in which the respiratory system fails to oxygenate or eliminate carbon dioxide or both. There are two types of insufficiency caused by problems in the exchange of these gases: hypoxemic respiratory failure, which results from pulmonary insufficiency and hypercapnic respiratory insufficiency, resulting from the failure of the respiratory mechanics (Phuong *et al.*, 2014).

Immunocompromised patients, i. e., patients with hematological neoplasms, solid organ transplants, acquired immunodeficiency syndrome, using corticosteroid or cytotoxic therapy for a malignant disease, present a progressive increase in the survival rate due to notable advances in diagnostic and therapeutical options (Brenner; Gondos; Arndt, 2007). However, the acute hypoxemic respiratory failure is the main cause of admission to the intensive care unit (ICU) in this group of patients (Azoulay *et al.*, 2013). Noninvasive ventilation (NIV) is used in individuals with acute and chronic respiratory insufficiency, indicated to relieve respiratory distress, decrease the breathing inspiratory work, improve gas exchange, revert respiratory muscle fatigue and prevent additional complications due to abnormal gas exchange.

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This therapy is present in the intra-hospital services and home care (Falsaperla *et al.*, 2013; Marohn; Panisello, 2013). It is defined as the positive pressure ventilation using interfaces (nasal, facial, full facial, nasal prong or helmets) without the need for an artificial airway, in different modalities (CPAP BIPAP, among others). The complications of this therapy refer to hemodynamic and respiratory effects, as well as lesions of the skin and mucous membranes (Ferreira *et al.*, 2013). The absolute contraindications of this therapeutic are cardiorespiratory arrest, total obstruction of the airways, severe encephalopathy, gastro intestinal tract hemorrhage, severe hemodynamic instability, facial trauma, inability of airway protection with risk of aspiration and hypotensive shock, uncontrolled cardiac ischemia, arrhythmia, compromised swallowing, not-drained excessive secretions, failure in several (two or more) organs, surgery on upper airways or high gastrointestinal tract, severe progressive respiratory insufficiency and pregnancy (Ferreira *et al.*, 2013; Nava; Hill, 2013; Peñuelas; Frutos-Vivar; Esteban, 2007).

Physiotherapy is part of the multidisciplinary care offered to patients in the Intensive Care Unit (ICU). Its performance is extensive and it is present in various segments of the intensive treatment, such as physiotherapy and respiratory insufficiency. In this phase, the physiotherapist has an important participation, assisting in the conduct of the ventilatory support (invasive and non-invasive mechanical ventilation), since the preparation and adjustment of the artificial ventilator through intubation, patient evolution during mechanical ventilation, interruption and weaning from ventilatory support and extubation (George *et al.*, 2007).

The physiotherapist, in the application of noninvasive ventilation (NIV), shall evaluate the need to establish and follow the procedure in the context of intensive therapy and has the important role in the conduct of protocols for screening of patients for discontinuation of mechanical ventilation (George, 2007; Ely, 2001). Taking into consideration the different possibilities of employment in this therapeutic and its complications, in this study, we have as the main question: *What is the outcome in the use of NIV in immunocompromised patients?*

METHODOLOGY

This is a study of integrative review, obeying the steps proposed by Mendes and Galvão (2008) in the period of January and February 2018, in the databases Latin American and Caribbean Literature on Health Sciences (LILACS), Scientific Electronic Library Online (SciELO), National Library of Medicine in the United States (Pubmed) and Latin American and Caribbean Center on Health Sciences Information (Bireme), articles published in the period of five years, in English, Spanish and Portuguese, using the following descriptors in English and Portuguese: Noninvasive ventilation; Respiratory Insufficiency, Physiotherapy, Lung Diseases, Immunocompromised host, composing different syntaxes using the Boolean operator "AND". Incomplete articles were excluded, as well as theses, dissertations, literature review, except systematic ones. After performing these steps, we achieved a sample of nine articles Figure 1. The information on the characteristics of the articles (journal, year, author, type of study and objective) will be presented in the form of tables and the content will be discussed in the light of two themes: favorable outcome to the patient and improvement aspects.

RESULTS AND DISCUSSION

The sample consisted of 09 scientific articles published in PUBMED (n=4) and BIREME (n=4), followed by SCIELO (n=1) and eight in the English language and one in Spanish from 2013 to 2017, with a predominance of 2016 (4 articles). Most patients were under intra-hospital care, as the main cause of immunodeficiency HIV patients, individuals in therapy with immunosuppressants, transplanted, hematological cancer. The most used interface was facial mask, oronasal and nasal mask, ventilatory modes described in articles were CPAP/BIPAP/PSV. The time of exposure to therapy (NIV) 8 hours/day in the first 48 hours. The information described in the synoptic frame will be discussed as favorable outcome (5 articles) and aspects of attention and improvement (4 articles).

Favorable Outcome to the Patient: The main causes of immunocommitment of patients included AIDS, hematological malignant tumors, cancer, chemotherapy and transplants, treatment with immunosuppressive drugs (Chertcoff *et al.*, 2018; Wang, 2016; Mokart, 2008; Lemiane *et al.*, 2014; Huang *et al.*, 2017). The patients had their best result in five of the studies analyzed and create new discussions for the use of NIV as first-line approach in this population (Huang, 2017; Bello, 2012). In this integrative review, we pointed out that the use of NIV proved to be effective in reducing the mortality rate. As described in the metaanalysis of HAUNG *et al.*, four out of five clinical trials showed reduced short-term mortality attributed to the use of NIV (Antonelli *et al.*, 2000; Squadrone *et al.*, 2010; Lemiale *et al.*, 2015). Chetercorf, five out of the five patients in the study had acute respiratory insufficiency; in these, four patients were immunocompromised and had been diagnosed with pneumonia.

In all cases, patients responded well without requiring invasive mechanical ventilation, supporting the use of noninvasive ventilation as the preferred modality for these patients, but they did not stratify the mortality rate in this study (Chertcoff *et al.*, 2018; Lemale *et al.*, 2014). The mortality rate was also reduced in the study of WANG *et al.* who compared the effects of NIV in relation to IMV in respiratory insufficiency in immunocompromised patients, data reflected by the Simplified Acute Physiology Score SAPS II < 60 in patients with AIDS and hematological cancer (Chertcoff *et al.*, 2018). In the same study, the author obtained a favorable result of the average rate of intubation after treatment with the NIV, which was 49.5%. A result similar to HAUNG *et al.*, in which NIV was associated with reduced rate of intubation (Wang, 2016). The benefit of NIV in preventing the endotracheal intubation or tracheostomy was evidenced by leaving the upper airway intact, thus preserving the defense mechanism of the airways. Therefore, issues related to IMV such as nasocomial pneumonia, aspiration, events associated with the mechanical ventilator, blunt teeth, pharynx, esophagus and trachea (Nava *et al.*, 1997; Hess, 2013; Namendys-Silva, 2010). Bello also reinforces the advantage of using the noninvasive ventilatory support in immunocompromised patients, avoiding side effects of tracheal intubation, ventilation-associated pneumonia (VAP), lesion of the upper airways and tracheomalacia (Bello *et al.*, 2012). Furthermore, adequate use of PEEP during NIV promotes alveolar recruitment, improves hypoxia, dyspnea and relief of muscle fatigue²⁹. Several studies support the benefits of reduced rate of intubation and mortality of NIV in two studies, one with 40 solid organ transplant patients, the percentage of patients who required orotracheal intubation was

Table 1. Characterization of the studies sample according to databases, journal and impact factor

Article	Database	Journal	Impact Fact
1.	SCIELO	Journal Critical Care	2.648
2.	PUBMED	The Journal of Infectious Diseases	6.273
3.		New England Journal of Medicine	72.406
4.		Annals Intensive Care	3.646
5.		Journal of the American Medical Association	44.405
6.	BIREME	Journal of the American Medical Association	44.405
7.		Journal Critical Care	2.648
8.		Klin Padiatrie	0.731
9.		Journal Critical Care	2.648

Synoptic Frame: Description of the information in the selected articles related to author, year, type of study, overall goal, sample and main results

Author/Year	Type of Study	Objective	Sample	Main Results
Chertcoff <i>et al.</i> (2013)	Case report	To describe the use of NIV in patients undergoing minimally invasive procedure with high risk for sedation or OTI.	It included nine patients (ICU) British Hospital, Buenos Aires who underwent bronchoscopies, digestive endoscopy, preparation of gastrostomy and trans-esophagus echocardiogram.	NIV in Bilevel mode during the procedures proved to be a valid, safe option and reduces the need for intubation and its complications.
Wang <i>et al.</i> (2016)	Systematic review / Metanalysis	To determine the effects of NIV compared to invasive mechanical ventilation (IMV) as an initial choice of mechanical ventilation for the treatment of IrespA in immunocompromised patients.	13 studies (2552 patients).	NIV presented significantly lower mortality rates, especially in less severe and immunocompromised patients with AIDS, hematologic malignancies and bone marrow transplantation. For more severe patients, however, the NIV showed no clear advantages in relation to the VMI.
FRAT <i>et al.</i> (2016)	Randomized Controlled Multicenter Clinical Trial	To compare the results of immunocompromised patients with IrespA treated with O ₂ under high-flow nasal cannula, standard O ₂ and high-flow nasal cannula associated with the NIV	82 immunocompromised patients with respiratory insufficiency treated with noninvasive ventilation, high-flow nasal canula.	The group of high-flow nasal cannula showed significantly lower rates of intubation and mortality than the noninvasive mechanical ventilation. No significant differences in the rates of intubation and mortality were observed between the oxygen standard and high-flow nasal cannula.
COUDROY <i>et al.</i> (2016)	Cohort	To compare results from immunocompromised patients treated with high-flow nasal cannula alone or NIV as first-line therapy for IrespA.	115 immunocompromised patients with acute respiratory insufficiency.	The OTI and mortality rates in the ICU were significantly lower in the high-flow nasal cannula group than in the NIV group.
MOKART <i>et al.</i> (2015)	Clinical Trial	To assess whether high-flow nasal cannula associated or not with NIV during IrespA is associated with a high mortality rate in a cancer patient admitted to the ICU.	178 cancer and IrespA patients received standard O ₂ , high-flow nasal cannula or through combination of high-flow nasal cannula-NIV or standard O ₂ -NIV.	O ₂ , high-flow nasal cannula and high-flow cannula + NIV group presented a lower mortality rate, longer ICU stay, longer period for OTI, but not a significant number of ventilator-free days. High-flow nasal cannula + NIV was associated with improved survival.
Lemale <i>et al.</i> (2014)	Controlled Randomized	To demonstrate that early NIV onset decreases mortality rates compared to standard O ₂ therapy in immunocompromised patients with IrespA.	374 patients in 29 ICUs	Most studies evaluated NIV without time control between the initiation of IrespA and the implementation of IMV, not identifying the etiology of the insufficiency, and/or knowledge of the presence of organic dysfunction at the time of NIV initiation.
Sun <i>et al.</i> (2014)	Prospective Cohort	To observe clinical features and critical patient outcomes with severe acute respiratory distress syndrome (ARDS) caused by HAdV-55 requiring MV and/or extracorporeal membrane oxygenation (ECMO)	5 immunocompromised patients with human adenovirus HAdV-55	O suporte ventilatório falhou em todos os pacientes. Quatro dos pacientes receberam ECMO um paciente recusou o suporte. Para pacientes com SARA grave, ECMO demonstrou ser uma escolha.
Fuchs <i>et al.</i> (2015)	Descriptive Observational	To investigate the mortality rate, success rate, prognosis, side effects of NIV in immunocompromised patients with IrespA.	41 children with immunodeficiency, after transplantation of stem cells or chemotherapy with oncological diseases.	The IrespA prognosis in immunocompromised children remains independent of the initial success or failure of NIV because of a high recurrence rate of failure with a better response in reversible causes such as bacterial sepsis.
Huang <i>et al.</i> (2017)	Systematic Review with Metanalysis	To assess the effect of early NIV in comparison to oxygen therapy alone in immunocompromised patients with IrespA.	5 studies (randomized clinical trial) with 592 patients.	Evidence indicates that early use of NIV may reduce short-term mortality in immunocompromised patients with IrespA.

Subtitle: OTI: orotracheal intubation; IrespA: acute respiratory insufficiency

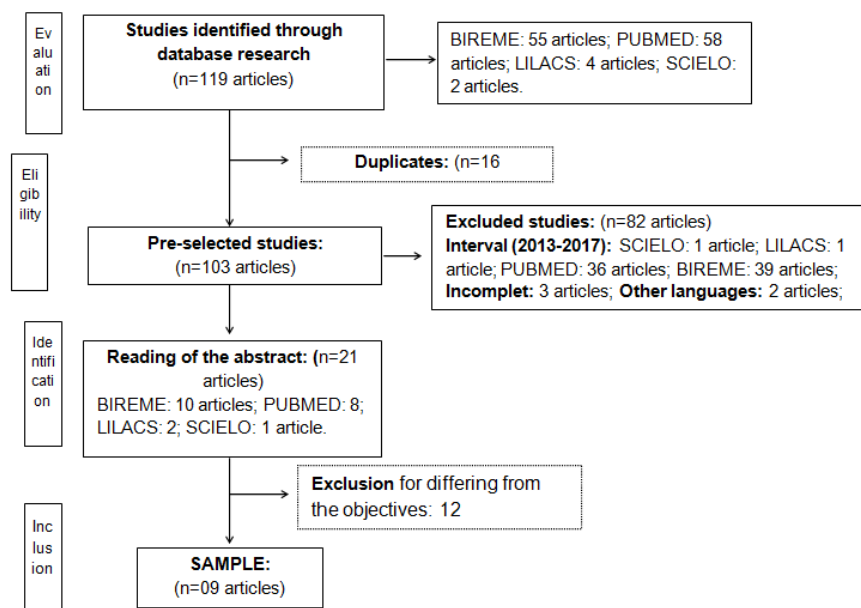


Figure 1. Flowchart of the studies selection

20% and in 52 patients, the intubation 12% and mortality, 13% rates were significantly lower than the control group that used supplemental oxygen. Azoulay *et al.*, in their study with the use of NIV, also resulted in reduced rates of intubation and mortality when compared to the use of standard therapy with oxygen (Antonelli *et al.*, 2000; Hilbert *et al.*, 2001; Azoulay, 2014). However, some recent studies have challenged the effects of NIV in immunocompromised patients with hypoxemic acute respiratory insufficiency using new alternatives of oxygen therapy. The studies that present more controversial results to outcomes reported until now are those that use the high-flow nasal cannula (HFNC). HFNC is a recent technique that offers heated and humidified oxygen at high flow rates (Squadrone, 2010). Mokart *et al.* (2016), in a retrospective study that included 178 immunocompromised individuals with cancer and respiratory insufficiency, assessed the use of high-flow nasal cannula associated, or not, with noninvasive ventilation and standard oxygen. The group that received the treatment with high-flow nasal cannula and noninvasive ventilation showed mortality rate of 37% vs 52% of other groups. This suggests that the best strategy consisted of using NIV associated with HFNC between sessions.

Controversial to the study of Mokart, a recent randomized controlled multicenter study, where patients were treated with standard oxygen, high-flow cannula alone and NIV interspersed with the cannula between the sessions of noninvasive ventilation, showed a decreased mortality rate lower in those treated with cannula alone than in the other groups. In addition, the rate of intubation was greater in the group of NIV interspersed with the cannula 65% of group (Frat *et al.*, 2016). Coudroy *et al.* (2016) presented similar results in their study, which sought to compare results of immunocompromised patients treated with high-flow nasal cannula in isolation or noninvasive ventilation. The article analyzed 115 patients, 60 treated with high-flow nasal cannula and 55 with noninvasive ventilation. Intubation and mortality rates were 55 and 40%, respectively, in patients treated with noninvasive ventilation greater than treated with high-flow nasal cannula 35 and 20%.

Aspects of Attention and Improvement: The ventilatory modality may undergo changes during the treatment, taking into consideration the clinical impact on patient. Sun (2014), in a prospective, observational study of patients with pneumonia caused by adenovirus type 55 with acute respiratory distress syndrome in immunocompromised adults. The sample consisted of 8 patients diagnosed with infection by adenovirus and acute respiratory insufficiency, 7 of them received the diagnosis of acute respiratory distress syndrome, 5 patients presented severe respiratory distress syndrome and were included in the review, the other two had mild symptoms. As a result, both noninvasive ventilation as the invasive mechanical ventilation failed in any of the patients and four of the patients required extra-membrane oxygenation and one patient refused therapy. Four of the five patients, 80% of the patients died despite receiving the appropriate respiratory support. Nevertheless, the high mortality rate reported in this study is probably linked to the large area of consolidation characteristic of the severe form of the disease that led to a severe lung shunt, which can lead to lack of response to positive pressure ventilation. Besides, even though the study had a small sample of two patients who survived had mild symptoms, suggesting that the ventilatory intervention of NIV is feasible in such cases. Therefore, some factors that were not described in studies or were confusing must be emphasized, early in the NIV implementation, portrayed in only one study of the sample Lemiale *et al.* It seems that the early NIV implementation in individuals with respiratory insufficiency can result in the prevention of the progression of certain diseases (Carteaux, 2015). In the clinical practice of a professional from the ICU, with patients with respiratory insufficiency, we must choose the best device of oxygen therapy between standard oxygen, NIV and IMV, depending on the different degree of pulmonary involvement. The NIV or standard oxygen should be applied to less severe patients. For more severe patients, the choice is limited to NIV and IMV. WANG' s review showed that, even in relatively more severe patients, the favorable effects of NIV may vary with different levels of disease, different causes of immunocommitment and types of respiratory insufficiency (Wang, 2016).

The importance of respiratory monitoring during the NIV procedure has not been described in any of the studies. The physiotherapist is the professional able to establish and follow the procedure in the context of intensive therapy. The failures can be linked not only to the severity of the pathology, time, it may be in the application protocol that is not well described in some studies, besides monitoring and criterion of applicability of ventilatory support. This statement is confirmed by the fact that patients under noninvasive ventilation that receive large tidal volumes > 11 ml/kg of predicted body weight died (Frat, 2016). Similar results were reported by CARTEUX: the authors intended to achieve a tidal volume of 6 ml/kg and 8 ml/kg of predicted body weight, and realized that this tidal volume was not achieved in half of the sample; the majority showed a tidal volume above 10 ml/kg that was associated with an increased risk of failure of noninvasive mechanical ventilation (Carteaux, 2015).

Conclusion

The favorable outcome to the patient submitted to NIV is associated with the lowest mortality rate, intubation, especially in patients with lower severity, immunocompromised patients with AIDS, hematologic malignancies and transplant. A positive point is the reduced period of hospitalization and stay in the ICU, as well as rates of nosocomial infection. However, for more severe patients, this alternative did not show sufficient favorable evidence when compared to invasive mechanical ventilation and oxygenation by extra-corporeal circulation membrane. The main difficulties identified by the authors were: NIV onset time, severity of the disease, failure of organs and lung injury induced by mechanical ventilation. The information mentioned in this text deserve reflection of health professionals who provide direct care to patients in a critical situation in the context of using/indicating the most effective therapeutic alternative taking into consideration the clinical presentation and the level of evidence from studies on the theme.

Authors' Contribution:

Thiago de Oliveira Pires: Conception and design, or analysis and interpretation of data, article writing. Gisele Torrente: Methodological guidance, relevant critical review of the intellectual content; final approval of the version to be published. Elielza Guerreiro Menezes: relevant critical review of the intellectual content; final approval of the version to be published. Yara Nayá Lopes de Andrade Goiabeira: relevant critical review of the intellectual content; final approval of the version to be published.

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