Use of an Alternative Oxygen High-Flow Nasal Cannula Device for Hypoxemic Acute Respiratory Failure in an Adult Emergency Department in Argentina. Quasi-Experimental Study

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Abstract
Objective: To describe changes observed in respiratory rate, heart rate and dyspnea score before and after using an alternative high-flow nasal cannula device in patients with hypoxemic acute respiratory failure in an Emergency Department.

Materials and Method: Quasi-experimental, retrospective study with adult patients who went to the Emergency Department with clinical signs of hypoxemic acute respiratory failure. Data from respiratory rate, heart rate and dyspnea score were gathered from the electronic medical records of the patients both before and after using a Venturi device connected to a high-flow nasal cannula system two hours.

Result: 43 patients were included. The mean age was 64.7 years (SD 16). The main cause of respiratory failure was pneumonia in 18 patients (42%). We observed a decrease of 8 breaths per minute (p < .001) in the respiratory rate, and 7 beats per minute (p < .001) in the heart rate; and there was a 2-point decrease in the dyspnea score (p < .001).

Conclusions: We observed a significant decrease in the three variables under study in patients who went to the Emergency Department with hypoxemic acute respiratory failure, using a non-conventional oxygen therapy device, which could become useful in countries with limited resources or in cases of overcrowding, so common in the Emergency Departments.

Key words: Oxygen therapy; Emergency medicine; Physiotherapy; Respiratory failure; Respiratory care

Introduction

Acute respiratory failure (ARF) is a frequent reason for admission to the Emergency Department (ED). According to the etiology and severity of the ARF, patients may be treated with conventional oxygen therapy, noninvasive mechanical ventilation (NIV) or invasive ventilation. The conventional oxygen therapy has certain limitations, such as low flow of gas, variable concentrations of medicinal oxygen...
and low level of heat and humidity provided by the gas mixture delivered\textsuperscript{1–3}. Some patients show low adherence to the NIV: they do not tolerate the selected interface, the excessive leaks or the discomfort caused by the harness or attachment systems, which are usually very tight\textsuperscript{4}. Also, the use of NIV in hypoxemic ARF is a controversial issue, whose failure is associated with unfavorable results\textsuperscript{5,6}.

The oxygen high-flow nasal cannula (HFNC) arises as a new oxygen therapy option for the clinical treatment of adult patients with hypoxemic ARF\textsuperscript{6}. There are turbine-driven or micro-processed equipments capable of generating flows of up to 50 or 60 liters per minute (L/min) of mixed gases humidified and heated at body temperature (37 °C) with an oxygen concentration of up to 100%. In this equipment, the flow is constant and is an independent variable, that is to say, no matter what happens with the system, the flow shouldn’t be modified. But there are also other devices capable of generating high flows, such as the WhisperFlow\textsuperscript{®} system. This or similar devices are available in most EDs, and their operation is based on the Venturi principle, using a gas supply (medical oxygen) and taking room air, increasing the outflow. So, the final flow is the result of the relationship between the inflow of gas and the ambient air that enters due to the pressure drop inside the device, reaching up to 150 L/min, with a fraction of inspired oxygen (FiO\textsubscript{2}) between 0.30 and 1 (30% and 100%).

There is growing interest in the use of HFNC in patients with hypoxemic ARF, after a controlled, randomized clinical trial proposed by Frat. et al\textsuperscript{7} reported favorable results. Also, two other reviews have shown the clinical efficacy of HFNC in patients with hypoxemic ARF caused by a variety of medical conditions. Results show dyspnea relief, reduced work of breathing and improvements in oxygenation and patient’s comfort\textsuperscript{1–5, 7–8}. There are a number of mechanisms that could explain these beneficial effects: generation of low levels of positive end-expiratory airway pressure, conditioning of inspired gas, improvement in lung mucociliary clearance, and also reduction of the metabolic cost of breathing, the anatomical dead space and the inspiratory resistance when matching or exceeding the inspiratory flow of the patient\textsuperscript{9–11}.

Most of the available scientific evidence about the use of HFNC is related to adult populations with hypoxemic ARF in Critical Care Units (CCU)\textsuperscript{3, 7, 9, 12–15}; however, there is little research on the use of HFNC in the EDs\textsuperscript{16–20}. We did not find any other work that used a Venturi device to generate high flows in an ED, so the objective of this study is to describe changes observed in the respiratory rate (RR), the heart rate (HR) and the dyspnea scale score, before and after the use of an alternative HFNC device in adult patients with hypoxemic ARF in our ED.

Materials and Method

Study Design: A quasi-experimental, retrospective study was conducted. The ED belongs to a teaching hospital that received more than 55,000 consultations in 2015. Argentina is a country with limited resources where conventional, high-flow systems are not available in most medical centers. So, in this case, in order to generate high-flow we used a Venturi device that is normally used to deliver continuous positive airway pressure (CPAP). The equipment uses an oxygen supply of 60 psi (412 kPa) that generates the outflow (Whisper Flow\textsuperscript{®}) together with ambient air entering the device through the Venturi mechanism. It may generate flows from 10 up to 150 L/min and deliver a FiO\textsubscript{2} between 0.30 and 1.0. Also, the setting of the FiO\textsubscript{2} in this equipment is not independent from the setting of the flow, so we begin therapy with the minimum necessary FiO\textsubscript{2} to keep oxygen saturation (SpO\textsubscript{2}) above 94% with a gas flow of 60 L/min, according to the patient’s tolerance\textsuperscript{9, 15, 21}. We used an active humidification system (MR850 with MR 290 chamber) to heat and humidify the gas mixture at a temperature of 37 °C and deliver it to the patient by means of a one line heated inspiratory circuit (RT241) through a nasal cannula (Optiflow\textsuperscript{®}). Also, we used an oxygen sensor (Criterion\textsuperscript{®} Oxicheck, Respironics\textsuperscript{®}) to measure the delivered FiO\textsubscript{2}, and a respiratory mechanics monitor (FluxMed\textsuperscript{®}, MBMed\textsuperscript{®}) to measure the airflow. (Figure 1)
Subject Selection
We included patients older than 18 years who arrived at the ED with clinical signs of hypoxemic ARF, with or without history of pulmonary disease, who required HFNC, and also patients with hypoxemic ARF with adequacy for life-sustaining treatment (ALST), during the period between July 1st, 2015 and January 31, 2017.

The decision to use ALST was made before admission to the ED by the treating medical staff, the patient and/or the patient’s family, and was then registered in the medical records as “patient with advance directives”.

The decision to begin with oxygen high-flow therapy was based on the clinical signs and symptoms of the patient: RR ≥ 25 breaths/min, SpO₂ < 90% breathing room air (FiO₂, 21%) and increase in work of breathing (WOB) evidenced by sensation of dyspnea, use of accessory muscles or diaphoresis, despite the use of conventional oxygen therapy at ≥ 6 L/min

In cases of hypercapnic ARF, we used NIV; but, in cases of mixed ARF we considered the use of oxygen therapy with HFNC, given that the available bibliography states that patients with mask intolerance may benefit from trying this therapy.

Variables and Measurements
Data gathered from the daily medical chart were included in the electronic medical records: RR, HR and dyspnea score according to the Modified Borg Scale. Variables were collected before and after using the HFNC for two hours. Also, the following data were collected: value of FiO₂ and flow used at the initiation of HFNC therapy, together with the average time of use, success or failure of treatment and hospital mortality after 28 days.
The therapy began with 60 L/min flow and was adjusted according to patient’s tolerance. The objective was to achieve the highest flow tolerated by the patient to match the patient’s inspiratory flow in the ARF, which may even reach 120 L/min. The partial pressure of oxygen (PaO₂) and the values of PaO₂/FiO₂ and SpO₂/FiO₂ were only available during the post-treatment period, 2 hours after the beginning of HFNC therapy, because during the common clinical practice of our ED the analysis of arterial gases is made once the arterial access has been placed. We also registered the basal characteristics of the population regarding age, gender, ARF etiology and history of respiratory or cardiovascular disease (diagnosed through lung function tests; computed axial tomography, echocardiography or lung ultrasound, as deemed appropriate).

Therapy with HFNC was considered successful when the patient did not need escalation to another type of ventilatory support, whether invasive or noninvasive, within the first 24 hours after beginning high-flow therapy. On the contrary, if the patient required NIV or invasive ventilatory support during the first 24 hours after beginning therapy, it was considered a therapeutic failure. The HFNC weaning criteria were: FiO₂ < 30% for SpO₂ ≥ 92% and RR ≤ 25 breaths per minute during at least 6 hours. Contraindications taken into consideration to receive high-flow therapy were: impairment of consciousness, claustrophobia, airway obstruction, facial lesion or malformation, risk of aspiration, untreatable arrhythmia or respiratory arrest. Intubation was considered if two or more of the following criteria were presented within the first two hours using the HFNC: impairment of consciousness, hypotension despite fluid resuscitation treatment, RR > 35 breaths per minute, PaO₂/FiO₂ < 150, increase in WOB, SpO₂ < 90%, secretions difficult to manage and decrease in blood pH.

Ethical Standards
All the procedures of this research were adjusted according to the ethical principles of the 1964 Declaration of Helsinki as subsequently amended, and received the approval of the Ethics Committee on Research Protocols of our Hospital. For this type of study, no formal informed consent was required, as no patient information was included in the original text.

Statistical Analysis
Continuous variables were presented as mean and standard deviation or median and interquartile range (IQR) according to their distribution, whereas categorical variables were presented as absolute frequencies and percentages. For the comparison of pre- and post-HFNC variables, we used the paired T test. A value of p < 0.05 was considered as statistically significant. Data were analyzed with STATA software (StataCorp, version 14.2).

Results
A total of 43 patients were included in the study; 23 (54.5%) were male, with a mean age of 64.7 years (SD 16). Table 1 summarizes the characteristics of patients before the beginning of the treatment. Seventy-two per cent of the patients had clinical history of respiratory diseases. The main etiology of hypoxemic ARF was pneumonia, diagnosed in 18 patients (42%). Ten (23%) patients with hypoxemic ARF were in a state of ALST. Eight patients had mixed ARF with intolerance to NIV and were treated with HFNC. We observed a significant decrease in RR, HR and the dyspnea scale after two hours of therapy with HFNC. The study population was divided in groups, one group with ARF and another one with ARF and ALST. A significant reduction of the three parameters under study was observed in the ARF group. But, in the ARF with ALST group we didn’t observe any significant change in the dyspnea score. These results are summarized in Table 2.

The mean time of HFNC therapy was 28.5 hours (IQR 13-50). HFNC therapy was successful in 21 patients (63.6%). Results are shown in Figure 2. Only seven patients were intubated and five patients...
required NIV. Two patients died within the group of ARF without ALST. One of them had history of congestive heart failure and kidney cancer and required chronic dialysis. The physician and the patient’s family decided to limit the treatment. The other patient had history of silicosis and chronic hepatitis C, was waiting for a lung transplant and died due to the progression of this pulmonary disease.

The mean value of FiO$_2$ administered at the beginning of treatment with HFNC was 0.46 (SD 0.15), and the initial gas flow rate was 59 (SD 16) L/min. The median of the PaO$_2$ value after two hours of HFNC therapy in 20 patients of the ARF group (61%) was 122 (IQR: 113-153), and the PaO$_2$/FiO$_2$ value was 282 (IQR: 230-395). The median of the SpO$_2$ and SpO$_2$/FiO$_2$ values after two hours of HFNC therapy in 31 patients of the ARF group (94%) was 97 (IQR: 95-98) and 220 (IQR: 163-250) respectively.

### Discussion

In our study, we found a significant reduction of RR, HR and the dyspnea scale score with the use of HFNC in patients with ARF in the ED. These results are supported by previous studies that also showed reductions in RR$^{12,13,16,19,20}$, HR$^{7,12,17,19}$ and the sensation of dyspnea$^{12,13,16}$ in the CCU and ED using conventional high-flow devices. Regarding the RR, our study shows some values similar to those documented by Rittamayani et al, or even below the values of other studies conducted in the ED$^{16,17}$. Lenglet et al observed a three-point reduction in the RR after 60 minutes of HFNC therapy, whereas we observed a higher reduction$^{16}$. According to Sztrymf et al, the significant reduction of the RR indicates

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**TABLE 1.** Basal characteristics of patients admitted to the ED before beginning HFNC therapy (n = 43)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Results N = 43</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>23 (54.5)</td>
</tr>
<tr>
<td>Age - years, mean (SD)</td>
<td>64.7 (16.0)</td>
</tr>
<tr>
<td>APACHE II, mean (SD)</td>
<td>13 (5)</td>
</tr>
<tr>
<td>Respiratory history, n (%)</td>
<td>31 (72)</td>
</tr>
<tr>
<td>IPF*</td>
<td>12 (39)</td>
</tr>
<tr>
<td>COPD†</td>
<td>9 (29)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (32)</td>
</tr>
<tr>
<td>Cardiovascular history, n (%)</td>
<td>26 (60)</td>
</tr>
<tr>
<td>Oncological history, n (%)</td>
<td>13 (30)</td>
</tr>
<tr>
<td>Other medical records</td>
<td>12 (28)</td>
</tr>
<tr>
<td>Etiology of ARF§, n (%)</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>18 (42)</td>
</tr>
<tr>
<td>IPF exacerbation</td>
<td>7 (16)</td>
</tr>
<tr>
<td>Septic shock</td>
<td>5 (12)</td>
</tr>
<tr>
<td>Cardiogenic pulmonary edema</td>
<td>4 (9)</td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Other§</td>
<td>8 (19)</td>
</tr>
</tbody>
</table>

*idiopathic pulmonary fibrosis; †chronic obstructive pulmonary disease; ‡lung cancer, breast cancer, renal cancer, meningioma, testicular cancer, Ewing’s sarcoma, glioblastoma, leukemia; §acute respiratory failure; ‡pulmonary-renal syndrome, rejection of lung transplant, Ewing’s sarcoma, portopulmonary hypertension, pneumoconiosis, lung metastasis, paraneoplastic pleural effusion, multifactorial acute respiratory failure. ED: Emergency Department; HFNC: high-flow nasal cannula.
**Figure 2.** Flow diagram of patients and results


**TABLA 2.** Respiratory rate, heart rate and dyspnea score before and after two hours of HFNC in patients with clinical signs of acute respiratory failure in the Emergency Department

<table>
<thead>
<tr>
<th>Variables</th>
<th>Results</th>
<th>N = 43</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before the CNAF</td>
<td>After the CNAF</td>
</tr>
<tr>
<td>RR, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patient</td>
<td>31 (7)</td>
<td>23 (5)</td>
</tr>
<tr>
<td>ARF group</td>
<td>30 (6)</td>
<td>22 (5)</td>
</tr>
<tr>
<td>ARF with ALST group</td>
<td>35 (8)</td>
<td>25 (6)</td>
</tr>
<tr>
<td>HR, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>98 (22)</td>
<td>89 (17)</td>
</tr>
<tr>
<td>ARF group</td>
<td>99 (23)</td>
<td>91 (18)</td>
</tr>
<tr>
<td>ARF with ALST group</td>
<td>97 (22)</td>
<td>84 (14)</td>
</tr>
<tr>
<td>Dyspnea, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All the patients</td>
<td>4 (3)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>ARF group</td>
<td>4 (3)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>ARF with ALST group</td>
<td>2 (2)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>


Note: 33 (77%) of the 43 patients included in the study were part of the ARF group and 10 (23%) belonged to the ARF with ALST group.
success of the HFNC therapy\textsuperscript{3,16}. With regard to dyspnea, our results show a two-point reduction, which means a significant reduction in the Modified Borg Dyspnea, from “Somewhat severe” to “Slight”. This reduction is similar to that reported by Schwabauer et al and slightly lower than the one reported by Lenglet et al\textsuperscript{11}. Despite the fact that the objective of the treatment in the ALST group was the palliative relief of dyspnea, we did not find a significant reduction in the dyspnea score within this group of patients\textsuperscript{29}. The reason for this may be the small number of subjects and the low initial dyspnea scores. As for the HR, with HFNC therapy we found a statistically significant difference, but could not find any clinically significant reduction relating to data reported by other authors\textsuperscript{9}.

In order to analyze the failure rate for HFNC, we excluded patients with ALST who received therapy in the context of palliative care. We found that one third of the patients failed therapy (15% of the patients required NIV and 21% required invasive mechanical ventilatory assistance). Despite the severity value of $\geq 12$ points as measured by APACHE, it has been reported by Rello et al as the cause for HFNC therapy failure, similar to data reported by Sztrymf et al (24%), Frat et al (38%), and Messika et al (40%) in the CCU\textsuperscript{3,7,15,27}. However, our failure rate was higher than other studies conducted in the ED, as for example Lenglet et al (11.8%), Hughes et al (5.2%) and Jones et al (3.6%) in the EDs\textsuperscript{16,19,20}. One possible explanation for this high failure rate could be the fact that some patients used NIV on a regular basis (for example, for treating the obstructive sleep apnea syndrome) or followed treatment protocols in other critical areas\textsuperscript{30}. Finally, Hyun Cho et al reported an association between the APACHE II score and the mortality rate in the CCU\textsuperscript{31}, but our hospital mortality rate for the ARF group was 6% at 28 days, similar to that reported by Sztrymf et al and Jones et al in the ED (9.1%)\textsuperscript{3,20}.

Our study has strengths. First, it addresses the management of patients with clinical signs of hypoxic ARF in an ED, an area where there is still a lot more to learn and research. Secondly, it describes the use of a new device to generate high flow that costs up to 10 times less than conventional devices and allows for higher gas flow rates. Thus, it could be an alternative option for countries with low resources and limited access to conventional HFNC devices. If we consider that the inspiratory flow of a patient during ARF can be as high as 120 L/min, then a higher flow could be beneficial if tolerated by the patient\textsuperscript{14}. On the other hand, the heterogeneity of the clinical presentations of our sample represents the daily reality of ED consultations.

The retrospective analysis of clinical data of a small number of subjects may limit the generalization of our findings. But, in contrast to other countries, exception to informed consent is not allowed in Argentina. Thus, making prospective studies within an emergency environment is unlikely. Also, an emergency situation complicates the explanation process, the patient is not in good clinical conditions and on several occasions the patient’s family is not present. Another limitation was the lack of FiO\textsubscript{2} values of gases in arterial blood before beginning therapy with HFNC. Also, we were not able to control other variables such as the use of bronchodilators, antibiotics, diuretics, hydrocortisone, etc. and so we may not attribute the whole magnitude of the effect, in terms of change in vital signs or sensation of dyspnea to the high-flow therapy. We should also bear in mind that dyspnea is a subjective parameter, so it is difficult to measure it precisely. Finally, there was not a control group without HFNC; the patients themselves were their own control.

**Conclusion**

In patients presenting to the ED with clinical signs of hypoxic ARF we observed a significant reduction in RR, HR and the dyspnea score with the use of a non-conventional HFNC device. These results were similar to those found in the CCUs and EDs when using conventional HFNC devices. So, this Venturi system may be an alternative therapy in places with limited resources or in cases of overcrowding with shortage of equipment, so common in the EDs. However, the efficacy of this equipment should be studied more thoroughly in controlled, randomized clinical trials.

**Conflict of interest:** The authors declare there is no conflict of interest.
Referencias


