Development of a New High-Oxygen Flow Nasal Device for Hypoxia Management in Patients With Pulmonary Limitation Arising from Covid-19 and Other Respiratory Diseases

Uma Nova Estratégia de Aporte de Oxigênio Por Alto Fluxo em Cateter Nasal para Manejo da Hipóxia em Pacientes com Limitação Pulmonar Decorrente da Covid-19 e de Outras Doenças Respiratórias

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Abstract

About 5.5 million people in the world have respiratory limitations, which is the 5th largest cause of hospitalizations in Brazil. Covid-19 has contributed negatively to this scenario. The choice of adequate respiratory support contributes to a better clinical outcome, also supporting an improvement in quality of life. A new way of providing oxygen therapy, with lower cost and capable of managing hypoxia, may be a promising alternative. With the use of common supplies, it is possible to provide a high flow of compressed air and oxygen, heated and humidified, optimizing ventilation-perfusion. With a view to addressing hypercapnia and hypoxemia, this newly designed new form can contribute to clinical practice. The results of this study showed the effectiveness of this strategy when using flows from 30l/min, since, in this way, the loss of gas supply to the patient is insignificant. In addition, the financial viability makes the strategy accessible to less favored institutions. The magnitude of respiratory disorders aroused the need for new approaches to this clinical scenario, as conventional oxygen therapy does not always meet these demands and the high-flow nasal catheter has already shown a promising strategy in cases of respiratory limitations.

Keywords: Rehabilitation. Respiratory Tract Diseases. Covid-19.

Resumo

Cerca de 5,5 milhões de pessoas no mundo apresentam limitações respiratórias, sendo esta a 5^a maior causa de internações no Brasil. A Covid-19 tem contribuído negativamente para este cenário. A escolha do suporte respiratório adequado contribui para um melhor desfecho clínico, auxiliando também na melhora da qualidade de vida. Uma nova forma de oferta de oxigenoterapia, com menor custo e capaz de controlar a hipóxia, pode ser uma alternativa promissora. Com o uso de insumos comuns, é possível fornecer um alto fluxo de ar comprimido e oxigênio, aquecido e umidificado, otimizando a ventilação-perfusão. Com o objetivo de abordar a hipercapnia e a hipoxemia, esta nova forma recém-desenhada pode contribuir para a prática clínica. Nossos resultados mostraram a eficácia dessa estratégia ao utilizar fluxos a partir de 301/min, pois, dessa forma, a perda de suprimento de gás ao paciente é insignificante. Além disso, a viabilidade financeira torna a estratégia acessível às instituições menos favorecidas. A magnitude dos distúrbios respiratórios despertou a necessidade de novas abordagens nesse cenário clínico, pois a oxigenoterapia convencional nem sempre atende a essas demandas e o cateter nasal de alto fluxo já se mostrou uma estratégia promissora em casos de limitações respiratórias.

Palavras-chave: Reabilitação. Doenças Respiratórias. Covid19.

1 Introduction

Estimates supports that 5.5 million people have been living with chronic obstructive pulmonary disease (COPD) in Brazil¹ and 52 million worldwide, accounting for 2.74 million deaths, the fifth main cause of deaths. Also, COPD is the fifth most significant cause of hospitalization among patients aged over 40 within the Brazilian public health system (which covers 80% of the population), with 196,698 hospitalisations and incurring an expense of approximate 72 million Brazilian Reais³.

Pneumopathies with respiratory limitations are characterised by a progressive limitation on air flowing, not fully reversible, and associated to an abnormal inflammatory response of the lungs to the inhalation of harmful particles or gases². Briefly, a chronic inflammatory process could bring

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changes to the bronchi (chronic bronchitis) and destruction of the pulmonary parenchyma (emphysema), resulting in a loss of elasticity. The clinical symptoms include chronic cough, production of expectoration, and dyspnoea on efforts. In addition, despite pneumopathies with respiratory limitations directly affecting the lungs, it can also produce significant systematic consequences for the muscular and cardiovascular systems.

Altogether, the changes comprising inflammation, excessive mucus secretion, the smooth muscles contraction during air passages, thickening of the bronchial walls, loss of elastic retraction and alveolar destruction, lead to limitation on air flow, and inappropriateness of the relationship between ventilation and perfusion, hyper-insufflating the lungs². The study of pulmonary mechanics in patients with pneumopathic respiratory limitations reveals significant changes in the

airway resistance and limitation to the expiratory flow, thus requiring to be considered for therapeutic decisions making, in order to minimize the damage caused by such condition⁴.

After 2019, the first cases of a new strain of pneumonia caused by a novel coronavirus, named as SARS-COV2, spread worldwide^{2,5}. The illness caused by this virus (Covid-19) was infectious, and its clinical spectrum would range from patients who have no symptoms or are oligosymptomatic, to situations where there were very serious acute shortage of breath, often requiring hospitalisation in Intensive Care Units (ICU). Usually, this illness progresses to a situation of Acute Respiratory Distress Syndrome (ARDS) with prolonged period of hospitalisation, leading to severe breathing complications, which, when not lethal, brings serious respiratory sequelae^{4,6}.

According to the Clinical Treatment Protocol of Covid-19, published by the Brazilian Ministry of Health⁷ in February of 2020, 80% of these patients had the disease ranging from mild to moderate form, which included cases both with and without pneumonia; 13.8% had severe form of the disease (dyspnoea, breathing frequency \geq 30/min, O₂ saturation in the blood \leq 93%, PaO₂/FiO_{2 ratio} < 300 and/or a lung with infiltrate taking up more than 50% of the pulmonary parenchyma within 24 to 48 hours); and 6.1% of them were critical cases that evolved fatally with breathing failure, septic shock and/or dysfunction and multiple organ failure (MOF)^{7.8}.

Changes in pulmonary structure are reflected through radiological imaging technique using the high resolution computed tomography (HRCT). The different tomographic findings can be combined to form typical pulmonary lesion patterns caused by SARS-COV2 virus infection⁹. These, together with the anatomical distribution of the findings, and clinical data, can narrow down the possible diagnoses of diffuse pulmonary interstitial diseases, and in many cases even suggest the correct diagnosis with a very high level of accuracy. The most common patterns shown in diffuse pulmonary interstitial diseases in tomography are the nodular, linear and reticular patterns, cystic lesions, opacities in glazed glass, and consolidations¹⁰.

In the tomographic findings what is most commonly observed in Covid-19 cases are pulmonary opacities in glazed glass and sometimes consolidations, with peripheral distribution predominantly, often linked to a small reticulate (mosaic paving), vascular thickening, and reversed halo sign¹¹. Damages to the central part of the parenchyma, the presence of lumps, cavities, enlarged lymph nodes, or pleural effusion corrur less frequently^{9,12}. Some authors described that the reversed halo sign suggests the possibility of pneumonia in organisation as one of the mechanisms behind the pulmonary lesions^{13,14}. The most evident distinction among these pulmonary lesions pattern consists of the identification of vascular marks on the opaqueness of glazed glass¹⁵. Recently analysis showed that this pattern can be found in the acute or chronic phases of the illnesses, and harm the interstitial regions or the alveoli, of a wide range of different natures¹⁶.

Also, it is remarkable that the severity of respiratory conditions, linked to chronic lung diseases, such as the harmful effects that Covid-19 has produced, brings a worse prognosis when not considered early. If not monitored, these patients would be a group with worse prognosis and that, in general, would need considerable time of hospitalisation¹. Finally, according to the reports in the literature, most of the population severely affected by COVID-19 ends up developing severe respiratory syndrome, and these individuals usually cease with respiratory limitations, whether they are mild, moderate or even incapacitating.

This present article brings the description of an innovative device fro the application of high-flow oxygen catheters using assembly of appropriate existent supplies in hospitals, within the pandemic scenario we have been living currently.

One important event arising from lung impairment, whether chronic or acute, is the effectiveness of mucus removal, which depends on the magnitude of the flow peak and the muscular breathing force necessary for the cough capability ¹⁷. The high intrapulmonary pressure, achieved after a deep inhalation, the glottis closure and the contraction of expiratory muscles bring high flows in the explosive cough phase ¹⁸. This high flow transfers kinetic energy from the air to the secretion, or foreign body, removing it from the bronchial walls and taking it to the pharynx or the mouth, where it can finally be expelled¹⁹. For such mechanism operates well, it is necessary to have neuromuscular activity intact and effective coordination²¹.

Alterations to any of the coughing process phases could reduce its efficiency, which could in turn lead to hypoxaemia and increasing of the breathing effort, resulting in demand for greater oxygen concentrations. The incompetence on closure, and inability to open the glottis, triggers a reduction of final positive expiratory pressure, thereby contributing to hypoxaemia²¹. Weakness of the breathing muscles is one of the main functional consequences of the breathing function worsening caused by chronic lung disease. This weakness leads to the onset of alveolar hypoventilation, formation of micro atelectasis, and the cough mechanism dysfunction, factors that increase the risk of respiratory failure²². Therefore, the measurement of the respiratory muscles strength must be hastily considered for clinical practice.

Among the methods used for the assessment of respiratory muscular force, the measurement of maximum respiratory pressures at the mouth can be mentioned: the maximum inspiratory pressure (MIP) and the maximum expiratory pressure (MEP). The MIP reflects the strength of inspiratory muscles and diaphragm, while MEP follows the strength of expiratory and abdominal muscles. A MIP value less than a third of the normal value is a predictor of hypercarbic breathing failure ($PaCO_2 > 45$ mmHg), while an MEP below 60 cm H₂O is a predictor of inefficient cough, with tendency

to retain secretion. While hospitalized, patients may show functional decline, interfering with their breathing function, which could increase the morbimortality of these individuals.

Few studies have addressed the respiratory function in relation to the length of stay hospitalized. However, it is still uncertain whether the negative effect is secondary only to hospitalization process, or is also influenced by other factors, such as disease severity, nutritional state, type of therapy used or unresponsive environment²³.

Considering the damages resulting from the Covid-19 in the lungs, and other respiratory diseases, it was aimed herein to develop a new method of handling hypoxia in patients with respiratory limitations through the use of a novel nasal device with high-oxygen flow, by increasing in volume and the lungs capacity, and promoting a consequent improvement in oxygen desaturation. Such an instrument was designed to be more affordable, and available to all institutions, for accessible pneumopathy patients' treatment. In addition, being that resource introduced within an appropriate time frame, the nasal device with high flow of oxygen would also be able to reduce the long periods of hospitalization characterized in these conditions.

Many studies have appraised the positive effects of respiratory physiotherapy in patients who have been hospitalized for a long time(24), but these studies do not mention a routine with the implementation of such a technique with high flow of oxygen. Also, considering the resources available on the market that are ready for use, the average cost of a kit to propose therapy with high-oxygen flow, as here suggested, is sure to be a hindrance for public health services. Even in private institutions, such procedure is used sparingly due to the high costs incurred thereby.

In this context, the nasal device proposed for the control of hypoxia in patients with Covid-19 and other respiratory diseases, was idealised taking advantage of components with recyclable assembly. Thus, these pieces are already available in hospital environments for other respiratory therapies, meaning that there is no need for additional costly packages. Additionally, this is a new type of oxygen-therapy that could not only bring a clinical improvement to the pneumopathies, but also carry a broadly usage of this novel device in all kinds of health services.

2 Material and Methods

2.1 Design of nasal high-oxygen flow device prototype

The nasal device prototype consists of a tracheal aspiration probe, made of silicone, widely used in hospital environments. The cannula is introduced two centimetres above the carina, the structure that branches the trachea into two source bronchi. The flow of gas shall consists of oxygen and compressed air, and this composition will then be dosed based on two flow metres of 30 litres/minute, connected to an extension which takes the gases over to a pitcher with water The device contains three extensions, with the first leading the flow of air, a second one controlling the flow of oxygen from the gas network to the pitcher with water, and the third taking the flow of air, as already composed, heated and humidified, from the pitcher to the catheter already inserted in the patient's nostril. A reducing and unifying piece, for the flow of gas coming from the network, is necessary to make a connection with the pitcher (Figure 1).





Source: The authors.

2.2 A new technique with high oxygen flow to control hypoxia

The final proposal of this approach is to integrate all these supplies to provide a high flow of O2 and, as a result, to show the benefits linked to speed and heat that would bring an increase in tidal volume, and a consequent increase in expiratory pressure positive final, with consequent alveolar dilation and better ventilatory perfusion for individuals with limited pulmonary function.

The proposal of the new nasal device with high oxygen flow to be clinically implemented is based on the following: removal of CO2 from the upper airway dead space (high gas flow), reversing the hypercapnia state; reduced respiratory effort by providing an adequate flow of oxygen (delivery of O2 = less exertion of the respiratory muscles), reversing hypoxemia; Improved pulmonary mechanics with the use of adequately heated and humidified gas (warming = respiratory tract distension and optimization of residual volume), generating positive pressure; and reduction in energy consumption for gas conditioning (heating and humidification).

Sometimes it may be hard to wonder why speed would matter. Well, if one device delivers 25 L of flow per minute and another device does the same, does the patient get 25 L/min? The answer is yes, but the way the device is working makes all the difference. A good analogy is to compare it to a garden hose. If you have two garden hoses operating side-by-side providing exactly the same volume of flow, your performance will be equivalent. However, as soon as you place your thumb on the end of one of the hoses, obstructing part of its opening (similar to a small-caliber cannula), the water will splash even more. The volume would remain the same, but the water that would pass through the opening would be smaller, meaning that the speed would be greater, reaching greater distances. Thus, delivering 25L/min without obstruction (larger caliber cannula) in the airflow circuit would lead to low oxygen flow (reduced velocity) to the alveoli and then it would only reach the proximal regions of the lungs (Figure 2A). On the other hand, the presence of an obstruction (small-caliber cannula) in the airflow circuit would lead to high oxygen flow (higher velocity) to the alveoli, also reaching distal areas of the lungs (Figure 2B).

Figure 2 - Illustration representing the garden hose analogy, which demonstrates the importance of the cannula of small calibre for ideal oxygen flow delivery for the treatment of patients with respiratory difficulties. A) Supply of O_2 with larger calibre cannulas in the air flow circuit delivering low speed oxygen flow to the alveoli, and reaching just the lungs proximal region . B. Supply of O_2 with the presence smaller calibre cannulas in the air flow circuit delivering high speed oxygen flow to the alveoli, and reaching also distal areas of the lungs



2.3 Experimental measurement of oxygen flow of the proposed device

This measurement was performed with a 7200 mm adult and infant peak expiratory flow meter (MEDICATE). In short, when the airflow goes through the device, a pin which works as an indicator of low is dragged to the peak of maximum flow, moment when the reading of the result was performed. For the measurements shown in these results, two identical Peak Flow devices were used. The Peak Flow 1 equipment was coupled between the flowmeter output (gas network) and the beginning of the circuit; The Peak Flow 2 was inserted at the end of the circuit (catheter), where the patient's airway begins. When the flow meter was activated, releasing the output of O2 and compressed air, the flow of the gas network was observed and measured using the flow at Peak Flow 1; meanwhile, the circuit flow (O^2 + compressed air), at the time of delivery to the patient, was measured by Peak Flow 2.

3 Results and Discussion

The accessing and understanding of a resource as the one proposed here, at much lower price available to different institutions, shall result in an improved treatment option for patients with lung diseases. This would also reduce invasive procedures, length of stay and provide greater comfort during the treatment, as the interface is nothing more than a catheter (Table 1).

	Optiflow	Airvo 2	Precision Flow	New Device
Flow	1-60L/min	10-60 L/min	1-40 L/min	1-30L/min
Temperature	31 or 37 °C, fixed temperature	31 to 34 °C or 37 °C, fixed temperature	33 to 43 °C, fixed temperature	33 to 37°C
Humidification	Yes	Yes	Yes	Yes
Movement	No	Yes	Yes	Yes
Assembly	30min	10 min	5 min	5 min
Single Use	Yes	Yes	Yes	Yes
Connectivity	No	No	Yes	No
Usage Time in the Circuit	7 days	14 days	30 days	7 days

Table 1 - Comparison between currently oxygen flow procedures available and the newly proposed nasal device of high-flow of oxygen

Source: Resource data.

The target public for using the nasal device with high oxygen flow to control hypoxia consists of patients with respiratory limitations, patients with SARS-CoV-2 infections who had their respiratory capacity affected, or individuals with chronic lung disease, which significantly occupy hospital beds for extended period worldwide.

There are two proposals, stratifying two specific groups of patients: 1) Terminal patients: these are individuals dependent on respiratory devices. For them, speech and swallowing difficulties become contraindicated in maintaining noninvasive ventilation, as this treatment causes oronasal obstruction resulting in respiratory discomfort; 2) Pediatric patients: they do not participate in the treatment that reduces breathing effort, as the impossibility of communication and the pressure on the face make them cry, which increases the respiratory effort, making it an unfeasible alternative.

Finally, by developing the proposed mechanism, these researchers intend to:

- ✓ consolidate collaborations with a variety of researchers in this area for the clinical implementation of a new method to deliver high oxygen flow.
- ✓ contribute to the explanation of the technique and its use in the hypoxia management.
- ✓ establish supplies for mounting the high-flow oxygen device to manage cases of hypoxia in patients with respiratory limitations arising from Covid-19.
- make it clear that this newly designed device is affordable and inexpensive to use in therapy, especially in disadvantaged institutions.
- ✓ disseminate the technical and scientific knowledge acquired.

Considering the importance of the benefits achieved with high flow for patients with pulmonary functional limitation, and to ensure that the flow titrated in the new device was effectively applied to the airway, an experimental measurement was carried out comparing the gases network outflow with the flow emerging from the circuit, when then it enters into the patient's airway.

The gas network flow measurements (Peak Flow 1) were performed at 10, 15, 20, 25, 29 and 30L/min, respectively. Thus, measurements of the circuit outflow (Peak Flow 2) throughout the catheter at the time of delivering to the patient resulted in 7, 12, 18, 23, 27 and 30L/min, respectively. Table 2 summarizes these measurements, and the gas flow loss resulting from differences for the flows analyzed. Of note, flows lower than 30L/min were not able to reach the end of the circuit with the same proportion and efficiency when supplying O₂ and compressed air to the patient's airway (Figure 3A). Thus, the results of this study showed that to be considered effective, without losses, the high flow oxygenation strategy using the new proposed device must use gas volumes from 30L/min and above, since it was demonstrated that there would be no significant flow losses to the patient during its passage through the circuit (Figure 3B).

Table 2 - Perspective of the loss of flow from the exit of the gas $(O_2 + \text{Compressed Air})$ network to the entrance of the patient's upper airway

Output of the Flow of the Gas Network (L/min)	Flow Arrival at the end of the Catheter (L/min)	Volume of Gas Loss (L/ min)	Loss of Gas (%)
10	7	3	30
15	12	3	20
20	18	2	10
25	23	2	8
29	27	2	6
30	30	0	0
40	40	0	0
45	45	0	0

Source: Resource data.

Figure 3 - (A) Comparison of the flow of gases (O_2 and compressed air), delivered to the patient, between existing equipment for pulmonary physiotherapy and the new device proposed for high oxygen flow. (B) Representation of the air escape occurring at lower flows, with consequent loss of flow delivering to the patient. Beyond high flow increasing, the air escape is reduced and the gases delivery to the patient's airway are enhanced **B**



Source: The authors.

Given the impact of respiratory diseases and the magnitude of the damage it can cause, both socially and economically, it seems plausible that an essential measure is to gather knowledge to improve or preserve the lives of people affected by acute and chronic respiratory diseases. Different types of oxygen therapy intend to obtain higher oxygen concentration than the one which is found in the atmosphere (greater than 21%), and this is currently the most frequently treatment applied in the hospital environment.

High-flow oxygen supply in a quick and efficient manner is fundamental for treating seriously ill people. However, this strategy requires spontaneous breathing capability. If there is a degree of respiratory failure with muscle fatigue, then the assisted ventilation should be provided.

The choice of the equipment is based on how much oxygen needs to be provided and on the patient's adaptation and comfort. The use of some devices can make the patient restless, worsening their clinical condition and increasing oxygen consumption. The right choice of O_2 implement is, therefore, essential for the patient's clinical improvement.

Conventional forms of oxygen delivery rely on simple supplies, such as face masks or nasal cannulas and devices. However, the use of these techniques is limited because of the disadvantages such as the requirement for oxygen flow above 15 L/min in cases of severe hypoxemia. For this reason, one of the oxygen therapy options recently receiving great attention is the use of heated and humidified high-flow nasal oxygen. This method is capable of delivering heated and humidified oxygen with controlled FiO_2 up to 60 L/min. In the last decade, the use of this approach has been considered for patients living with recurrent and hypoxemic acute respiratory failure (ARF). Recent reports suggest that such strategy can also be used for safe intubation and for preventing ARF after extubation²⁵.

In fact, the comparative oxygen and compressed air measurement results in this study revealed reduced loss-offlow percentage of gases to be delivered to the patient for input flows equal to or greater than 30L/min using the new proposed method. Considering that the airway has a physiological resistance of $3 \text{cmH}_2\text{O}$, when a ventilatory strategy flow lower than 30L/min is applied, it will not reach the distal end of the airway (alveoli) with the same avidity, since this anatomical resistance will also contribute to decreasing the flow. Thus, flows greater than 30L/min did not present losses, and are able to overcome the airways physiological resistance, bringing benefits to the functional limitations, because there will be dilatation and consequent improvement of the ventilationperfusion ratio, as proposed in this study.

In addition, high-flow devices have already proven to be a competent system that offers heated (37 °C) and humidified (100% relative humidity) oxygen, with a system that uses high flow, generating positive pressure. Other studies have shown good results for oxygen therapy with high-flow tubes, even in children living with acute bronchiolitis, who have greater resistance to air intake. In this high-flow system, there is a reduction in dead space, with an increase in oxygen supply and a reduction in $PaCO_2$ in the alveolus^{26,27}.

Before Covid-19, millions of people were already living with respiratory diseases in Brazil and worldwide. This scenario had already an important impact on health systems. This devastating disease is expected to increase significantly the number of pulmonary diseases, as patients with preexisting respiratory diseases are one of the main risk groups for Sars-Cov2. Pneumopaths or people with respiratory limitations have more severe respiratory conditions when they are positive for Covid-19, as they have previous inflamed lungs, which upon viral infection develops worse clinical outcomes.

Finally, as respiratory diseases are well known to have social and economic impacts, gathering knowledge to improve or preserve the health of individuals affected by respiratory diseases is definitely a necessary step. There are several treatment strategies, but above all, oxygen therapy is essential. There are some forms of oxygen administration, however, it is observed that the conventional form does not seem to meet the most serious conditions, while the invasive form must be avoided. The use of traditional high oxygen flow has been shown as an important tool in the hypoxia management, but the high cost makes common access impossible.

Considering the described perspectives, the new highoxygen nasal device proposed for the hypoxia management in patients with pulmonary limitation, including post-Covid-19 conditions, not only treats patients by promoting increased lung capacities and improving oxygen desaturation, but it is also available at lower costs, making it an accessible instrument for patient treatment in all thepublic and private health institutions.

4 Conclusion

Although conventional oxygen therapy is a more accessible resource, its limitations do not always meet the ventilatory need, sometimes further impacting the patients' clinical outcome, particularly the ones with pulmonary limitation. In that case, the high-flow strategy emerges as a promising resource for the management of these patients.

Some technologies have already come up with resources and implemented benefits through high oxygen flow. However, the mandatory use of expensive supplies has an impact on accessing this technology, and limiting common use.

The possibility of implementing a new method for high flow oxygen-therapy to the patient's clinical improvement, taking advantage of reprocessable components available in hospital environments, which means no need for new financial investments and its usage expansion to cover all types of health services.

As this technique is accomplished using an assembled system, professionals wishing to use this novel high-flow oxygen strategy must understand the organization of the supplies and be aware that when poorly indicated, they can cause harm, as it is the case with any new implemented therapy. This means that the professional team must be trained to implement this therapeutical strategy carefully and progressively.

Although this proposal brings a promising and more efficient way to treat respiratory limitations, it is clear that further clinical studies are needed to determine subgroups of patients with better chances of benefiting from the use of highflow nasal oxygen therapy.

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