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Review Article

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Pandemic and High Flow Ventilation in Patients with Covid 19

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Summary

Introduction: COVID-19 disease is caused by the new SARS-CoV-2. The understanding of the disease has led to the use of NIMV and high flow (VAF) with good results in the treatment of patients with ARDS. , this strategy has gained strength due to its benefits and good results in terms of reducing mortality, hospital stay and return of the patient to useful life with a reduction in sequelae.

Objective: Describe the general context of the current pandemic, NIV and high flow oxygen source (HFFOV) strategies, as well as provide an alternative algorithm for the use of the latter.

Material and Methods: An exploratory documentary review of research articles in recognized databases, published between 2000 and 2021, was carried out; carrying out the analysis stages according to Calderón Villafañez et al.

Results: 82 academic articles were included, including experimental and non-experimental studies, as well as reviews, distributed as follows: articles on the general context of the pandemic 31.6%, articles on NIV and high flow 23.9%, Documents reviewed for algorithm proposal 33.7%.

Conclusions: FoAV is an easy strategy, widely available in high and medium complexity centers, general hospitalization wards and special care units; it is presented as an alternative strategy to treat patients with moderate to severe hypoxemia with COVID-19, with a reduction in care costs, and a significant decrease in sequelae. Taking into account some physiological conditions, the appropriate FoVV device can be chosen with which the better the patient benefits.

Keywords: *COVID-19; Coronavirus; Oxygen therapy; SARS-CoV-2; High flow ventilation; Pandemic*

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Introduction

Coronavirus disease 2019, COVID-19, Coronavirus 2019, is a human respiratory disease caused by a new coronavirus identified with the acronym SARS-CoV-21, 2, began in Wuhan, China, in December of that same year, and due to globalization it expanded with great speed to the 5 continents, being declared a pandemic on March 11, 2020 by the World Health Organization (WHO), providing pertinent indications to humanity for care. That must be taken into account in order to contain the spread of contagion [2-4].

It is known that the incubation period of the virus is 2 to 14 days and it is evident that most of the infections occur person to person, being highly transmissible and the symptoms vary from asymptomatic cases to febrile symptoms presenting symptoms such as cough and difficulty. Respiratory disease, pneumonia and respiratory distress, it can also be accompanied by gastrointestinal alterations; Primary cases are mainly seen in elderly patients and with comorbidities (diabetes, chronic kidney disease, hypertension, heart disease and chronic lung diseases) [5].

The course of this disease was described according to its characteristics in clinical phenotypes such as:

1. Initial or viral phenotype: In which mild symptoms occur such as dry cough, nasal congestion, odynophagia, and may be accompanied by anosmia, as well as fever, headache, arthralgia, as well as patients who do not present symptoms.
2. Inflammatory phenotype, but with respiratory repercussion: In this clinical stage, progressive dyspnea can be found, which can trigger ARDS or reverse in which the titers of inflammatory markers develop in 10%-20% of patients.
3. Hypercoagulative or thrombotic phenotype: In which episodes of thrombosis predominate in different vascular bed territories, predominantly venous and arterial.
4. Phenotype with cutaneous and vascular inflammation: Some of these manifestations are considered late onset, more common in young patients, such as: rash, vesicular lesions, morbilliform rash, multiple petechiae, fixed erythematoedematous plaques, violaceous plaques, from the point of view cardiovascular, cardiac involvement due to coronary vasculitis and myocarditis have been described, in the peripheral vasculature more frequent ischemic phenomena have been observed in the toes.
5. Phenotype with reactive inflammatory lung lesions and pulmonary fibrosis: This occurs particularly in patients who suffer from significant or severe lung disease without targeted treatment [6,7].

Given the significant number of cases globally (more than 11 million by July 2020) and understanding that it is an emerging virus for which there is no knowledge of effective treatment and oxygen therapy measures, the urgency to investigate new effective options to reduce mortality, need for ventilator support, and hospital stay [8].

The understanding of the disease has led to the use of different ventilation strategies for the group of patients who require it; this is why non-invasive ventilation has been used in large clinical centers in order to provide oxygen to patients with respiratory failure. This strategy has gained strength so far in the pandemic due to statistical data that shows its benefits and better results in terms of mortality, reduction in hospital stay and return of the patient to useful life with a reduction in sequelae in patients, in contrast we already know that mechanical ventilation is associated with a greater risk of the appearance of pneumonia associated with mechanical ventilation, showing which is the main cause of death due to hospital-acquired infection [4].

It is for this reason that high flow oxygen source ventilation has become an alternative strategy, which could reduce the occupancy of intensive care units, reducing costs in patient care and reducing the sequelae of the treated patient. In intensive care and connected to mechanical ventilation. This review aims to describe the general context of the SARS-CoV-2 pandemic, non-invasive and high-flow ventilation strategies and provide an alternative algorithm for the use of the latter in patients suffering from this disease.

Disease and may be useful in addressing the treatment of this pathology.

Materials and Methods

Study design

An exploratory documentary review of research and review articles was carried out in the following databases PubMed, Elsevier, Scielo, Springer, Biomedcentral, Medigraphic published between 2000 and 2021; following the recommendations of Calderón Villafáñez, Londoño Palacio and Maldonado Granados, in which the following stages are considered: a) search for articles; b) selection; c) organization; d) provision of information sources for rational treatment; e) integration of information based on the analysis of the messages contained in the sources9. The review answered the question: What is the general context of the SARS-CoV-2 pandemic, and the most used high-flow ventilation strategies?

Inclusion and exclusion criteria.

To carry out this work, the following inclusion criteria were taken into account:

1. Publications on the general context of the pandemic, due to SARS-CoV-2, that deal with the statistical data of each region analyzed, these could be theoretical publications (narrative reviews or letters to the editor), that the language of the publication was English or Spanish and that they were publications published between 2000 and 2021. In the case of clinical trials, those completed were included.
2. Articles that were inaccessible in full text and/or duplicates were excluded. Additionally, the search was carried out around the purpose of each work, taking into account the observation goals of this review: current state of the pandemic, non-invasive ventilation and high-flow ventilation.

This study did not require approval by an ethics committee, because the unit of analysis were published works.

Results

According to the bibliographic search carried out between 2000 and 2021, a total of 322 articles were found that contained information on the topic being searched, and 45% were published in English, followed by 65% in Spanish, of which 240 were discarded. Because they are duplicates, incomplete articles, without access to full text, and with unclear methodologies.

82 academic articles were included in the review, including experimental and non-experimental studies, as well as reviews, all on the general context of the SARS-CoV-2 pandemic, and the high-flow ventilation strategies used, distributed as follows: articles on the general context of the pandemic 31.6%, articles on NIV and high flow 23.9%, Documents reviewed for algorithm proposal 33.7%

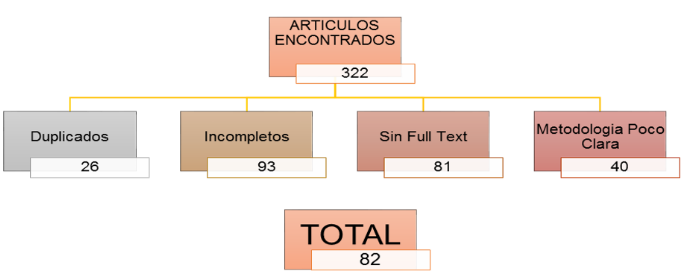

Figure 1: *Articles.*

World Statistics

The World Health Organization (WHO) estimates that the real number of deaths from coronavirus is 2 or 3 times higher than the 3.4 million deaths currently reported to the agency, as explained in the report on World Health Statistics 2021; That is, the real death toll could be between 6.8 and 10 million. As of December 31, 2020, preliminary estimates suggest that the total number of global deaths attributable to the COVID-19 pandemic in 2020 was at least three million, which is 1.2 million more deaths than the 1.8 million officially reported; The WHO highlights that the COVID-19 pandemic poses a significant threat to the health and well-being of the population worldwide, the coronavirus disproportionately affects vulnerable populations, and those living in overcrowded environments are at greater risk of contracting it, Furthermore, the study points out that the lack of data disaggregation favors inequality in health outcomes, since only 51% of countries include disaggregated data in their national statistical reports [10].

Regional Context

Since the appearance of the SARS-CoV-2 pandemic, as of June 20, 2021, 3,945,166 cases have been registered in Colombia, 69,963 in the Department of Norte de Santander and 44,211 in Cúcuta; Cúcuta being the municipality that contributes 63.2% of confirmed cases and 51.9% of active cases in the Department, of which 91.8%, which corresponds to 40,664 recovered cases, 2.75%, which is equivalent to 1,215 cases, are active to date and 4.84 % belongs to deceased cases with a total of 2,140 [11,12].

In relation to Norte de Santander, it is located nationally in position 24 in case rate per 100 thousand inhabitants and position 8 in death rate per 100 thousand inhabitants; presenting a transmission rate of 1.12% in the Department and a residence index of 0.38 in Cúcuta. Currently, a test positivity rate of 25% is recorded, the highest in the entire course of the pandemic, affecting 60% of the department, with a total of 27 municipalities with a high impact [13].

Situation that generates an increase in efforts in health personnel and in healthcare centers, since there are no physical resources to care for positive COVID-19 patients, given the shortage of ventilators to face the pandemic, led healthcare personnel to begin using alternative positive pressure ventilation devices connected to an oxygen source to adequately provide oxygen therapy to patients with COVID-19 infection.

All of this has led to the assumption that the use of high-flow oxygen therapy in primary hypoxemic respiratory failure in a pandemic is shown as an alternative to the management of respiratory therapeutic support in these subjects, both to stop the progression of the condition in well-selected subjects, as well as intermediate support in situations of system saturation [14,15].

Due to the above, devices began to be used, which are detailed later, with the aim of providing timely care to patients who entered hospital centers in need of oxygen.

It is worth mentioning that mechanical ventilation refers to any artificial respiration procedure that uses a mechanical device to help or replace respiratory function, and can also improve oxygenation and influence lung mechanics; recognizing two types main methods of mechanical ventilation: invasive and non-invasive, the difference lies in the use of endotracheal intubation, but both have the same objective, which is to increase or replace the cyclic change in alveolar air volume that occurs with respiratory movements [15, 16].

Since the beginning of the pandemic, the treatment of patients with acute respiratory failure (ARF) associated with COVID-19 has evolved rapidly, based on an increasing number of reports on respiratory system mechanics, cytokine storm, and ventilator treatment [17].

Pathophysiology of SARS-CoV-2 infection in the Taxonomy of viruses, Coronaviruses correspond to the Orthocoronavirinae subfamily, which is included within the family, and is made up of four genera, according to their Genetic structure: Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus, SARS-CoV-2 it is classified within the genus Betacoronavirus [18].

SARS-CoV-2 infection activates the innate immune system, generating an excessive response that could be related to greater lung injury and worse clinical outcome, when the immune response is not capable of effectively controlling the virus, such as in older people with a weakened immune system, the virus spreads more effectively, producing lung tissue damage, which activates macrophages and granulocytes with the massive release of Pro-inflammatory cytokines [18,19].

Early in infection, SARS-CoV-2 targets cells, such as nasal and bronchial epithelial cells and pneumocytes, through the viral structural spike protein that binds to the angiotensin-converting enzyme 2 receptor (ACE2) [19]. Transmembrane serine protease type 2 (TMPRSS2), present in the host cell, promotes viral uptake by cleaving ACE2 and activating the SARS-CoV-2 S protein, which mediates the entry of the coronavirus into host cells [20-21], ACE2 and TMPRSS2 are expressed in host target cells, particularly type II alveolar epithelial cells, similar to other respiratory viral diseases, such as influenza, profound lymphopenia may occur in individuals with COVID-19 when SARS-CoV-2 infects and destroys T lymphocyte cells. In addition, the viral inflammatory response, which consists of the innate and adaptive immune response, alters lymphopoiesis and increases lymphocyte apoptosis [22,23].

Although upregulation of ACE2 receptors by ACE inhibitor and angiotensin receptor blocker medications has been hypothesized to increase susceptibility to SARS-CoV-2 infection, large observational cohorts have not found an association. Between these medications and the risk of infection or in-hospital mortality due to COVID-19 [24-25].

In later stages of infection, when viral replication accelerates, the integrity of the epithelial-endothelial barrier is compromised. In addition to epithelial cells, SARS-CoV-2 infects pulmonary capillary endothelial cells, which accentuates the inflammatory response and triggers an influx of monocytes and neutrophils [26].

In severe COVID-19, there is a fulminant activation of coagulation and the consumption of coagulation factors [27-28]. A report from Wuhan, China, indicated that 71% of the 183 people who died of COVID-19 met the criteria for disseminated intravascular coagulation, inflamed lung tissues and lung endothelial cells can lead to the formation of microthrombi and contribute to high blood pressure. Incidence of thrombotic complications, such as deep vein thrombosis, pulmonary embolism, and thrombotic arterial complications, the development of viral sepsis, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, may further contribute to multi organ failure [27].

Pandemic and oxygen therapy

The course of the pandemic and the understanding of the disease has meant that different ventilation strategies are used for the group of patients who require it; this is why non-invasive ventilation has been used in large clinical centers in order to provide oxygen to patients with respiratory failure. This strategy has gained strength so far in the pandemic due to statistical data that shows its benefits and better results in terms of mortality, reduction in hospital stay and return of the patient to useful life with a reduction in sequelae4. In contrast, we already know that mechanical ventilation is associated with a higher risk of pneumonia associated with mechanical ventilation, showing that it is the main cause of death due to hospital-acquired infection [4-29].

The fatality of patients on invasive mechanical ventilation (IMV) for more than 48 hours is ~20 to 25%, with an additional 1% incidence for each day of mechanical ventilation (MV). It is estimated that the risk of acquiring pneumonia is 21 times greater in patients exposed to MV, compared to patients not subjected to the procedure. The additional mortality caused by ventilator-associated pneumonia (VAP), or attributable mortality, has been studied, observing a wide range from 30 to 70%, according to different studies [2-28]. On the other hand, these and other reports show that survivors' hospital stay is significantly prolonged between 19 and 44 days [29].

Non-invasive ventilator support

The use of non-invasive ventilation (NIV) during the pandemic in the world has varied, and has been reported between 2% and 19%, with Chilean figures close to 5% and 6%. 30 The recommendations that discuss the role of NIV in primary hypoxemic respiratory failure in a pandemic, where there is no evidence to support or refute this support alternative [2], likewise, different interfaces have been used in non-invasive mechanical ventilation with significant differences in the impact on the reduction of mortality. Among which we find the Helmet in different series showing better clinical results and reduced mortality [31,32].

An Argentine study compared continuous positive airway pressure (CPAP) by face mask, high-flow nasal cannula (CAF), and conventional oxygen therapy; showing that there was a lower risk of aerosolization; better tolerance; and even better performance in prone wakefulness, when using NIV and "Helmet" as an interface in a H1N1 influenza pandemic, the failure was 28%, with 0% failure in people who had pure hypoxemia; For that same pandemic, a series of 337 patients who underwent NIV reported greater survival for the NIV user group (24% versus 13%; P=0.02), with a calculated relative risk of surviving of 1.62 (95% CI 1.0 to 2.6), and a number needed to treat (NNT) of 13 [33].

In a study carried out by (Maclans & Cols), also during the H1N1 pandemic, in an observational methodology of 148 ICUs in Spain, 685 confirmed cases were admitted, 489 ventilated, and 177 on NIV; The latter showed effectiveness in 40.7% of the subjects, despite the low success rate compared to the other series, those who were successful with NIV required less ventilation time, a shorter ICU and hospital stay, compared to the that failed. Furthermore, mortality was similar when compared with early intubation (26.5 versus 24.2%) [15].

In the current COVID-19 pandemic, results presented by a group from China, 5.1% of subjects used NIV compared to 2.3% assuming a maximum calculated NIV failure of 45%, leaving at least one 55% that works properly with VNI [34].

Other current studies have shown the use of CAF and NIV in 30% of hospital admissions and in 72.6% of subjects with ARDS; of these, only 6% of 84 subjects included in this subgroup of patients were invasively ventilated. The cohort, who had no association with higher mortality [35,36].

In a systematic review, which involved 9 clinical trials and 2,093 patients, an association was found between the combined outcome of requiring intubation or therapeutic escalation with the use of NIV with RR = 0.71 [95% CI 0.51 to 0.98], no as well as support like 4 CAF12. The systematic review and meta-analysis by Leeies & Cols,

Compared CAF and NIV in hypoxemic primary respiratory failure, in 7 clinical trials with 1771 subjects, they found no differences in mortality. The PaFi ratio was significantly lower in the CAF group (Mean difference -53.3 [95% CI -71.9 to -34.7]), strongly recommending clinical trials that evaluate the real efficacy of CAF in this type of pathology [37].

In a retrospective study on non-invasive ventilation (NIV) in patients with moderate or severe ARF due to COVID-19, carried out by Mukhtar et al., it was identified that NIV was initiated following "predefined" criteria and an algorithm was used to detect failure of NIV and initiate invasive mechanical ventilation (IMV) if necessary. This included 55 patients, of which 71% (n = 39) presented signs of ARF that required mechanical ventilation. Of these 39 patients, NIV was successful in 77% of the cases (n = 30) and not were intubated, while 23% (n = 9) were intubated with an in-hospital mortality rate of 10% and 78% respectively. Based on these results, the authors support that NIV is feasible with a high success rate and helps prevent IMV among patients with severe COVID-19 [38].

Likewise, in the study developed by Mehta et al., in 2011, adult patients who received NIV were identified, considering that patients had an SEC for NIV if they had an acute exacerbation of chronic obstructive pulmonary disease or heart failure. Multivariable hierarchical logistic regression was used to determine the association between hospital rates of NIV use for ECS and patient risk of NIV failure (need for IMV after NIV). As a result of the 22,706 hospitalizations with NIV as the initial ventilator strategy, 6,820 (30.0%) presented SEC. Patients with SEC had a lower risk of NIV failure than patients with weak evidence conditions (vs. 18.2%, P < 0.0001). Regardless of the underlying diagnosis, patients admitted to hospitals with greater use of NIV for ECS had a lower risk of NIV failure (adjusted odds ratio quartile 4 vs. quartile 1 = 0.62; 95% CI = 0 .49-0.80), even patients without an ECS benefited from admission to hospitals that used NIV more frequently for patients with ECS (adjusted odds ratio of quartile 4 versus quartile 1 for NIV failure = 0.68; 95% CI = 0.52–0.88) [39].

Finally, Zangrillo et al, in a study where the objective was to describe the characteristics, daily care and outcomes of patients with COVID-19 acute respiratory distress syndrome (ARDS), in the large tertiary hospital of Milan; Daily demographic and clinical data were collected to identify predictors of early mortality from mechanically ventilated patients with confirmed COVID-19 admitted to the intensive care unit (ICU) between February 20 and April 2, 2020. The results were that, of the 73 patients included in the study, the majority were men (83.6%), the median age was 61 years (interquartile range [IQR], 54-69 years) and hypertension affected 52.9 % from the patients. Lymphocytopenia (median, 0.77 x 10^3 per mm^3; IQR, 0.58-1.00 -269.1 mg/dL) and pro-coagulant status with D-dimer (median, 10.1 µg/m; IQR, 5.0-23.8 µg/m) were present. Median tidal volume was 6.7 ml/kg (IQR, 6.0-7.5 ml/kg) and median positive end-expiratory pressure was 12 cm H_2O (IQR, 10-14 cm H2O). In the first 3 days, the prone position (12-16h) was used in 63.8% of the patients and extracorporeal membrane oxygenation in five patients (6.8%). After a median follow-up of 19.0 days (IQR, 15.0-27.0 days), 17 patients (23.3%) had died, 23 (31.5%) had been discharged from the ICU, and 33 (45.2%) were receiving invasive mechanical ventilation. in the ICU. Older age (odds ratio [OR], 1.12; 95% CI, 1.04-1.22; P = 0.004) and hypertension (OR, 6.15; 95% CI, 1.75 -29.11; P = 0.009) were associated with mortality, while early improvement in arterial partial pressure of oxygen (PaO_2) to fraction of inspired oxygen (FiO2) ratio was associated with discharge alive of the ICU (P = 0.002 for the interaction) [40].

Current devices in high flow oxygen source ventilation

Acute respiratory failure caused by SARS-CoV-2 pneumonia (COVID-19) generates a significant compromise in oxygenation in patients, where oxygen therapy in an efficient and timely manner is essential and necessary for timely patient care. Who suffer from this infection, thus avoiding fatal outcomes? It is for this reason that high-flow oxygen therapy emerges as an alternative to conventional oxygen therapy in patients with acute respiratory failure, especially when other rescue therapies have been questioned due to their high particle dispersion [41].

The most used devices are described below:

High flow nasal cannula (CNAF)

High-flow nasal cannulas (CNAF) are a type of respiratory support instrument through which humidified and warm air is administered, with or without oxygen, using flows higher than the patient's maximum spontaneous inspiratory flow [42].

High flow oxygen therapy consists of the application of a gas flow of up to 60 L/min through nasal cannulas. This system is tolerable by the patient because the inspired gas is heated and humidified (temperature of 34–37ºC, delivering a relative humidity of 100%), as effects of high-flow nasal cannula therapy, a lower dilution of the administered oxygen with ambient air, a decrease in dead space (and CO2 scavenging), generation of positive pressure in the airway (CPAP), increase circulating volume and respiratory work and improve mucociliary transport [41].

The use of HFNC in COVID-19 can provide a specific positive end-expiratory pressure, which could have a potent effect in mild to moderate hypoxemic respiratory failure. It also delivers a flow of adequately heated and humidified gas to through the nasal pharynx, which reduces metabolic work; in addition, HFNC has been observed to reduce the intubation rate and improve the clinical prognosis in patients with acute respiratory failure; it also has advantages such as: [41].

1. Generates less claustrophobia, as the cannula is smaller and more comfortable than a facial mask.
2. NIV is more dependent on the operator and patient tolerance.
3. CNAF requires less complicated installation and management than NIV.
4. The risk of particle dispersion is much greater in NIV and requires the use of negative pressure rooms, high-efficiency virobacterial filters, and minimizing the possibility of leaks as much as possible, which is practically impossible.
5. It has been shown that particle dispersion with CNAF decreases significantly when used with a surgical mask on the equipment.

Likewise, it is considered as a therapeutic alternative in the management of patients with COVID-19, once it has been shown that the degree of aerosolization is minimal with these devices, and it is now recommended as the oxygenation therapy of choice in patients with respiratory distress; The use of HFNC is framed in the early recognition of severe hypoxemic respiratory failure, identification of the non-favorable response to conventional oxygen therapy, selective use of HFNC, intubation and early, but not premature, invasive ventilation [43].

Helmet

Oxygen delivery via helmet-based continuous positive airway pressure (CPAP) is a feasible option that allows for higher positive end-expiratory pressure (PEEP) and may theoretically reduce the need for intubation compared to with HFNC, but direct comparative evidence is lacking [44].

Due to the above, the "helmet" is useful, which is an interface to provide ventilator support through pressures with relative control of them. For this, it is necessary to have a system that manages to deliver the necessary flow to pressurize the interface and to the subject, in addition to a restrictor, such as an exhalation valve or a PEEP valve [45].

This device, being a transparent hood that covers the patient's entire head, with a soft seal on the neck, helps eliminate support areas around the face, generating greater comfort and reducing leakage, and can increase PEEP at desired levels without worrying about its control [46].

Many groups suggest the use of NIV through the "helmet" interface due to its better clinical performance in mortality reduction [46] compared to CPAP by face mask, high-flow nasal cannula (CAF) and oxygen therapy; leading to lower risk of aerosolization; better tolerance; and even better performance in prone position [47-49].

Helmet masks, over the years and in conjunction with the modernization of technologies, reduced in size, improving comfort and efficiency; leading to them being better tolerated and more suitable for patients with dyspnea who did not meet all the requirements for intubation, since they had better adherence to treatment even for first-line management in cases of exacerbation of Chronic Obstructive Pulmonary Disease (COPD). With decreased work of breathing, improved gas exchange, lower risk of intubation and decreased pneumonia associated with mechanical ventilation [45].

Among the reported benefits are that patients can stay awake, the materials are soft, comfortable and also adjustable; Currently, face masks in NIV are the most used and among the difficulties reported are the presence of non-tolerance, skin damage, pain and claustrophobia, which can lead to escalation in treatment, leading to intubation [45].

The main characteristics of this interface is that it covers the entire surface of the head, including part of the neck where its seal is located, using strap systems under the arms, which is why they are an alternative to ulcerations in the nose or adjacent areas. Caused by interfaces that fit the face (full facial) or the mouth and nose (oronasal). In addition, it has been found that in many cases it is better tolerated than facial masks, reducing the leakage of particles, since due to the conformation inherent to the "Helmet" it is possible to selectively filter the air exhaled by the patient, and in some studies they have also reported that higher positive end-expiratory pressure (PEEP) values could be used compared to face masks. As is recommended for prolonged use in users with continuous positive airway pressure [50].

- The device can be used in a prone position, where the "Helmet" must be completely rotated so that the air, oxygen or MV connections are in the back. A prone mattress can be used to promote comfort, in case if this is not available, pillows should be used that prevent the weight of the device from remaining in the cervical area [49].
- Finally, tolerance has been one of the important factors in the success of NIV therapy, for which this interface has seemed to improve patient acceptance, however, there are some complications, including carbon dioxide scavenging. (CO_2) and subject-ventilator synchrony as the most reported [51].

CPAP O2 MAX Trio System

The use of devices that provide continuous positive airway pressure has shown improvement in various pathologies that cause respiratory failure. In the COVID-19 pandemic, the use of these devices has become widespread, but, due to the shortage of conventional continuous positive airway pressure (CPAP) devices, alternative devices that connect to sources have been manufactured. Of oxygen and do not need a mechanical ventilator [52].

Oxygen source CPAP therapy represents a preferred method to avoid the progressive deterioration of patients with predominantly hypoxemic respiratory failure and especially in its initial phase. It quickly improves vital signs, gas exchange and respiratory effort. In addition, by reducing the sensation of dyspnea and improving hypoxemia, in some cases it avoids the need for invasive therapy. The CPAP system – O2 MAXTRIO offers continuous positive pressure in the airway in patients with spontaneous breathing at hospital level. And Pre hospital. With a simple control of the adjustable positive pressure, between 5cm H20 and 20cm H20, with a constant flow of 02 that allows FIO2 of 30%, 60% or 90%, we achieve timely management of hypoxemia. All these benefits allow us to use this therapy in a wide range of clinical conditions related to respiratory difficulty [53].

In a descriptive observational study at the IFEMA Field Hospital, a patient with SARS CoV-2 pneumonia who presented respiratory failure (oxygen saturation [$SatO_2$] < 93 and oxygen saturation/inspired fraction of oxygen [$SatO_2/FiO_2$] < 300), where the reservoir mask or Ventimask Venturi effect was compared vs. alternative CPAP devices in a total of 23 patients, which resulted in: alternative CPAP was used in five patients (21.7%), while, in The remaining 18 (78.3%) used ventilatory support with a reservoir mask or Ventimask Venturi effect; A progressive increase in saturation was observed in those patients in whom alternative CPAP was used (from 94% on average to 98 and 99% on average, after 30 and 60 minutes with the mask, respectively), significant changes were observed in the [$SatO_2/FiO_2$] in patients who used alternative CPAP (p = 0.040), its use is recommended after the use of conventional oxygen at [15].

It/min with oxygen saturation (SpO_2) below 93%, start at pressure between 8-10 cm H_2O, can be applied in scenarios, such as, trial therapy, as a bridge to a mechanical ventilator, as therapeutic ceiling and as an aid in weaning off the invasive mechanical ventilator; the response should be evaluated within 30-60 min, it is suggested to verify the patient's tolerance to therapy and positive pressure, SpO_2 should be maintained between 92-96%, tidal volume should be maintained between 6-8 ml per kg of ideal weight and the respiratory rate is maintained ≪ 35 per minute [52].

Physiological and pathological aspects analyzed for the development of the high-flow oxygen therapy algorithm for oxygen sources in patients with COVID 19.

Breathing Modes

Nasal breathing

It is one that is carried out nasally, through the nostrils, through which the air enters and leaves, in conditions of rest without effort, while the simultaneous closure of the oral cavity occurs, through lip closure and the attachment of the tongue to the palate [54-55]; Breathing, considered normal, is considered correct because when the passage of air occurs, as a mechanical event, the surrounding nerve endings are stimulated, generating certain responses, among the most important of which we find chest movement, the three-dimensional development of the nasal passages, the ventilation and size of the maxillary sinuses, as well as the secretion of certain endocrine hormones that regulate the behavior of pleasure and displeasure. Nasal breathing, in addition to conditioning the air breathed and allowing oxygen to reach all organs, participates in important reflexes from its sensitive, sensory and neuro vegetative innervation that mainly affect the respiratory and cardiovascular system, such as increased blood pressure. Vasodilation and secretion of the nasal mucosa, glottic closure and sneezing as mainly defensive functions [56,57].

Mouth breathing

The loss of the normal respiratory mode is defined as the change from the physiological nasal respiratory regime to the oral one, which can be total or partial, mixed or intermittent, and is considered normal in situations of physical effort, on the contrary, it is considered abnormal in resting conditions, originating from multiple factors such as respiratory infections of the upper airway, airway obstructions or as a consequence of other pathologies, this is classified as organic; which is due to a real disorder that hinders the passage of air through the natural and functional route: in which, without a structural impediment, the oral route is used, it is also considered a bad habit as long as once the obstruction is eliminated The patient maintains oral respiratory mode, usually mouth breathing is related to poor permeability of the upper airway, either due to adenoid hypertrophy, palatine tonsils, allergic rhinitis, deviations of the septum and narrow nasal cavities with turbinate hypertrophy [57,58].

Naso-buccal breathing (mixed)

It is a combined form of nasal and mouth breathing, with one or the other predominating. For the mixed respiratory mode to occur, the soft palate adopts a certain position, in which the soft palate rises until it comes into contact with the posterior wall of the pharynx, closing access from the oropharynx to the nasopharynx and all airflow. The expiratory flow is directed towards the mouth, so that when the soft palate rises, the posterior entrance to the oral cavity opens at the same time [59].

The distribution of the respiratory flow occurs between the mouth and the nose, which not only occurs with the lips semi-closed, but is activated on all occasions when, with the mouth open, the air can pass either through the nose, through the mouth, or through both routes at the same time, it is the soft palate that causes the oronasal distribution, approaching the tongue or moving away from it, approaching the posterior wall of the pharynx. Likewise, the evaluation of the respiratory mode is essentially clinical, with different methods available, such as: Glatzel test, Rosenthal test, observation of nasal flaring, among others [57].

The above indicates that, when changing the nasal respiratory mode to an oral, or mixed, respiratory mode, due to pathological or dysfunctional obstruction of the nasal passages, the air that will reach the lungs will do so through a shorter and more efficient route. Easy, without being filtered or moistened, generating a greater tendency to respiratory infections and preventing the correct stimulation for the development of the paranasal structures and respiratory capacity, in addition to generating alterations at the level of the entire organism [60].

Neurological status and use of high-flow oxygen therapy

It is important to highlight that of the total number of patients requiring mechanical ventilation (MV) in intensive care units (ICU), around 20% correspond to neurological pathologies. This group of patients has a longer stay on MV and higher mortality [61].

This is explained because brain injuries such as traumatic brain injuries (TBI), cerebrovascular events, metabolic encephalopathies, among others, which manifest mainly with impaired level of consciousness and Glasgow score less than or equal to 8, are associated with respiratory compromise due to altered reflexes. Airway protectors and inadequate management of oro-nasal secretions with high risk of pneumonia and respiratory failure due to aspiration, making it necessary to provide oxygen therapy invasively through endotracheal tubes 62, and non-ventilation devices are contraindicated. Invasive such as CPAP MAX TRIO, high flow cannula, Helmet chamber (connected to an oxygen source) and/or non-invasive ventilation with a mask connected to mechanical ventilation, due to its high risk of favoring the penetration of oro-nasal secretions into the bronchial space. And therefore increase ventilator deterioration [63].

Definition of old age and physiological changes

Old age is not definable exclusively with chronology but rather by the sum of the physical, functional, mental and health conditions of people; as well as, it is identified from the physiological age according to the aging of organs and functions, the psychological or mental age, according to the degree of maturity, psychological aging; Therefore, it is a dynamic concept, once it must be taken into account that biological age can differ markedly from chronological age, and both from subjective age [64].

The World Health Organization (WHO) considers an older adult to be any person over 60 years of age 65,66, considering people from 60 to 74 years of advanced age, from 75 to 90 years old or old, and those over 90 years old are called old, old or long-lived [67]. Likewise, PAHO, in April 1994, decided to use the term older adult, meaning people 65 years of age or older [68].

During aging, common age-related conditions occur, including hearing loss, cataracts and refractive errors, back and neck pain and osteoarthritis, chronic obstructive pulmonary disease, diabetes, depression and dementia; as you age, the likelihood of experiencing several conditions at the same time increases. This life cycle is also characterized by the appearance of several complex health states that usually occur only in the last stages and do not fall into specific morbidity categories; this is a consequence of multiple underlying factors that include, among others, the following: frailty, urinary incontinence, falls, delirious states and pressure ulcers [69].

Physiological changes in the muscle mass and respiratory system of the elderly

Aging is considered as a dynamic process of morphological, functional, psychological and biochemical modifications that begin at birth and develop throughout life; understood as a universal phenomenon, a dynamic, irreversible, inevitable and progressive process, involving a certain number of physiological changes, mostly simply a decline in the function of the organism; producing changes in organs and systems.

Some of the most complex and sophisticated human movements are performed in the oral sphere, the lips and tongue perform very specific movements that are modulated by a neuromuscular control mechanism, the chewing and skin muscles lose 20% of their effectiveness when moving from 30 years to 65 years, facial muscles lose elasticity and resistance due to dehydration and an increase in fibrous tissue, muscle weakness is a recognized aspect of physiological aging, muscle tissue slowly atrophies and happiness Involution is manifested by increasing fragility and progressive difficulty in executing the slightest effort, with a decrease in muscular work capacity [70].

Skeletal muscle decreases in mass, is infiltrated with fat and connective tissue, there is an especially significant decrease in type 2 fibers, disarray of myofibrils, a decrease in motor units, and a decrease in blood flow [71]; At the subcellular level there is an accumulation of molecules with damage due to oxidative stress, mitochondrial dysfunction, accumulation of lipofuscin, failure in the synthesis of new proteins relevant to the formation of myofibrils, among others [72], generating a lower capacity of the muscle to generate force [73].

The loss of muscle mass and function associated with age is known as sarcopenia [74], which is defined as a syndrome characterized by the generalized and progressive loss of skeletal muscle mass, usually accompanied by physical inactivity, decreased mobility, slowing of gait. , reduced ability to perform resistance exercises [75]; It has important metabolic repercussions, both in the regulation of glucose, bone mass, protein balance, temperature control, among many others [75,76].

Sarcopenia causes a decrease in strength and exercise capacity [73], it is a predictor of morbidity and mortality in older adults [77], it has also been proposed that the decrease in muscle strength and the reduction of muscle mass would participate in the genesis, associated with the reduction of muscle fibers and the denervation of the motor units, which are reinnervated by slower neurons [71]. Likewise, shared characteristics are generated with the frailty syndrome [72], understood as the cumulative deterioration in multiple physiological systems including the neuromuscular, which results in sarcopenia [77].

Another of the important changes that occur during the aging process are those that occur in the respiratory system in which there is a decrease in lung elasticity and an increase in thoracic rigidity, which do not allow good pulmonary contraction-distension, With the consequent deficit in gas exchange, there is an increase in residual volume and total lung capacity, with a decreased response to hypoxia and hypercapnia; The speed and production of tracheal mucus is altered, as well as the functioning and efficiency of the ciliary apparatus, in addition to a decreased antitussive reflex, all of which does not allow good movement of the bronchial secretions that are normally produced and adequate cleaning of the bronchial tree. , with the consequences of a tendency to develop respiratory infections and decreased respiratory function, processes that frequently deteriorate [78], as well as a decrease in thoracic compliance and an increase in residual volume, the volume of closure of the airway. Small increases. PaO_2 decreases, which accounts for the increase in the alveolar-arterial gradient with age; FEV1 also decreases, residual volume increases in both sexes and vital capacity decreases, that is, total lung capacity is lower [79].

During the aging process the lungs begin to lose part of the tissue, a decrease in elasticity is also observed, partly due to the loss of elastin in the lung tissue, a slight increase in the anteroposterior thoracic diameter, dorsal curvature is observed. of the spine may be affected due to a reduction in bone mass and mineral deposition in the costal cartilages, the diaphragm is weakened, as are the intercostal muscles, the cilia that line the airways are less able to move the mucus upwards and out of the airways, there is a lower production of IgA through the respiratory passages and, therefore, a higher incidence of viral infections, changes also appear such as a decrease in maximum lung function, the amount of oxygen that is transferred decreases, a greater tendency is generated for the airways to collapse by not breathing deeply or by remaining immobilized for a long time, and with this a greater risk of developing respiratory infections or other lung problems, less response to the decrease in levels of oxygen and an increase in carbon dioxide levels [80].

Anxiety in the patient with COVID 19

The COVID-19 pandemic has had a great impact on the mental health of hospitalized patients, whether due to isolation, uncertainty, or their own state of health, generating various emergencies and psychiatric emergencies that must be addressed [81]; Thus, the psychological and social impact of this pandemic is indisputable; This is why several lines of research have worked on understanding how society defines the origin and impact of epidemics and how they deal with them, emotional coping being key in this process [82].

In the research called "Levels of stress, anxiety and depression in the first phase of the COVID-19 outbreak in northern Spain", the levels of stress, anxiety and depression upon the arrival of the virus were analyzed and the levels of Psychological symptoms according to age, chronicity and confinement. With a sample of 976 people using the DASS scale (Depression, Anxiety and Stress Scale), the results obtained show that the younger population and those with chronic diseases have reported higher symptoms than the rest of the population. The study predicts that symptoms worsen as the pandemic goes on and suggests interventions and treatment to reduce the psychological impact that this pandemic may create [83].

In a study carried out in 2020 with 1,210 people in 194 cities in China, and which aimed to evaluate the level of psychological impact, anxiety, depression and stress in the initial stage of the COVID-19 outbreak and carrying out the application of the Depression, Anxiety and Stress Scale (DASS-21). The result was that 16.5% of the participants showed moderate to severe depressive symptoms; 28.8% moderate to severe anxiety symptoms; and 8.1% reported moderate to severe stress levels. Poor health status was significantly associated with a greater psychological impact on higher levels of stress, anxiety and depression [84].

A study of 1,354 Canadian adults in early February 2020 indicated that a third of people surveyed were worried about the virus and 7% were "very worried" about the infection. In which 7% of the population, that is, 2.6 million people, were very worried. Likewise, globally, fear of COVID-19 is much greater than fear of seasonal flu outbreaks, although the latter has killed considerably more people [85].

Finally, it is important to mention that, in any biological disaster, fear, uncertainty, and stigmatization are common and this is why it is important to carry out appropriate medical and mental health interventions [86]; interventions aimed at knowing the specific psychological situation of the potential group on which one wants to act, since each group can perceive the risk differently [87], as, for example, in the 2009 influenza A (H1N1) epidemic it was found that The university population surveyed was not worried about the pandemic situation, nor did they think it was serious. In fact, the youngest respondents (ages 20-34) were the most likely to believe they were not susceptible to H1N1 flu, despite being the most affected group in previous flu pandemics [88].

Recommendation algorithm for high-flow oxygen therapy in patients with COVID 19

In the first instance, the algorithm helps us identify the type of patient who is a candidate for high-flow devices, starting with clinical and oxygenation characteristics that allow the clinician to define the device to use, as well as the criteria for not using them, based on in widely described physiological aspects and results of series of research available to date.

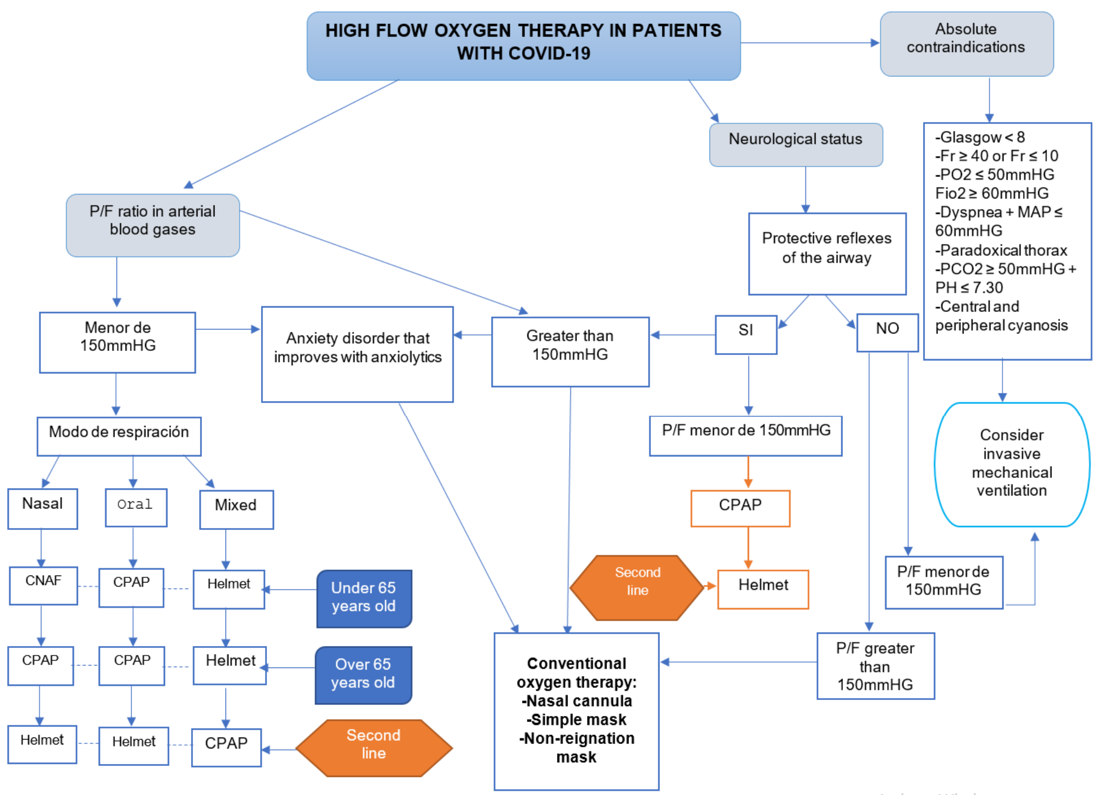

Figure 2: *Algorithm. Own elaboration (2021).*

Legend: P/F=PaFi ($PaO_2/Fi0_2$), PO_2= Oxygen Blood Pressure, FiO2= Inspired Oxygen Friction, RR= Respiratory Rate, MAP= Mean Blood Pressure, PCO_2= Carbon Dioxide Blood Pressure, CNAF= Cannula High Flow Nasal, CPAP = Continuous Airway Pressure System, Second Line = Refers to alternative devices that can be used if the main device of choice is not available or there is a contraindication for it.

Evaluation of the degree of hipoxemia

It is definitely the most important aspect to evaluate in the patient with infection by the SARS CoV 2 virus, since it is already known that the level of hypoxemia in these patients behaves differently than patients with other interticiopathies, leading to the coining of the term silent hypoxemia in patients, where basically a disproportion is observed between the sensation of dyspnea reported by the patient and the clinical symptoms, contrasted with the oxygenation levels found in the patient by pulse oximetry or arterial gases, this is attributed to multiple factors such as the genetic, the altitude of residence of the patient [89] and also in recent studies it has been found that SARS-CoV-2 has affinity for the receptors in the nervous system that could explain the inadequate perception of dyspnea [90].

Therefore, this consideration of hypoxemia must be evaluated to define the most appropriate oxygenation device. This must be measured through arterial blood gas, taking as a reference its consideration and start with a PAFI index of less than 150, since the start of oxygenation High flow rates above this value have shown no differences between placing the device or not [91].

As previously defined, the state of consciousness determines the most appropriate oxygenation device for the treatment of the patient, because its deterioration is associated with respiratory compromise due to alteration of the protective reflexes of the airway and inadequate management of secretions. oro-nasal with a high risk of pneumonia and ventilator failure due to aspiration [62], in which the use of high-flow ventilation devices or non-invasive mechanical ventilation is not indicated; Opposite case in which protective reflexes such as cough, gag reflex, bite reflex, swallowing reflex, are present are present.

You can use CPAP and Heltmet as a second line because these devices guarantee oxygenation through the nose and mouth in patients with discrete alterations in the level of consciousness and loss of muscle tone that prevent correct occlusion of the oral cavity [63].

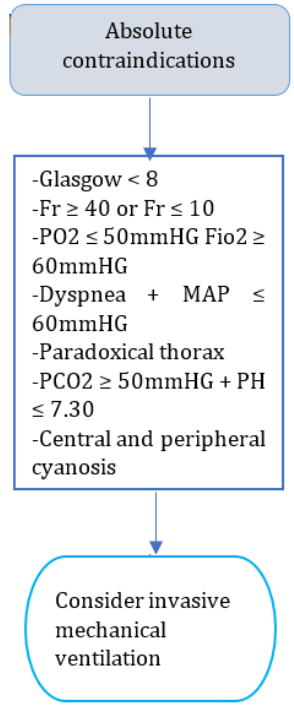

Figure 3.

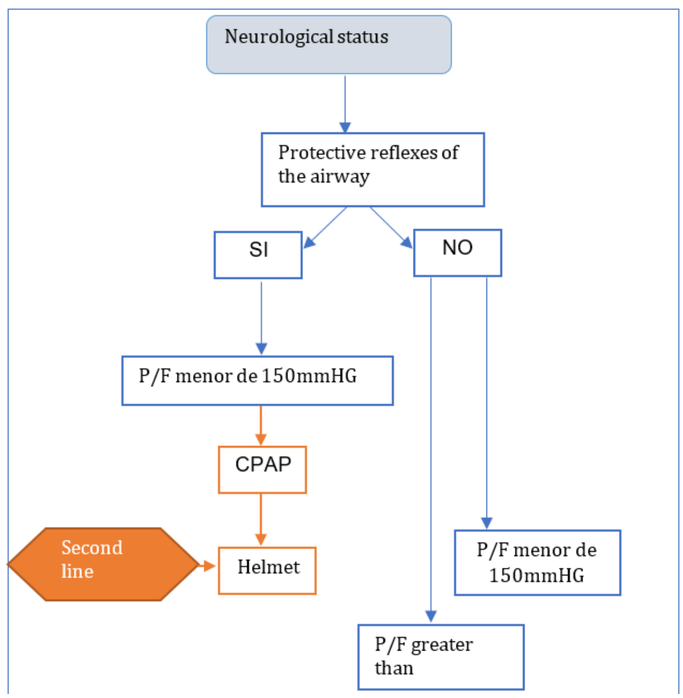

Figure 4.

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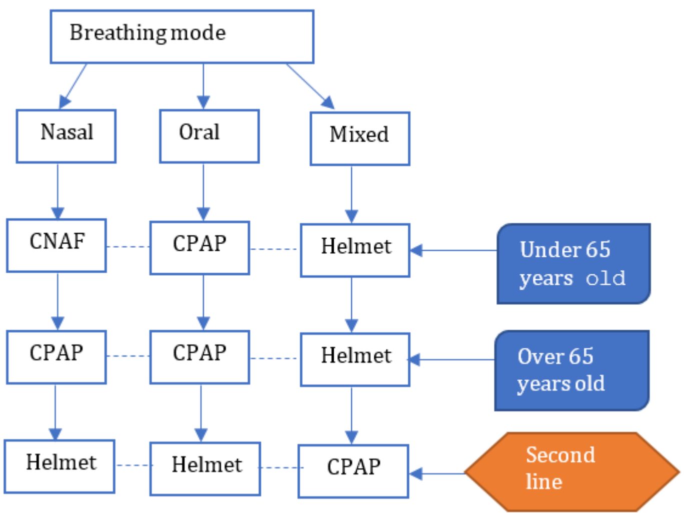

Figure 5.

2, nasal breathing therefore allows us in patients under 65 years of age who still retain good muscle tone to keep the mouth closed for as long as possible, use the high-flow nasal cannula, and take greater advantage of its properties, such as: the lowest dilution of oxygen administered with ambient air, reduction of dead space (and CO_2 sweep), generation of positive airway pressure (CPAP). Increase in circulating volume and decrease in respiratory work.41 unlike patients over 65 years of age in whom physiological sarcopenia prevents this, therefore oxygenation devices that can administer oxygenation through the nose and mouth are suggested for patients with mixed and mouth breathing such as CPAP and Helmet.

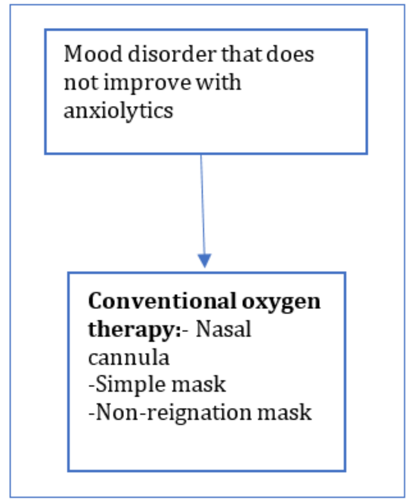

Figure 6.

Mood disorder is a topic that is little talked about, due to the few clinical and treatment studies carried out on it during the current pandemic, but it has been observed that mood disorders in hospitalized patients are important factors that determine the evolution patient clinic of the patient with this infection [81]; It is absolutely important that the patient is sufficiently cooperative to interact effectively with the oxygenation device, in such a way that he tolerates it for long hours, and his breathing is as adequate as possible, resulting in correct oxygen delivery to the units. functions of the lung, some of the aspects that must be taken into account in this recommendation are the adequate positioning of the device, the adequate time of use, the non-interruption of the use of the device or its manipulation by the patient, who is usually found with high levels of anxiety and anguish, which should be treated with antipsychotics, anxiolytics and/or antidepressants if applicable [83-84].

It is then recommended that patients in whom the symptoms of anxiety, psychosis, agitation, etc., which make the use of high-flow oxygenation devices impossible, should begin treatment with traditional oxygenation if their clinical condition allows it.

Discussion

Currently there are no consensus or well-established protocols on the formal indications in the choice of candidate patients for the use of high-flow oxygen source oxygenation devices, the data related to their use are increasingly encouraging in terms of its benefits due to its versatility, availability and reduction in health expenses and consequences for patients and their family environment [31,32].

González-Castro, et al, in their letter to the editor, state that High Flow Oxygen Therapy (HFO) would be the modality of first choice. Non-Invasive Ventilation (NIV) is the second option in cases of insufficient response and without immediate criteria for intubation [95].

Well-supported recommendations from the WHO, which places OAF and NIV at the same level since both therapies could be used only in well-selected patients with hypoxemic respiratory failure. It is also stated that when standard oxygenation therapy was compared, OAF reduces the need for intubation, data well described in the European/American clinical practice guideline. This guideline also explains that according to the FLORALI-REVA study, the end point primary intubation was not significantly different. It is these reasons and the rationality of resources that invite health professionals to try to avoid intubations, and perhaps consider NIV and OAF as the first choice without strong recommendations between one and the other, according to WHO recommendations [95].

Likewise, Ferreiro et al. They describe in their systematic review and meta-analysis when standard oxygen therapy was compared vs. the non-invasive oxygenation strategy, the latter being associated with a lower risk of death, similar data obtained in the FLORALI-REVA study, which showed in a post hoc subgroup (patients with a PaO2/FiO2<200) that the intubation rate was lower in patients treated with HFNO compared to those treated with NIV or standard oxygen96-97-98; We believe that the first reported experiences with high flow oxygenation in patients with ARDS due to COVID 19, escalated to NIV and invasive ventilation PAFI rates that could keep the patients stable, could be said "rushed", increasing the failure rates related to complications. Typical of invasive ventilation as shown (Colaian - ni-Alfonso & Castro-Sayat, 2020) where they studied 17 subjects to whom they applied TNAF as a first-line treatment. Of the 17 subjects with TNAF, 7 (41%) failed treatment. Failure was considered the need to escalate treatment to non-invasive mechanical ventilation (NIMV), where 2 patients finally required IOT. The P/F ratio in the success group was 209 (179-376) vs 142 (130-188) in the failure group (p= 0.03) [96].

High-flow oxygen therapy is used in patients with COVID-19 who have developed mild hypoxemic respiratory failure and there is greater compromise in PaO_2/FiO_2, and this, within non-invasive ventilation procedures, however, this procedure does not provide positive effect for the patient, the patient moves on to the stage of assisted mechanical ventilation, through orotracheal intubation.

When the use of CPAP, facial mask, CAF, and conventional oxygen therapy was compared; In the previous H1N1 pandemic, better tolerance was found; less aerosolization with NIV, with 0% failure in people who had pure hypoxemia; In a series of 337 patients in Argentina, greater survival was reported for the NIV user group (24% versus 13%; P=0.02), with a RR of survival of 1.62 (95% CI 1.0 to 2,6) [33]. Similar data were obtained (Maclans & Cols) in Spain, during the H1N1 pandemic, comparing 489 ventilated and 177 on NIV; For a total of 685 cases, the latter showed effectiveness in 40.7% of the subjects, those who were successful with NIV required less ventilation time, and a shorter ICU and hospital stay, compared to those who failed. Furthermore, mortality was similar when compared with early intubation (26.5 versus 24.2%) [15].

In a retrospective study on (NIV) in patients with moderate or severe ARF due to COVID-19, carried out by Mukhtar et al., it was identified that NIV was initiated following "predefined" criteria and an algorithm was used to detect failure of NIV and initiate invasive mechanical ventilation (IMV) if necessary. This included 55 patients, of which 71% (n = 39) presented signs of ARF that required mechanical ventilation. Of these 39 patients, NIV was successful in 77% of the cases (n = 30) and not were intubated, while 23% (n = 9) were intubated with an in-hospital mortality rate of 10% and 78% respectively. Based on these results, the authors support that NIV is feasible with a high success rate and helps prevent IMV among patients with severe COVID-19 [38].

Conclusion

High-flow oxygen source ventilation is an economical strategy, easy to use, and widely available worldwide, it can be used in high and medium complexity centers, as well as in general hospitalization wards and special care units; It is presented as an alternative strategy to treat patients with moderate to severe hypoxemia with COVID-19, with a reduction in care costs, compared to patients treated in the intensive care unit, in whom a significant decrease in sequelae related to the treatment of critically ill patients; Taking into account some physiological conditions, the appropriate high-flow oxygenation device can be chosen that best benefits the patient. However, it also opens up the possibility of carrying out complementary studies where the effectiveness of this proposed treatment algorithm is evaluated. .

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