

OXYGEN TENTS AS SUPPORT THERAPY TO FACING COVID-19: A PATENT**LANDSCAPE****Tendas de oxigênio como terapia de suporte ao enfrentamento da covid-19: um cenário de patentes**

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Abstract

Over the past 20 years, coronavirus outbreaks have been responsible for a large number of infected people and deaths. Currently, the pandemic caused by SARS-CoV-2, COVID-19 is still increasing that number daily. Infected people have mild to severe symptoms such as difficulty and respiratory failure and shortness of breath. In the most severe cases, oxygen therapy and mechanical ventilation are often used. As supportive therapy, oxygen tents can act as a strong ally in this fight. Therefore, the present review describes a worldwide panorama of patented oxygen tents that can act as supportive therapy to combat COVID-19. Of the selected patents, countries such as China, the United States, Japan, the Republic of Korea and the United Kingdom lead the ranking. The tents found have metal or plastic structures, flexible and transparent plastic material, portability, atmospheric pressure, oxygen concentration and temperature controlled. Therefore, based on the characteristics of the oxygen tents, this device we can used as an alternative to provide effective oxygen therapy to patients infected with SARS-CoV-2 who need therapeutic support.

Keywords: Coronavirus, COVID-19, Oxygen tent, Oxygen therapy, SARS-CoV-2, Pandemic.

Resumo

Nos últimos 20 anos, os surtos de coronavírus foram responsáveis por um grande número de pessoas infectadas e mortes. Atualmente, a pandemia causada pelo SARS-CoV-2, causador da COVID-19, ainda está aumentando esse número diariamente. As pessoas infectadas apresentam sintomas leves a graves, como dificuldade e insuficiência respiratória e falta de ar. Nos casos mais graves, a oxigeno terapia e a ventilação mecânica são frequentemente usadas. Como terapia de suporte, as tendas de oxigênio podem atuar como uma forte aliada nessa luta. Portanto, a presente revisão descreve um panorama mundial de tendas de oxigênio patenteadas que podem atuar como terapia de suporte no combate a COVID-19. Das patentes selecionadas, países como China, Estados Unidos, Japão, República da Coréia e Reino Unido lideram o ranking. As barracas encontradas possuem estruturas metálicas ou plásticas, material plástico flexível e transparente, portabilidade, pressão atmosférica, concentração de oxigênio e temperatura controlada. Portanto, com base nas características das tendas de oxigênio, este dispositivo pode ser usado como uma alternativa para fornecer oxigeno terapia eficaz para pacientes infectados com SARS-CoV-2 que precisam de suporte terapêutico.

Palavras-chave: Coronavírus, COVID-19, Tenda de oxigênio, Oxigênio terapia, SARS-CoV-2, Pandemia.

1. INTRODUCTION

Coronavirus disease appeared in December 2019 in the Hubei, China, and became globally distributed, on an exponential outbreak (Sorbello et al., 2020) with a high human-to-human transmission rate (Zhang, Huang, Zheng & Dai, 2020). The disease develops pulmonary symptoms in the patients, and due to this the virus was named as severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2) (Sorbello et al., 2020). Similar to this, in 2003 emerged, also in China, the highly pathogenic severe acute respiratory syndrome-related CoV (SARS-CoV) and almost a decade later, in 2012, the Middle East respiratory syndrome-related CoV (MERS-CoV) appeared in Saudi Arabia (Alsaadi & Jones, 2019).

The coronaviruses are considered as a zoonotic disease (Di Gennaro et al., 2020) and replicate through proteases (Nascimento Júnior et al., 2020), thus they can be transmitted across species barriers. Moreover, there are other ways to transmit the virus, such as human-to-human contact, mainly between family members (Guo et al., 2020), aerosol transmission, touch, and respiratory droplets during coughing or sneezing (Yang et al., 2020). The “hidden transmission” can also happen through asymptomatic infected people or carriers who are infected unknowing (Chan et al., 2020).

Besides, the coronaviruses have peculiarities and affect humans in different ways (Nascimento Júnior et al., 2020), most of the symptomatic patients exhibit clinical manifestations such as fever, fatigue, dry cough, malaise, shortness of breath, and acute respiratory distress syndrome (Chen et al., 2020; De Wilde, Snijder, Kikkert, & Hemert, 2018). The coronaviruses initially provoke lower respiratory tract disease and can lead to progressive lethal atypical pneumonia, inducing a bilateral lung infiltration in severe cases (De Wilde, Snijder, Kikkert, & Hemert, 2018; Gralinski & Menachery, 2020). Despite the risk of death that the disease can cause, there have not effective therapies for the treatment of patients (Nascimento Júnior et al., 2020).

Although there is no standard treatment for all patients with COVID-19 who that develops the most severe form, the most usual approaches trying save the patients can be highlighted in three fields: A) Consider aspects similar to a thrombotic disease and treat it as such using anticoagulants; B) The use of dexamethasone (or similar corticoids) seeking to control inflammatory aspects that often resemble sepsis and mitigate the cytokine storm syndromes; C) Optimize oxygen support through approaches with the use of high-flow nasal oxygen therapy, non-invasive ventilation or using oxygen tents (Barnes et al., 2020; Oxford, 2020; Ñamendys-Silva, 2020). However, even with all therapeutic support seeking to mitigate the most severe effects of COVID-19, the severe pneumonia called of acute respiratory distress syndrome (ARDS), improving oxygen availability is pivotal.

Moreover, due to the lack of effective therapy and aggressive pulmonary involvement, the COVID's treatment is mostly based on supplemental oxygen therapy (Sorbello et al., 2020), to achieve the oxygenation adequated with the lowest fraction delivered oxygen (Walsh & Smallwood, 2017). The methods to deliver oxygen can be classified into non-invasive, semi-invasive, and invasive. Moreover, they should be safe, simple, effective, and inexpensive (WHO, 2016). However, all oxygen administration methods carry risk as aerosolization and disease transmission (Sorbello et al., 2020).

The oxygen tent is a non-invasive oxygen delivery method with a plastic enclosure that surrounds the whole patients' body to maintain a continuous flow of humidified oxygen. The oxygen concentrations should be maintained between 22 to 80%, thus the flow used in the tent should reach a minimum of 15–30 L/min (Walsh & Smallwood, 2017). Therefore, the oxygenation's support effects comprise an increase in oxygenation and alveolar ventilation and a reduction in breathing work (Frat, Joly & Thille, 2019).

Recently, research report brought the global oxygen tent market to 2020-2026 due COVID-19 outbreak who showed statistics for 2020 and forecasts for next few years, thus it was demonstrating that is a booming market, that companies were not prepared for the wide demand that occurred during the current pandemic; innovations, cost-benefit and availability are unquestionable points (MarketWatch, 2020). This review aims to evaluate patents that treat oxygen tents as supportive treatment for oxygen therapy and to provide an overview of a possible ally in the fight against the new coronavirus; bringing hope to patients and health professionals in the fight against SARS-CoV-2.

2. METHODS

In this present patent review, the European Patent Office (EPO) database was searched using the code A61G 10/04 (Oxygen tents) in field International Patent Classification (IPC). A total of 415 patents were identified for preliminary assessment from the database, of which 25 patents were excluded as they were duplicates, 167 because the text was unavailable, 93 for being outside the focus (vaccine) of our review after reading the title and abstract, and a further 19 patents were excluded after reading the full patent for being outside the focus of the review. This resulted in 111 patents being selected for our critical analysis according to the objective of the study. Figure 1 illustrates the systematic guidelines, based on PRISMA methodology, used for the patent search and screening in this review.

Cluster analyzes were applied to determine the basis of intellect in the field of coronavirus vaccines through patents obtained through the Web of Science and use of the VOSviewer software. The clusters obtained by VOSviewer define terms in a group based on their similarity (Chen, Wu,

Xie & Li 2016). Thus, a search was carried out on the Derwent Innovations Index with IPC A61G 10/04. A total of 203 patents were obtained. During the process of obtaining the clusters map, terms whose frequency was greater than 10 were selected. Thus, of 3,578 terms, 65 meet the threshold. For each of the 65 terms, a relevance score was calculated. Resulting in the 39 terms. Some terms have been excluded because they do not meet the search criteria or are not relevant. Finally, a co-occurrence map composed of 29 terms divided into four clusters was obtained.

Figure 1: Flowchart of patent search and screening.

3. RESULTS AND DISCUSSION

3.1. Clustering

The great occurrence of keywords present in a patent represent its main content, in the same way that they reflect themes focused on a special field to a certain extent. The five terms with a high frequency of co-occurrence found in obtaining the cluster map are pressure (63), patient (61),

treatment (51), structure (37), door (36). In addition to demonstrating that to high individual frequency and co-occurrence, demonstrate to attract more attention and have a close relationship with other search terms.

A graph showing the co-occurrence relationship between terms was obtained (Figure 2). Terms derived from the Derwent Innovations Index have been separated into four clusters that display different colors. When the terms are grouped in the same cluster, they tend to reflect similar field. In addition, each cluster has a number of different terms, thus indicating that the search fields in oxygen tents as supportive therapy.

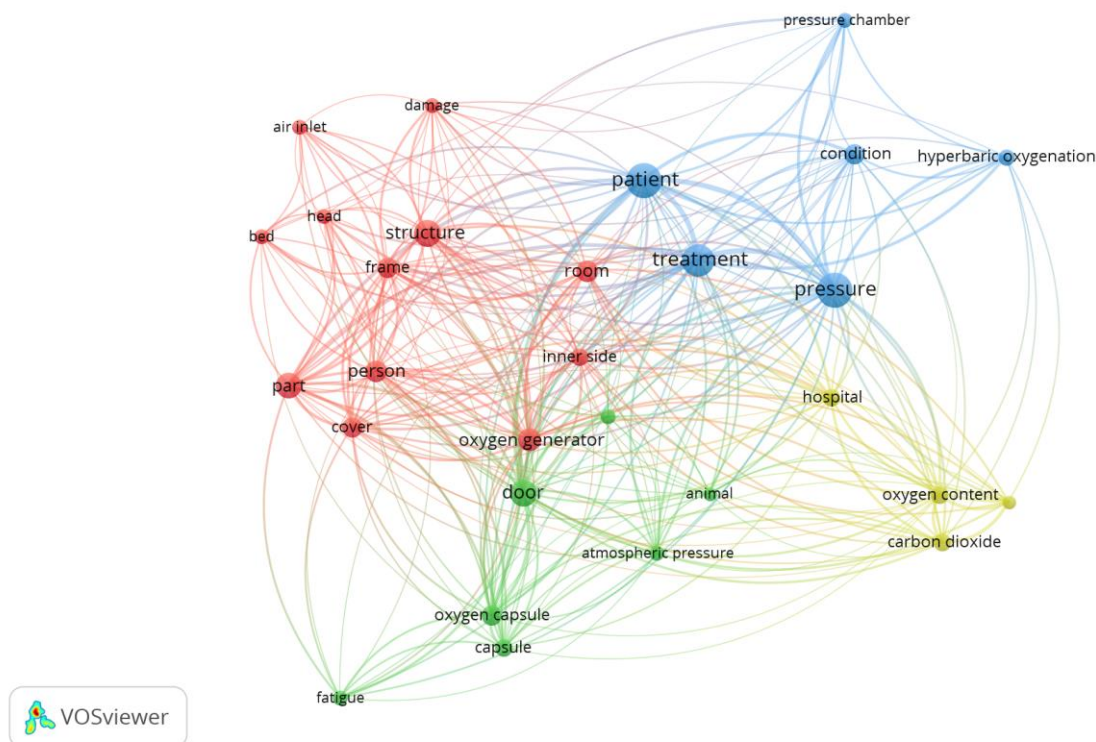


Figure 2: Co-occurrence map of clusters regarding oxygen tents. Made by the author in software VOSviewer.

Detailed information for each cluster are present in Table 1. The cluster 1 has a higher number of terms, making this a most centralized field. Doing so, that the terms present in this cluster have more attention in the field about oxygen tents. The cluster map based on co-occurrence expresses the frequency of terms according to the size of the node. Whereas, the thickness of the line, represents the proximity of the connection between the keywords (Chen et al., 2016). Therefore, according the Figure 2, pressure, treatment, structure, door, pressure chamber, and oxygen capsule has the highest frequency of the keywords. The connecting lines between the terms have a strong connection attributed to the thickness of the line. Similarly, the terms, pressure

chamber, atmospheric pressure, hyperbaric oxygenation, oxygen content, capsule have a connection, but are weak.

Table 1: Composition of clusters regarding oxygen tents

Cluster	Number of items	Items
1	12	Air inlet; Bed; Cover; Damage; Frame; Head; Inner Side; Oxygen generator; Part; Person; Room; Structure
2	7	Animal; Atmospheric pressure; Capsule; Door; Fatigue; Human body; Oxygen capsule
3	6	Condition; Hyperbaric oxygenation; Patient; Pressure chamber; Treatment
4	4	Carbon dioxide; Dust; Hospital; Oxygen content

3.2. Patent search and screening

Infection induced by SARS-CoV-2 has acute respiratory failure as the main clinical manifestation. Thus, the use of effective respiratory support therapies is essential in the treatment of those infected with virus which develop ARDS (He et al., 2020). Statistical data demonstrate that about 80% of patients have a mild or asymptomatic clinical picture, while 15% have a severe condition, requiring oxygen and the rest are in critical condition and use ventilation (Rokni, Ghasemi & Tavakoli, 2020). Thus, about 20% of those infected need supportive care, and oxygen therapy represents the main therapeutic intervention (Nicola et al., 2020).

Tissue hypoxia leads to further inflammation from the attraction of neutrophils and others inflammatory cells (Zanboni et al., 1993). The vicious cycle where inflammation is tied to hypoxia can only be broken by an increase in the oxygen available to organs and tissues (Abbot et al., 1994; Eltzsching & Carmeliet, 2011). Intubation and positive pressure ventilation causes micro-trauma to already damaged lung tissue and extra corporeal membrane oxygenation is very complex, invasive and does not treat the pulmonary pathology caused by COVID-19 (James, 2020).

In this context, COVID-19 is responsible for several symptoms ranging from flu complaints to life-threatening cardiac and pulmonary complications. Especially in individuals in the risk group, such as elderly people and those with an underlying disease who need mechanical ventilation and the mortality rate grows exponentially. Thus, an alternative that has been used is hyperbaric oxygen therapy (HBO), which avoids the use of mechanical ventilation. Studies have already shown that the use of this therapy, in addition to increasing oxygen saturation levels, decreases inflammation markers in those infected (Thibodeaux, Speyrer, Raza, Yaakov & Serena, 2020).

Based on the year of publication of the patents, the first was filed in 1922, followed by other deposits over the years until 2000 with 35 patents. From this period, the number of patents related

to oxygen tents and oxygen therapy increased, totaling 76 applications. Such fact may be associated with the use of oxygen therapy for the treatment and support of various clinical conditions, such as fatigue, diabetes, wound treatment, supportive therapy (Chan, Lee & Kang, 2010; Drugs, 2020; Maalej et al., 2020; Mayoraless-Alises, Carratalá & Díaz-Lobato, 2019).

In this sense, according to Figure 3, countries such as the Republic of Korea, the United States, Japan, the United Kingdom and China are the largest patent applicants for oxygen tents and hyperbaric oxygen therapy. These present a grand total of 94 of the 111 selected patents. This fact is associated with economic and social characteristics, which characterize them as countries that register more patents. In addition, due to the high rate of pollution in cities, people develop respiratory problems and require supportive oxygen therapy (Boogaard, Walker & Cohen, 2019; Guo, Chang, Wu & Li, 2019; Mokoena, Ethan, Yu Shale & Liu, 2019). As well, in the case of individuals infected with coronavirus, they also need this type of treatment, seeking to relieve respiratory symptoms (Alhazzani et al., 2020; Li, Lu & Zhang, 2020).

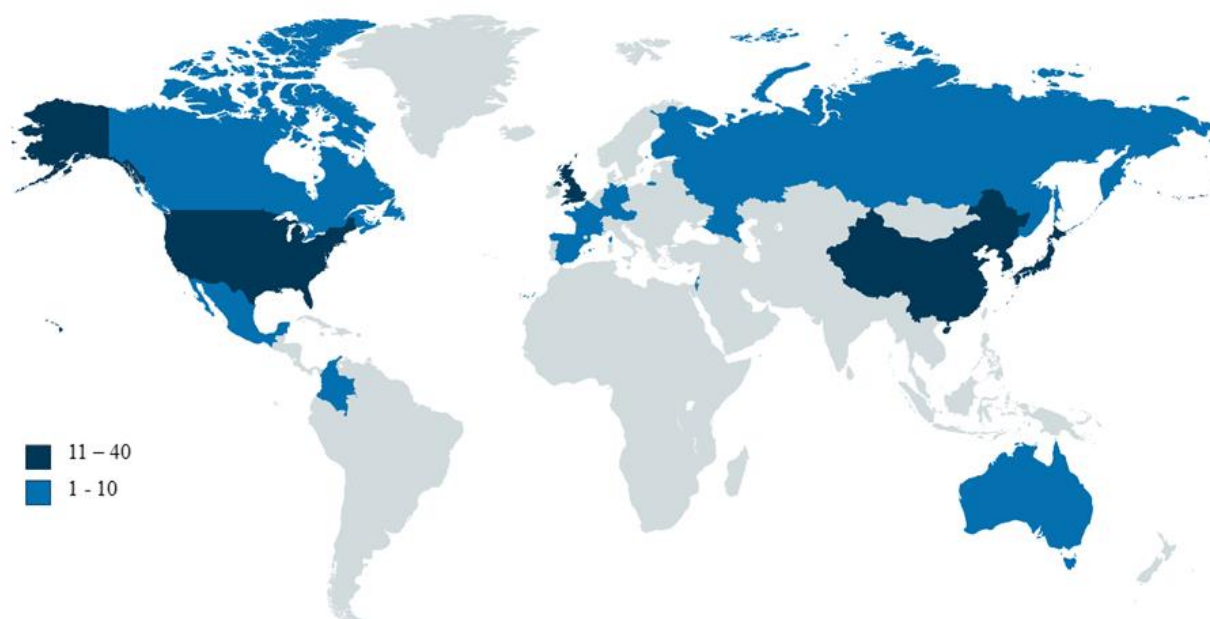


Figure 3: Number of patent filings by countries.

In addition, the selected patents were also evaluated according to the type of depositor. Since, documents for protection of invention can be deposited by several entities such as, industry, universities, hospitals, and freelance researchers (Donald, Kabir & Donald, 2018). As shown in Figure 4, the industry sector and independent researchers represented 48 processes each. As expected, industries are always creating new and updated alternatives to problems existing on the world market. In the case of oxygen tents, they seek to improve the practicality of assembly (Kotliar, 2003), raw material (Weibin, 2016; Zhang, 2019), product size (Lee, 2019) and methods of monitoring patients (Park, 2013; Yang, 2017).

In the case of independent inventors, the number of patents found can be attributed to the low cost of manufacturing and raw materials for the tents. Finally, universities and partnerships between industries and inventors represent a quantity in the request for protection of their inventions, corresponding to five and seven patents, respectively.

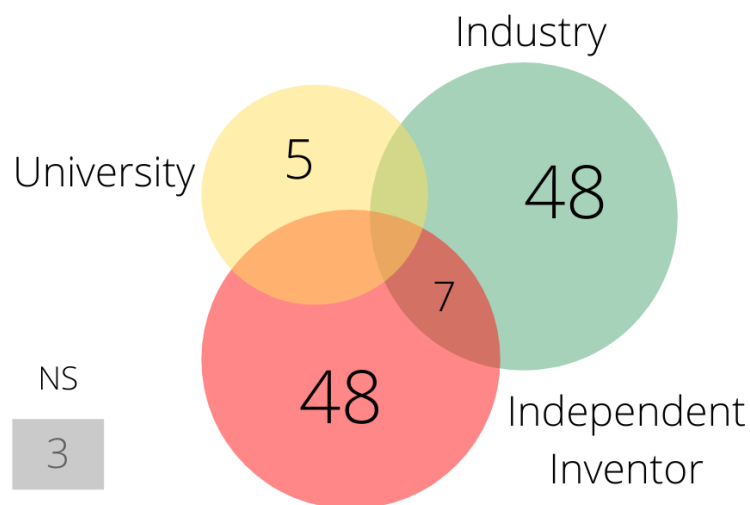


Figure 4: Final selection of patents: type of applicant.

3.3. Technological scenario of patents

Several devices and structures can be widely used to provide a closed environment in order to maintain an atmosphere containing a specific gas for a patient. As far as this is concerned, the most commonly used method is oxygen tents, placed around the patient's head or entire body providing an atmospheric rich gas (Heath, 1974). The tents can be used in medical treatments that require the administration of air enriched with some type of gas, especially oxygen (Air reduction, 1954).

In recent decades, oxygen therapy has often been used for several purposes, such as treatment of metabolic syndrome, recovery from physical and mental fatigue (Yoshida & Nakamura, 2010). In addition to assisting in air purification and improving respiratory health problems (Wennerstrom, 2019). As well, they help in anti-aging, in improving immunity, in preventing arteriosclerosis (Yang, 2017). Studies have already shown that the survival rate of patients with respiratory failure improves with the use of oxygen therapy. The physiological effect is based on the ability of the absorbed oxygen to be able to reduce the progression of pulmonary hypertension (Lee, 2019). Thus, this device and its method of use are of paramount importance for patients infected with SARS-CoV-2 and who need frequent therapeutic support of oxygen.

Another alternative to using oxygen tents is the use of high-flow nasal cannula may reduce the need for invasive ventilation and escalation of therapy compared with conventional oxygen therapy in COVID-19 patients with acute hypoxemic respiratory failure, this benefit must be

balanced against the unknown risk of airborne transmission (Agarwal et al., 2020). One of the advantages of using oxygen tents is the non-invasiveness of the method, avoiding laryngeal edema (McGrath, Wallace & Goswamy, 2020) and bacterial pneumonia which is very common in the intubation process (Póvoa, Chianca & Iorio, 2020).

Oxygen tents have several characteristics, ranging from their types of structures and sizes, types of materials, pressure concentrations and portability (Table 2). With a focus on its structure, the tents can be designed with the use of metals or rigid plastics, on which a flexible cover or canopy is arranged. Plastic structures are strongly recommended, as they provide easy sterilization and cleaning with germicidal agents (Dixon, 1972), they are also used in intubation of patients with COVID-19 and have the advantage over acrylic structures (Canelli, Connor, Gonzalez, Nozari & Ortega, 2020) due to the easier handling of the patient more comfortably (Matava, Yu & Denning, 2020). While, metal alloys tend to undergo a process of corrosion and rust due to the moisture present in the atmosphere of the tents (Deaton, 1974). However, there are inflatable structures that do not require the use of support materials, in which internal and external sealing strips containing adhesives are used to seal the environment and keep the atmosphere constant and stable (Wang, 2020).

Based on size, they vary according to need and space available in the treatment environment. However, they improve patient comfort, as the use of an oxygen absorption mask is unnecessary. Thus, this type of model can be applied to comatose patients, the elderly, babies, young children and patients who have maxillofacial injuries (Zhiming, Liansheng & Cai, 1996). They can be found in different sizes, ideas for patient beds in hospitals, double beds, in the case of home use, or coupled only to cover the head (Dixon, 1972; Trammell, 2005). Based on their portability, they can be easily disassembled and transported to another environment when needed (Davis, 1922).

In the case of materials used to provide an environment containing an appropriate gas, transparent plastic materials are the most used because they allow observation of the patient by doctors (Abdalla, 1936). As described in Table 2, they must be flexible, light (Deaton, 1974), present around an inch thick (Wren, 2018), and impervious to any contaminants (Bongiovanni et al., 1999). In addition, they have equipment, such as a zipper or magnetic tape, that allow the entry and exit of health professionals to monitor the patient's clinical condition (Kotliar, 2003).

Finally, the atmospheric pressure in the tents seeks to be above 1 atm, around 1.2-1.4 atm, as it facilitates the dissolution of oxygen in the patient through tissue fluids as the pressure increases (Lin & Lin, 2019). As well, a low oxygen concentration (<50%), used mainly in the treatment of respiratory problems (Li et al., 2016). Taken together, as information selected and explored here, they can be used to make proposals for oxygen for auxiliary supportive oxygen therapy for those infected with new coronaviruses.

Table 2: Main features of the oxygen patents of the selected patents.

Advantages	<ul style="list-style-type: none"> - Improves convenience; - Enable use while patient is seated; - Highly airtight; - High safety and anti-fog factor; - Quick temperature adjustment, oxygen pressure; - Temperature, humidity, oxygen and carbon dioxide sensors.
Structure	<ul style="list-style-type: none"> - Rectangular shape; - Format for headboard; - Semi-cylindrical structure from head to toe; - Entrance sealed with magnets, zippers, fastening straps; - Composed of metal or plastic tubes; - Accessibility for healthcare professionals.
Pressure	<ul style="list-style-type: none"> - Oxygen pressure: 1.25 atm and 1.4 atm; - Oxygen concentration: 27-30% and 36-39%.
Material	<ul style="list-style-type: none"> - Transparent, porous, thin and light flexible polymeric plastic; - Thermoplastic, rigid and gas-proof; - Impervious to any contaminants; - Easy cleaning and disinfection; - Examples: Polyester 5%, nylon, polyethylene, polypropylene, cellulose acetate; vinyl chloride, polyvinyl, acrylonitrile-butadiene-styrene; EVA resin (ethylene vinylate copolymer).
Size	<ul style="list-style-type: none"> - Adjustable size around the patient; - Dimensions for hospital beds, single and queen size; - Adaptable for newborns, children and adults.
Portability	<ul style="list-style-type: none"> - Portable and detachable.

4. CONCLUSION

Infections caused by respiratory viruses, such as COVID-19, present clinical complications that affect the respiratory system of sick individuals, especially the lungs. With regard to the current pandemic, a portion of those infected have severe symptoms, such as difficulty breathing and shortness of breath, and other respiratory failure and organ failure. Thus, this group of patients needs to receive effective oxygen therapy, while also maintaining their comfort and quality of life. In this case, the oxygen tents are great alternatives for this situation. Its characteristics enable a

hermetically sealed environment providing a suitable gas in a stable and constant manner. In addition, based on the patents found, these devices allow monitoring of temperature, oxygen, humidity and vital signs of the patient. As well as, ease of use, portability, easy cleaning, and adequate oxygen supply, flexible, light and heat resistant plastic material. Therefore, one must look for several alternatives to support patients with COVID-19, such as oxygen tents. Since mechanical ventilation is an invasive technique and tends to increase the mortality of those infected.

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