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Palliative Care in SARS-CoV-2: A Systematic Review

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Abstract

Objective: Gather information about an important aspect of SARS-CoV-2 disease, regard to palliative care.

Introduction: SARS-CoV-2 disease started by the ending of 2019 in Wuhan-China and given the lack of a specific treatment, the role of palliative care in SARS-CoV-2 infection has been drawn to the spotlight.

Method: A systematic review was carried out between June and October of 2020.

A total of 25 articles were totally reviewed.

Results: The management of symptoms, is the main objective of palliative care in SARS-CoV-2. We find ourselves with the interrogant of when to start palliative care and with what medications and measures it is preferred to do so. Discussion: As SARS-CoV-2 currently does not have a curative treatment, palliative care is the centerpiece of its management.

Conclusion: Palliative care should be considered as a protocol in any disease with no curative treatment at the moment, just like SARS-CoV-2.

Keywords: Palliative care; COVID-19; Coronavirus; SARS-CoV-2

Introduction

SARS-CoV-2 disease started by the ending of 2019 in Wuhan-China and ever since it has spread worldwide bringing severe consequences along [1]. Later on, on January 30, 2020 the World Health Organization declared the outbreak as a Public Health Emergency of International Concern [2].

SARS-CoV-2 is a Beta coronavirus enveloped and positive-sense single-stranded RNA (+ssRNA) virus, member of subfamily Coronavirinae of the Coronaviridae family (Figure 1) [2].

Transmission occurs mainly via respiratory droplets produced when an infected person coughs or sneezes. Fomites also may be a large source of transmission, as SARS-CoV-2 has been found to persist on surfaces up 9 days [2].

Risk factors

SARS-CoV-2 infection has a higher incidence in male patients between 34 and 59 years old. People with chronic comorbidities such as cardiovascular and cerebrovascular diseases and diabetes are more susceptible to this disease. Thus, the fatality rate varies worldwide, presenting a higher risk of death among black and Asian race, older people, male, multimorbid, and from areas of higher deprivation [2,3].

Pathogenesis

The host immune system response to the infection is critical to inhibit viral replication and dissemination of this disease. However, excessive immune responses and lytic effects on the host cells could also unchain severe symptoms and may complicate the outcome [2].

In the serum from patients diagnosed with SARS-CoV-2, increased levels of proinflammatory cytokines have been found, such as: IL-1, IL6, IL12, IFNγ, IFN-γ-induced protein 10 (IP10). Additionally, patients in the Intensive Care Unit (ICU) have a significantly higher level of GSCF, IP10, MCP1 (which are associated with pulmonary inflammation and severe lung damage), and TNF-α than those non-ICU patients, suggesting that a cytokine storm might be an underlying cause of disease severity. Given this, cytokines may be functional as severity markers and useful for ethical decisions towards palliative care [2].

Clinical manifestations

The most common symptoms of SARS-CoV-2 infection include fever, dry cough, dyspnea, chest pain, fatigue and myalgia. Less common symptoms include headache, loss of taste and smell,

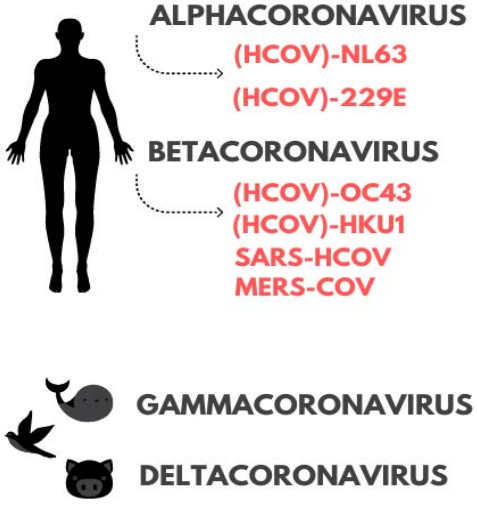

Figure 1: Coronaviruses families and species susceptible.

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dizziness, abdominal pain, diarrhea, nausea, and vomiting [2].

However, symptoms can escalate rapidly among patients with severe covid-19, unleashing several systemic complications, such as Acute Respiratory Distress Syndrome (ARDS), hypoxaemia, arrythmia, shock, acute cardiac injury, acute kidney injury, among others [2,3].

Treatment

Currently, curative treatment for this particular disease is still under investigation. Until there is a fist-hand medication, different strategies have been established for its management, such as: prevention of co-infections with antivirals and antibiotics, support measures with oxygen and mechanical ventilation, especially in patients with intractable hypoxemia. Thus, given the lack of a specific treatment, the role of palliative care in SARS-CoV-2 infection has been drawn to the spotlight [4,5].

Palliative care is often misunderstood and therefore underestimated by physicians, however, it is focused on the relief of symptoms and suffering by comprehensive and compassionate care, through de journey of life-threatening illnesses [6].

In SARS-CoV-2 patients, palliative care are needed, especially for the relief of refractory symptoms, and given their rapid progression since onset to hospitalization, an anticipatory approach to symptom management is key [3,7].

Among decedents and survivors with SARS-CoV-2 infection, breathlessness, cough and fatigue are the most common and disturbing symptoms, hence, they are among the main concerns of palliative treatments [3].

The primary aim of this study is to gather information about an important aspect of SARS-CoV-2 disease, that most of the current guidelines have overlooked or have not deepened into; palliative care. Given this, it is intended to compile the current published material and discuss the accurate management of COVID-19 symptoms, in order to relieve and improve the patients' outcome.

Methods

A systematic review was carried out between June and October of 2020. Initially, a detailed search of original articles was performed among various scientific databases, such as: PubMed, Cochrane, Web of Science and Up To Date, in which the following keywords were established: "Palliative Care", "COVID- 19" and "Coronavirus" in order to obtain an overview of the research topic.

After reading the title and abstract, a total of 36 articles were pre-selected to apply the inclusion and exclusion criteria:

Inclusion criteria:

- Review articles.
- Articles written in English or Spanish.
- Articles from indexed scientific journals.
- Articles related to the topic of palliative care in COVID-19.

Exclusion criteria:

- Articles other than reviews.
- Articles not written in English or Spanish.
- Articles from non-indexed scientific journals.
- Articles unrelated to the topic of palliative care in COVID-19.

Procedure

After a full text review of those 36 articles, gathered in the primary search, 16 studies were discarded, due to the lack of one or more inclusion criteria. On the other hand, those studies that met the inclusion criteria and without any exclusion, were used, leaving a total of 20 articles included.

Afterwards, given the constant research on the subject of this protocol, a second research was considered pertinent, to include the most recent articles on the topic and complement the information already obtained.

Within this second research, seven articles were obtained, in which the same inclusion/exclusion criteria were applied, including five of these new articles. Therefore, a total of 25 articles were totally reviewed (Figure 2).

Results

The management of symptoms, mainly acute respiratory failure associated with pneumonia, fever, dyspnea, pain, anxiety and delirium, is the main objective of palliative care in SARS-CoV-2. Along with this and given the recency of the subject, we find ourselves with the interrogant of when to start palliative care and with what medications and measures it is preferred to do so.

Fusi-Schmidhauser et al. catalog the severity of the patients based on the National Early Warning Score 2 (NEWS2), according to the respiratory rate and oxygen saturation, which allows to categorize patients as stable or unstable, so the appropriate palliative treatment is decided. In terms of dyspnea, if the patient remain stable, oral opioid treatment (2-5mg) is suggested, while if the patient is unstable,

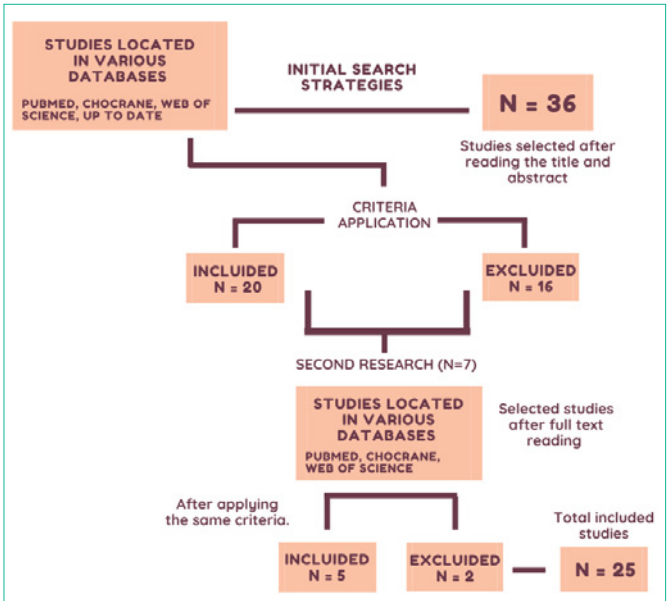

Figure 2: Systematic procedure followed in this review.

intravenous is preferred (5mg). Regard to anxiety, in stable patients, treatment with lorazepam is suggested (1-2.5 mg), while diazepam is preferred for unstable patients (2.5-5 mg IV). Fever and pain are managed with acetaminophen in stable patients and with intravenous diclofenac in unstable or complicated patients [8]. In summary, this study establishes the importance of palliative care in patients with SARS-CoV-2, regardless of the severity of the symptoms and guides us to apply them as required.

Aiming to find the most accurate treatment, Mottiar et al. carried out a study that focused on the symptoms that cause suffering and anguish on patients with positive COVID-19 test. Dyspnea, is indeed the first one on the list, usually treated with supplemental oxygen (6L per min), and if necessary accompanied with low-dose opioids. Followed by pain and cough, also managed with opioids and positioning measures for secretion management, along with glycopyrrolate 0.4mg sc/iv x 4 hours. On the other hand, restiveness, agitation and anxiety also represent a major cause of anguish, for which, the use of haloperidol, levomepromazine and benzodiazepines is recommended [9].

Another study conducted by the Specialized Services in Palliative Care of Waikato, New Zealand, proposes a similar approach, managing dyspnea with opioids, such as oxycodone and morphine, agitation and delirium with haloperidol and levomepromazine and adds hyoscine butylbromide to the secretion management scheme [10]. Additionally, focused on the breathlessness and drowsiness, one hundred and one patients with confirmed COVID-19 were reviewed in a study carried out in London, by Lovell et al. where palliative treatment with benzodiazepines and opioids was administered, showing improvement [10,11].

Given the increased necessity of palliative care in patients on the ICU during the COVID-19 pandemic, the UW Medicine program was created, with a focus on formulating a strategy to provide quality service in an ethical manner. The most affected areas by the pandemic were classified and the role of the palliative care team was detailed, taking into account the current capacity, contingency capacity and capacity crisis. Different strategies were proposed, one for the ER, one for intensive care unit and one for acute patient care, and it was concluded that the capacity crisis was the most important to address and in which care should be prioritized, followed by contingency capacity and finally the conventional capacity, as expected. Finally, it was demonstrated that during the COVID-19 pandemic it is essential to develop strategies to provide palliative care and a well-developed palliative care program that improves the quality of medical attention [12]. On the other hand, according to PRISMA guidelines, the medical team needs to be flexible and quickly redistribute the resources to the changing needs. The use of protocols for the control of symptoms and the training of non-specialist doctors is recommended to be able to attend a larger number of patients [13].

Regarding palliative treatment in patients who do not require hospitalization, it is well known that health systems have collapsed around the world due the pandemic, generating family and economic losses and increasing the number of deaths [14]. According to Borasio et al. the primary goal of advanced care in the context of Covid-19 is to avoid unwanted hospitalization and intensive care treatment, this can be achieved by doing an objective triage by a palliative expert, and only allowing patients at great risk to be hospitalized [15]. Just as Brian Nyatanga highlights in the recent review "Covid-19 Pandemic: Changing the way we live and die" mortality rate of patients that enter the intensive care unit in England, amounts to 50%, affecting hundreds of patients and families.1 Added to this, Bowers et al. explains how the covid-19 pandemic has changed the mode of operation of palliative care, preferring in many cases management from home given the risk of spreading the virus [16]. Ever since, many authors have addressed this topic. Cochrane made the first systematic review of the virtual interventions of chronic pain. He identified small to moderate reductions in pain, disability and distress in the intervention groups.

Given de circumstances, this is making a better option to manage chronic pain remotely [17]. Also, Arjun Gurmeet et al. established that is necessary to avoid hospital visits of patients that may not need to go. He also suggested that virtual medical attention can reduce risk of complications and improve how palliative treatment is executed [18].

Hence, Amit et al. proposed the possibility of offering palliative care kits with opioids, haloperidol, scopolamine, acetaminophen and midazolam during the pandemic. With the intention of carrying out home management by trained health personnel [19].

Let's not forget that mortality rate of COVID-19 is high, especially in patients with acute respiratory syndrome (SARS-CoV-2) that require mechanical ventilation. Therefore, early palliative treatment from home, allow us to prevent and anticipate possible complications. Medication for the most common symptoms at home is slightly different, adapted for an oral administration and lower doses. Fever is managed with acetaminophen and physical methods, as usual. Respiratory distress, cough and pain requires supplemental oxygen, if available, along with morphine 2% drops. Midazolam and Lorazepam are recommended for anxiety and haloperidol for delirium. Finally for nausea, metoclopramide is suggested, along with regular hygiene and oral hydration [20].

With that being said, according to Natalie Pattinson, in order to improve the outcome of patients in palliative treatment, either in hospital or at home, four key aspects need to be addressed: Stuff, referring to all the equipment needed to take care of the patient. Staff, as for, the ones who have been educated and have the expertise regarding palliative care. Space, as in the specialized areas for the palliative support. And finally, systems, meaning, the way to improve the assessment and attention [21].

The emotional aspects that the current situation worldwide has generated, we see panic, anxiety and uncertainty among patients and their families. Therefore it's understandable the stress caused by being diagnosed or being close to someone diagnosed with COVID-19. Emotional support from the family and health personnel is essential, as well as, constant communication between medical team and the patient and his family where the process to be followed is explained and doubts are resolved [22].

Consequently, various strategies have emerged, from telephone assistance, remote psychological support, and support groups. In March and April 2020, within a study conducted by Mills et al. the hashtags: #comcomcovid, #PallANZ and #PalliCovid were used on Twitter to create community chats between patients with a diagnosis

of COVID-19 and different health professionals, aiming to share and support patients in palliative care, and establish communication strategies with relatives of people affected by COVID-19. Given the good results and the enthusiasm of the people involved, is proposed to expand this dynamic to other social networks/platforms [23].

The pandemic has also interfered with grief context, as normal processes has been affected by the limitation of the family and the patient communication. In the new normative established in some states, hospitals and other facilities are limiting and banning the presence of visitors and relatives, which sometimes does not allow the family to say goodbye, unchanging a complicated grief.

In order to mitigate or avoid the effects of complicated grief, is necessary for the healthcare personal to prepare the patients and their families for the possible outcomes [24].

Finally, another important matter within emotional support during this pandemic, is how to address this topic with children. A study executed by Weaver et al., suggest that the communication process with children experiencing COVID-19 in the palliative care area should be based on the age and maturity of the children and needs to be in an honest and informative way.

This review also embrace that is normal to experience anxiety, stress, irritability, and sadness, among other symptoms. This feelings should not be hidden from children, on the contrary, it is important for them to be part of the situation [25].

Discussion

Due to the uncertainty of the situation, the pandemic has inspired a global fear. SARS-CoV-2 has been responsible of over a million deaths around the world, and sadly we all remain in a great danger.

According to the World Health Organization (WHO), palliative care is the discipline that aims to improve the quality of life of patients and their relatives when they face problems inherent to life-threatening diseases [26]. As SARS-CoV-2 currently does not have a curative treatment, palliative care is the centerpiece of its management. This in order to minimize symptoms and improve the quality of life of infected patients, as long as the infection ceases. Therefore, knowing the proper management and promoting treatment at home if possible, according to the studies previously exposed, has a better outcome and a lower emotional impact on patients.

As exposed, treatment can be carried out from home or in the hospital, depending on the severity of the symptoms. However, multidisciplinary treatment is of utmost importance. Palliative care not only focuses on the management of physical symptoms, such as: dyspnea, fever, pain, etc. but also emotional symptoms (anxiety, depression, etc.), and accompaniment of the patient.

On the other hand, in this particular disease, palliative approach, also focuses on the accompaniment of family members more than ever. Due to the social distance and the personal protection that is required to avoid spreading the virus, isolation, which is a major cause of stress, can come from not allowing patients to deal with the disease and the possible complications with the support of your loved ones.

Palliative treatment makes coping with this disease easier for both patients and their families, and we must not forget the importance of the support network where different strategies have been proposed, such as, virtual family meetings with the patients in order to help mitigate grief amongst family members. Finally, maintaining excellent doctor-patient and doctor-family communication, to prepare patients regarding possible scenarios, denying possible fake news and to accompany and reassure them during the process.

Conclusion

We must remove the stigma that typify palliative care as only useful and applicable to terminal patients or patients in agony.

Palliative care should be considered as a protocol in any chronic disease and any disease with no curative treatment at the moment, just like SARS-CoV-2.

It is especially important to embrace palliative care as it may be the only means to diminish the patient's and their families, afflictions. COVID-19's death toll is at a high end; physicians should be ready to ease a patient's pain and health care facilities must be prepared with the necessary equipment to help patients suffering, as per described within this review.

On the other hand, hoping that curative treatments that are under investigation will become first-hand treatment soon, palliative treatment will continue to be a key piece as a support to improve the symptoms and quality of life of patients with this disease, will continue to be a must.

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