

Adimod as a potential therapy for post-covid-19 syndrome

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ABSTRACT

This systematic review was carried out to find new evidence that demonstrates the efficacy of adimod as an immunomodulatory therapy that facilitates the overcoming and inactivation of viruses, fungi and bacteria that support our immune system. It is important to highlight that the use of adimod in post-covid syndrome is related to a faster resolution of infectious symptoms, prevention of recurrences, lower drug requirements for the underlying disease and return to daily activities in less time. In addition, it reduces the severity of symptoms by 44% and airway infections by 22%. The advantage of this is that they lead to a state of health free from respiratory infections for a longer time and positively impacting society and health systems.

Keywords: Adimod, post-covid syndrome, therapy.

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INTRODUCTION

As a result of the new reality created by the development of a new pandemic that has set records in mortality and morbidity rates, it is almost an obligation to find and develop pharmacological therapies that minimize the impact of a respiratory infection such as Covid-19 (Tan and Aboulhosn, 2020).

Post-covid syndrome is usually characterized by the sudden appearance of viral symptoms such as arthralgias, dysgeusia, anosmia, chest pain of the oppression type, headache, fever, among other symptoms, which are installed in a variety of 5 to 8 days after the Contact with another person in the same general conditions or with respiratory fluids or objects or material surfaces that present particles of respiratory aerosols of the infected person and usually lasts up to 3 months or

more. After the appearance of these symptoms (Table 1), the picture may become more intense, making respiratory distress and clinical symptoms of a more critical state appear, the product of a so-called "cytokine storm" or a systemic inflammatory response that can result in death (Mao et al., 2020).

That is why it was necessary to make a careful warning regarding this coronavirus pandemic, establishing preventive measures such as hand hygiene, covering properly when coughing or sneezing, avoiding contact with people who have flu symptoms, the use of the vaccination against influenza, improve dietary habits, and pharmacologically it is possible to use immunomodulators that strengthen our respiratory system and reject the probability of respiratory infections (Cao et al., 2020).

Table 1. Clinical symptoms of post-covid syndrome.

Clinical symptoms of post-covid 19 syndromes	Percentage of patients with post-covid syndrome presenting these clinical symptoms (%)
Malaise and fatigue	62
Fatigue	47.19
Dyspnea	19
Broncho-obstructive syndrome	25.8
Chest pain (unspecified)	13
Confusion	16.85
Tachycardia (unspecified)	13
Intolerance exercise	14.6
Insomniuous	10
Pain all over the body	10.11
Cough	9
Dyssomnia	7.86
Headache	7
Fever (unspecified)	6
Dysgeusia	6.74
Joint pain	6

MATERIALS AND METHODS

A bibliographic search was carried out that spanned from 2019 to 2021 in databases of PubMed, Elsevier, SciELO, Update, medline, national and international libraries. We use the following descriptors: immunomodulators, Adimod, post-covid syndrome drug therapy. The data obtained oscillate between 7 and 20 records after the use of the different keywords. The search for articles was carried out in Spanish and English, it was limited by year of publication and studies between 2017 and 2021 were used. The main exclusion criteria were articles that had more than 3 years of publication.

RESULTS

At present, antiviral therapy for SARS-CoV-2 infection presents very few alternatives. Some studies have shown that the implementation of remdesivir, a polymerase analog drug, reduces hospitalization time in patients with COVID-19 but without any impact on mortality (RECOVERY collaborative group, 2020).

The efficacy of hydroxychloroquine has not been demonstrated in hospitalized patients or as post-exposure prophylactic treatment. With ritonavir-boosted lopinavir, no improvement in survival has been demonstrated in critically ill patients with SARS-CoV-2 infection and post-covid syndrome hospitalized in a double-blind, randomized clinical trial, although in this case the drug was initiated in advanced stages infection (Figure 1) (Arabi et al., 2020).

Subsequently, the RECOVERY clinical trial, an open and randomized trial, did not show a reduction in mortality in hospitalized patients with COVID-19, even in patients in whom treatment is started in the first 7 days of symptoms (Prescrire, 2020). Finally, a triple-blind, randomized clinical trial of combined treatment with

lopinavir and interferon beta 1b in patients with Middle East Respiratory Syndrome (MERS) has shown a reduction in mortality in hospitalized with this condition (Tan, nd). This trial seems to suggest that lopinavir may be effective in hospitalized patients with SARS-CoV-2 infection in combination therapy with other drugs and as monotherapy in other settings, as early or prophylactic treatment. Several ongoing clinical trials are evaluating these strategies (<https://english.prescrire.org/en/81/168/58810/0/NewsDetails.aspx>).

Currently, clinical trials have shown that although Pidotimod does not have direct antibacterial and antiviral activity and, it can play an important role in the treatment of bacteria (*Dippneumonia lococcus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus*, etc.) and influenza viruses, viruses herpes simplex and sars-cov-2 for promoting the body's immune function (Zuccotti and Mameli, 2013). The conclusion of these trials is usually the same, although there were no drugs that had a rapid effect, adimod trials showed an effective unexpected therapeutic effect (Mahashur et al., 2019) (Table 2).

DISCUSSION

The treatments used so far are directed against different targets. Broadly speaking, we can say that: Antivirals act at the level of viral replication, preventing their binding to the cellular ACE2 receptor and, within the cell, preventing the use of their machinery to synthesize new viral proteins and RNAs, thus minimizing the risk of developing post-covid syndrome in patients previously infected with Sars-Cov-2 (Puggioni et al., 2019).

For their part, those treatments that include monoclonal

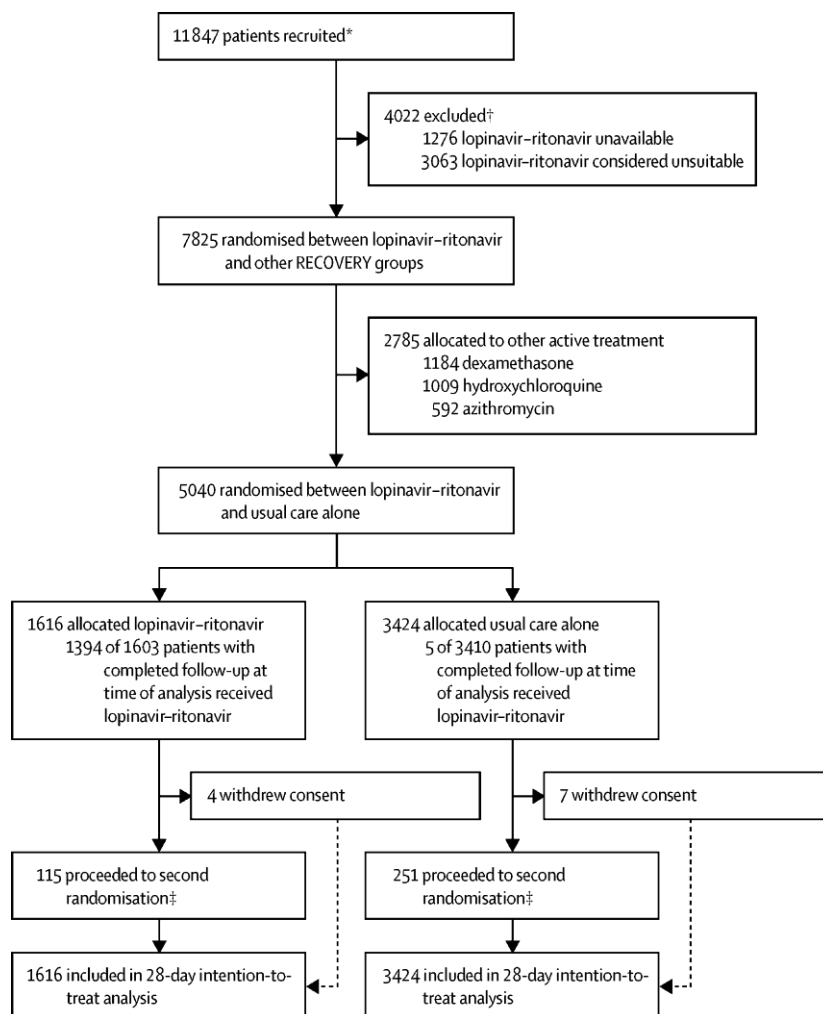


Figure 1. Medical study on the effectiveness of lopinavir-ritonavir therapy.

Table 2. Studies carried out on the use of adimond.

Reference	Population of Muestra	Results
RECOVERY collaborative group. Lopinavir-ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomized, controlled, open-label, platform trial. Lancet. 2020; 396: 1345-52.	N = 61 patients with covid-19 treated in more than 20 hospitals on three continents.	Implementing the use of Remdesivir reduces hospitalization time in patients with clinical symptoms of covid-19 or post-covid syndrome
Arabi YM, Asiri AY, Assiri AM, Balkhy HH, Al Bshabshe A, Al Jeraisy M, et al. Interferon Beta-1b and Lopinavir-Ritonavir for Middle East Respiratory Syndrome. N Engl J Med. 2020; 383: 1645-56.	N = 11,847 patients randomized when the lopinavir-ritonavir group, 1,616 patients were randomized to lopinavir-ritonavir, and 3,424 were randomized to usual care.	The use of hydroxychloroquine has not shown efficacy in hospitalized patients or as post-exposure prophylaxis to Sars-Cov-2. The use of lapinavir-ritonavir has not shown efficacy in hospitalized patients with a diagnosis of post-covid syndrome whose treatment was started in advanced stages of infection.
Covid-19 and severe breathing	N = 4,321 patients in 176 British	The RECOVERY trial did not

Table 2. Continues.

problems: dexamethasone reduced mortality in one trial. Prescrire 2020.	public sector hospitals.	demonstrate that the use of systemic corticosteroids reduces mortality in hospitalized patients with COVID-19, not even in those patients in whom lopinavir-ritonavir was used in the first 7 days of symptoms.
COVID-19 Ring-based Prevention Trial with Lopinavir/Ritonavir (CORIPREV-LR).	N = 1220 participants post exposure to covid-19.	The combined therapy of lopinavir - interferon b1 in patients with Middle East respiratory syndrome coronavirus (MERS) demonstrated a reduction in mortality in those hospitalized patients in patients with a diagnosis of post-covid syndrome.
Trial of early therapies during non-hospitalized outpatient window for COVID-19 (TREATNOW).	N = 600 participants with active symptoms of covid-19 infection.	The administration of Lopinavir in combination therapy with other drugs and as monotherapy in other contexts as prophylactic or early treatment, demonstrated efficacy in patients hospitalized for post-covid syndrome or active covid-19 infection.
Puggioni F, Alves-Correia M, Mohamed MF, Stomeo N, Mager R, Marino M, et al. Immunostimulants un respiratory diseases: Focus on Pitodimod. Multidiscip Reapir Med. 2019; 14:31.	N = 20 patients, men, and women of Caucasian ethnicity.	Pitodimod showed beneficial results that make it considered as a drug that promotes an immune response in the human body, which reduces mortality and complications of Sars-Cov-2 infection and post-covid syndrome.
Mahashur A, Thomas PK, Mehta P, Nivangune K, Muchhala S, Jain, R. Pitodimod: In-depth review of current evidence. Lung India. 2019; 36: 422-33.	N = 674 hospitalized patients with a diagnosis of post-covid syndrome.	An effectively unexpected therapeutic effect was demonstrated in reducing the mortality rate from covid-19 and post-covid syndrome.

antibodies act at the extracellular level, preventing the entry of the virus into them (preventing their binding to ACE2) (Wang et al., 2018).

Inhibitors of the inflammatory response act by neutralizing the effects triggered by the coronavirus on the immune system via the cytokine cascade, even reaching a situation of hyperinflammation known as cytokine storm (or cytokine release syndrome), ultimately responsible for the acute respiratory distress syndrome (SARS) but without the possibility of evolution to a clinical picture of post-covid syndrome (Devaux et al., 2020).

Plasma from convalescent patients acts both directly on the virus, neutralizing it by immediate immunity and indirectly by preventing its binding to ACE2 receptors, as do vaccines, which would also generate a long-lasting immune response (Gautret et al., 2020). Many of the drugs that are currently under study and those in the test phase have shown mixed mechanisms of action that can

shorten the progression of infection by covid-19 to a subsequent post-covid syndrome established with irreversible sequelae in patients. Among the most mentioned and with the best record of results in patients infected with Sars-Cov-2, is Pitodimod (The Lancet Infectious Diseases, 2020).

Pitodimod dispersible tablet is a synthetic oral immunostimulant that plays a role in stimulating and regulating the cell-mediated immunity of the immune response (Li et al., 2019).

It is commonly used in the auxiliary treatment of chronic infection or recurrent infection of the respiratory tract or the urinary tract (Ya et al., 2019). The research effect of Pitodimod in the treatment of children with recurrent respiratory tract infection due to the post-covid syndrome is significant; the drug can stimulate natural non-specific immunity and significantly improve the level of IgA and IgG in the body (18). It can also regulate the function of T

lymphocytes and B lymphocytes, the generation of antibodies increases chemotaxis, phagocytosis, and macrophage migration improves the immune function of the body, and achieves the purpose of treating respiratory tract infection (Ucciferri et al., 2020).

Pidotimod may play a therapeutic role by enhancing the body's immunity through these mechanisms. The new coronavirus and post-covid syndrome can cause severe respiratory disease, such as SARS and MERS, pidotimod, as an immune promoter, can not only promote the non-specific immune response but also provide a noticeable boost to the immune system so that the eradication of viral particles is more effective and without causing alterations in the immune balance (Barone et al., 2020).

Conclusion

Although there is no universality when considering adimod as the treatment of pneumonia due to post-covid syndrome, there is sufficient evidence that provides a new idea for clinical treatment and the implementation of immunomodulators as an ally in the clinical task of improving the general condition of the patient with the post-covid syndrome and as material for the prevention and strengthening of the immune system to prevent the onset of this syndrome.

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