Pharmacological Therapies for COVID-19: A Comprehensive Review from 2022 Updated NIH, IDSA and ICMR Guidelines

Ab Ahad Wani a≡, Kar Tahir Ashraf a≡, Malik Latief Ab aŒ, Jawhar Ul Islam aœ, Aamir Shafi aœ*, Wani Mubashir a†, Aleena Ahmad a†, Khan Azra a†, Dawood Ahmad a†, Nayarah Altaf a† and Shahid Ahmad a†

a Department of General Medicine SKIMS Medical College, Bemina, Srinagar, India.

Authors’ contributions
This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information
DOI: 10.9734/AJMAH/2022/v20i330444
Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/84129

Received 09 February 2022
Accepted 13 March 2022
Published 21 March 2022

ABSTRACT
Coronavirus disease 2019 (COVID-19) has had catastrophic results on the world’s economy and demographics leading to more than 4 million fatalities. This has been the most devastating world crisis after the 1918 pandemic which was caused by influenza. The main concerns regarding the disease have been lack of specific antiviral therapies. Results from recent trials have given some hope and promising results for the treatment of COVID-19 especially Molnupiravir, Monoclonal antibodies and Janus kinase inhibitors. This review article gives a comprehensive update on various pharmacological therapies in the light of recently published standard treatment guidelines based on large clinical trials for the treatment of COVID-19.

Keywords: COVID-19; Monoclonal antibodies; molnupiravir; baricitinib.

≡Assistant Professor;
$j$Registrar;
#In charge Pharmacist;
†Junior resident
*Corresponding author: E-mail: amirshafi400@gmail.com;
ABBREVIATIONS

IDSA : Infectious disease society of America;
ICMR : Indian council of medical research;
COVID : Corona virus disease.

1. INTRODUCTION

Although there is rapid and significant progress and lot of ongoing research about the covid 19, there is still paucity of data as far as drug therapy is concerned in particular when it comes to continuous mutant strains rendering the drug therapy as well as vaccination with substantial challenges. The National Institutes of Health (NIH) classified COVID-19 into following distinct types based on severity of clinical symptoms and imaging findings as:

Asymptomatic COVID-19 infection: patients who test positive for COVID-19 on real time polymerase chain reaction (RT-PCR) but do not have COVID related symptoms [1,2].

Mild illness: presence of covid 19 related symptoms but no breathlessness or any radiological findings [3].

Moderate illness: it is defined as the presence of covid 19 related symptoms with associated radiographic abnormalities but oxygen saturation more than 94% when breathing ambient air [4]. However, ICMR guidelines define moderate disease as anyone of the two parameters [5].

1. Respiratory rate >24 breaths per minute.
2. $\text{SpO}_2$ 90% to 93% on ambient air.

Severe illness: it is defined as the presence of radiographic abnormalities in more than half of lung field with an oxygen saturation of less than 94% when breathing ambient air or respiratory rate of more or equal to 30 per minute. However, ICMR guidelines define severe disease as anyone of the two parameters [5].

1. Respiratory rate >30 breaths per minute.
2. $\text{SpO}_2$ ≤90% on ambient air.

Critical illness: Patients who have acute respiratory distress syndrome or shock with indications for non invasive or invasive mechanical ventilation are said to have critical disease. It usually develops after the first week of covid onset. Following are the different pharmacological therapies that received FDA approval from time to time in the management of covid 19 [6].

1.1 Antiviral Therapies

Molnupiravir: In a meta-analysis of phase 1-3 studies, molnupiravir showed a significant reduction in hospitalization and death in mild COVID-19 disease [5]. In a landmark clinical trial (MOVEOUT) molnupiravir at a dose of 800 mg twice a day for 5 days showed significant reduction in hospitalization and death in at risk mild to moderate covid 19 patients who had at least one risk factor for progression to severe or critical disease [8]. January 2022 updated IDSA guidelines recommend molnupiravir for ambulatory patients with mild to moderate disease at risk of progression to severe disease who have no other treatment options within 5 days of symptom onset [40]. Current ICMR guidelines do not recommend molnupiravir in the treatment of COVID-19 [41].

Paxlovid (ritonavir in combination with nirmatrelvir) on an interim analysis of phase 2-3 data demonstrated 89% reduction in hospital admission rate in comparison to placebo when started within three days of symptom onset [10]. Further studies are ongoing to establish the efficacy reported [11]. On 22 December 2021, the FDA issued a EUA for Paxlovid to be used in patients with mild to moderate COVID-19. January 2022 updated IDSA guidelines recommend paxlovid for ambulatory patients with mild to moderate disease at risk of progression to severe disease within 5 days of symptom onset [40]. Current ICMR guidelines do not recommend paxlovid in the treatment of Covid-19 [41].

Remdesivir: There is evidence from three clinical trials which showed shortened clinical recovery time when remdesivir was compared with placebo [12,13] leading to EUA for remdesivir for patients who had indication for hospitalization due to covid 19 and were at least 12 years old and having above 40 kg body weight. [14][15][16]. However, the large WHO SOLIDARITY trial disappointed the infectious disease experts across the world when it demonstrated no mortality benefit in hospitalized covid 19 patients. A ray of hope emerged again when a recently published randomized double blind placebo controlled trial [PINETREE] reported an 87% lower risk of hospitalization or death in comparison to placebo when at-risk non hospitalized patients with COVID-19 were treated with a 3-day course of remdesivir [35-37].
January 2022 updated ICMR guidelines do not recommend remdesivir use in non hospitalized or mild disease patients. However, in moderate and severe disease it is given EUA/off label use [41]. IDSA guidelines recommend remdesivir for non hospitalized patients with mild to moderate disease at risk of progression to severe disease [40]

1.2 Anti-SARS-CoV-2 Neutralizing Antibody Products

The FDA approved convalescent plasma therapy under a EUA for patients with severe life-threatening COVID-19 [17][11]. The national registry of United states demonstrated from a prospective study the lower risk of death in hospitalized patients who were not on mechanical ventilation and who received a high titre convalescent plasma therapy [18]. However conflicting data emerged from many randomized controlled trials including large PLACID trial that showed insignificant benefits [19][20][21]. January 2022 updated IDSA and ICMR guidelines recommend against CPT use in COVID-19 disease [9,5].

REGN-COV2 (Casirivimab 1200 mg and Imdevimab 1200 mg): A monoclonal antibody cocktail that targets viral spike protein showed reduced hospitalization rates in a double blind randomized controlled trial in patients with mild to moderate covid 19 with at least one risk factor for severity [22] [23]. January 2022 IDSA guidelines recommend use of REGN-COV2 in patients with mild to moderate disease at risk of progression [40]. IDSA guidelines also recommend sotrivimab for non hospitalized mild to moderate disease patients at risk of progression to severe disease [40].

1.3 Immunosuppressive Agents

1.3.1 Glucocorticoids

The largest randomized controlled trial(RECOVERY) involved 2104 patients in steroid arm and 4123 patients in the control arm. Patients who received dexamethasone 6 mg daily for 10 days or till hospital discharge which ever came earlier had lower 28 day mortality. The benefit was not demonstrated in patients who did not require supplementary oxygen [24]. Based on the results of this landmark trial, dexamethasone is currently considered the standard of care in hospitalized patients who require supplemental oxygen or non-invasive or invasive mechanical ventilation. January 2022 updated IDSA and ICMR guidelines also recommend methylprednisolone as an alternative to dexamethasone in a dosage of 0.5 to 1 mg/ kg for moderate disease and 1 to 2 mg/kg for severe and critical disease respectively [40,41].

Tocilizumab: An Interleukin 6 inhibitor was studied in large randomized controlled trial(COVACTA) in which 294 patients received tocilizumab and 144 received placebo treatment. The trial failed to show a significant 28 day mortality benefit in severe and critical covid 19 patients [25,26]. Another double blind randomized trial involving 243 patients failed to prevent intubation rate or death in critically ill covid 19 patients [27,28,29]. However The REMAP-CAP and RECOVERY two large randomized controlled trials demonstrated mortality benefit in patients with rapid worsening of hemodynamic status [30]. January 2022 updated IDSA and ICMR guidelines recommend tocilizumab for severe covid disease with rapid decompensation and high inflammatory markers (IL6 and CRP) in absence of bacterial or TB infection [40,41]. In the largest clinical trial on the treatment of tocilizumab criterion for systemic inflammation was defined as CRP > 75 mg/L.

1.4 Janus Kinase (JAK) Inhibitors

Baricitinib, a Janus kinase 1 and 2 inhibitor has been shown to have beneficial effects in patients with severe covid 19 due to its inhibitory effect on viral endocytosis and thus preventing late cytokine storm phase [31,9]. In a retrospective observational study across many centres baricitinib at an oral dosage of 4 mg daily for 14 days improved 14 day mortality in severe and critical covid 19 patients. The large ACTT 2 trial demonstrated superior effect of baricitinib plus remedesivir combination than remedesivir alone in reducing time to recovery and allowing rapid clinical improvement in severe and critical COVID-19 patients [32,33]. January 2022 updated ICMR guidelines do not recommend baricitinib for use in COVID-19 irrespective of severity [5]. IDSA guidelines recommend use of baricitinib for severe and critical disease patients with high inflammatory markers [40]. Patients who can not receive steroids IDSA guidelines recommend use of baricitinib in combination with remedesivir [40].

2. CONCLUSION

Pharmacotherapy for covid 19 continues to emerge with extensive research going on. The
disease caused huge devastation due to its high mortality and economic crisis [42] Promising results have been seen with some pharmacological therapies like molnupiravir, monoclonal antibodies, remdesivir and baricitinib in latest clinical trials described above. This review aims to give comprehensive and consolidated update on recent standard guidelines for management of COVID-19 based on latest clinical trials and recommendations.

ACKNOWLEDGEMENT

Dedicated to all patients who lost their precious lives battling the covid pandemic.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


Respiratory Failure: The HENIVOT Randomized Clinical Trial. JAMA. 2021;325(17):1731-1743.

40. www.idsa.com Infectious disease society of America Updated in January 2022


© 2022 Ahad et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history: The peer review history for this paper can be accessed here: https://www.sdiarticle5.com/review-history/84129