

Analysis and Efficacy of Current Therapeutic Options for the Treatment of SARS-CoV-2

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Abstract: SARS-CoV-2 (COVID) has been at the forefront of medical discussion and research after the onset of the global pandemic. With many individuals not vaccinated for COVID, it became important to determine what treatment options are available for the treatment of COVID, what the efficacy of these treatment options is, and to determine which of these options does not hold any benefit in administration for patients hospitalized with COVID. Efficacious treatment options were determined by decreased hospital stay of the patient, decreased overall mortality of patient when receiving the treatment compared to a placebo, decreased oxygen use, or had a shorter hospital course leading to discharge earlier. An analysis of the literature revealed that treatment options that were found to have an efficacious effect on treating COVID were antibody therapy, cell therapy, Paxlovid, Remdesivir, Hydroxychloroquine used with Azithromycin, Favipiravir, Sofosbuvir and Daclatasvir, Tocilizumab, drinking tea, edaravone, IL1, IL6 inhibitors, teicoplanin, low and high dose dexamethasone, methylprednisolone, as well as ivermectin. There was most support for the use of remdesivir, followed by hydroxychloroquine, and then low dose dexamethasone. The literature strongly suggested against the use of Lopinavir-Ritonavir. Further research is recommended for the use of Hydroxychloroquine with Azithromycin, though thus far the research has been generally supporting its use in the treatment of COVID. Further research is also suggested in the treatment of Ribavirin.

Keywords: COVID-19 treatment, efficacy, Remdesivir, dexamethasone, research recommendations

1. Introduction and Background

The relevance of SARS-CoV-2 (COVID) came at an all time high in 2020, with the onset of the global pandemic affecting many lives all around the world. As the incidence and prevalence of the virus increased, so did the mortality from it. The race to determine and develop effective treatment options to improve the morbidity and mortality became important, with many trying current available treatment options to determine any efficacy toward COVID, while others attempting to develop new treatment options. Vaccines have been the most effective prophylactic agent, but it is important to evaluate options related to treatment when one already has the disease. The purpose of this literature review is to analyze the various treatment options that have been discussed in the literature thus far and to discuss any efficacy from these options, as well as recommend further areas of research for possible therapeutic potential. Though there have been previous literature reviews of COVID treatments, most were aimed toward analyzing treatments that had been given in the early part of the pandemic around 2021. More recent literature reviews have been written, but most focus on a few treatments and their efficacy, rather than analyzing all the treatments together and determining which treatment options are most discussed and supported in the literature. This review thus aims to bridge the gap between earlier and newer treatments that have been given, as well as determine which treatments are more discussed in the literature and supported. Finally, this review aims to provide further recommendations for treatment of COVID, both through clinical trials as well as through further literature review.

2. Methods

This literature review was conducted utilizing articles that are peer reviewed in a medical journal or library, specifically obtained through PubMed. Articles discussing clinical trials performed by the authors themselves as well as literature reviews were both utilized and analyzed in this review. The specific criteria involved articles that were published in 2020

and onwards involving treatment of the strain of COVID that caused a global pandemic. Of these articles, those were chosen that specifically discussed therapeutic options in the treatment of COVID. Specific keywords used to find these studies included COVID-19, COVID-19 treatment, COVID-19 mortality, COVID-19 research. A total of 50 articles from the literature were reviewed, and the recommendations of each will be considered and compared amongst each other. There was no specific criteria for language of studies. Thus, this review will analyze articles from the earlier part of the pandemic as well as current recommendations, and determine which treatment options are most discussed and also supported throughout the entire course of the pandemic, which is in general lacking in the literature.

3. Review

In general, the results thus far for the treatment of COVID have either had a generally positive patient outcome or no outcome at all, and thus not recommended by the literature. Positive patient outcomes were delineated by outcomes that decreased hospital stay of the patient, decreased overall mortality of patient when receiving the treatment compared to a placebo, decreased oxygen use, or had a shorter hospital course leading to discharge earlier. For those treatment options found to have no outcome at all as compared to a placebo, those were determined to not be favored by the literature and further recommendations were given to evaluate other options for treatment of COVID. In general, the outcomes of these treatments did not have a partially favorable or unfavorable outcome, and for sake of analysis were then classified into the categories of “favorable” or “unfavorable” for analysis.

There has been a few reports of antibody and cell therapy leading to positive outcomes in patients with COVID, but the evidence has been limited to a few patients.1 PAXLOVID has also been found to be generally favored, with an 89% reduction in the risk of COVID-19 related hospitalization or death in comparison to a placebo. This was in reference to

patients who were specifically treated within three days of their symptom onset.¹

The therapeutic agent most supported by the literature by Remdesivir.² The outcomes related to Remdesivir use involved possible acceleration of clinical improvement, with a faster time to recovery by around 31%.³⁻⁶ On average, the use of Remdesivir was found to have a decreased time to recovery in comparison to placebo by four days.⁷⁻¹¹ The overwhelming majority of studies tend to favor the use of Remdesivir, however there are some studies that believe that, through the studies conducted by the authors, there is little to no effect on all-cause mortality as well as in hospital mortality in patients who are admitted and unvaccinated with COVID.¹² These studies are in the minority, however.

Other therapeutic against that are not found to be in favor have been Umifenovir, with no difference noted in treatment of COVID in comparison to a placebo.² Another medication that has not been found to be favorable has been the combination of Lopinavir and Ritonvir.¹³ This has been shown to not significantly accelerate clinical improvement also in comparison to a placebo, and the treatment of COVID is not recommended through various studies conducted.^{8-9, 14-17}

The combination of Hydroxychloroquine with Azithromycin has also been researched extensively since the onset of COVID as a potential treatment option. The majority of articles delineate that there is a favorable outcome of treatment with COVID, with the potential for decreasing viral load and accelerating the recovery of COVID patients.^{4-5, 8, 10, 17-20} There are, however, other articles that do not favor this combination, detailing multiple observational and cohort studies that have not shown a benefit in treatment.^{8, 19-20} Even the studies that documented favor of the treatment of this agent mentioned that the use of it led to adverse cardiac effects, including QT interval prolongation.²¹ Other articles detailed that further research is necessary, including recommendations that mentioned the need for large scale, randomized, double blind placebo controlled trials.^{11, 21-22} Some trials mentioned that the findings themselves were not promising, and this eventually led to the drug falling out of favor.²³ In addition, the use of Azithromycin alone was only not favored.²⁴

Another therapeutic agent that has been found to be effective is Favipravir.⁵ However, this has been found to be only marginally effective in terms of clinical improvement.⁸ Another combination that has been found to be favorable has been Sofosbuvir and Daclatasvir.⁶ It has been shown to have mild clinical recovery in patients.⁶ Tocilizumab has also been found to be a therapeutic strategy for severe COVID pneumonia.^{7, 9, 14} It has been found to decrease the cytokine storm, which has shown to lead to overall decreased mortality.^{25, 26} Edaravone has also been found to decrease organ damage, clinical complications, and mortality in cases of hospitalized COVID.¹⁶ Inflammation inhibitors such as IL-

1 and IL-6 inhibitors have also been found to show decrease in hospital course related to COVID.²³ Teicoplanin has also been found an effective treatment in comparison to a placebo.^{9, 19, 23}

Other treatments that have been found to be favorable have been methylprednisolone. This has showed dose-response efficiencies, and pulse therapy of this has been shown to benefit critically ill patients.²⁷ It has been shown that it can also be an effective intervention to increase survival rates in patients at risk of developing a COVID hyper-inflammatory response.²⁸ Ivermectin has also been found to be favorable, with improvement in dyspnea as well as oxygen saturation noted when it was used in the treatment of COVID patients, as well as a reduction in recovery time.²³ Drinking tea has also been found to be favorable, with active ingredients in it inhibiting RNA replication of the virus.²⁹

Dexamethasone has also been a treatment agent widely used in treatment, and the studies have been split the use of low and high dose dexamethasone. Low dexamethasone has overall been found to be favorable, which has been shown to decrease the mortality rate related to COVID, as well as increase the resolution of all symptoms by day 14.^{10, 30-32} There is still further research that is recommended, however.³³ High dose dexamethasone has had more outcomes in its' favor, with some studies mentioning that its' use may benefit patients aged 70 years or less with severe acute respiratory failure.^{28, 34, 35} However, there have been other studies that mention there may be little or no impact overall on clinical improvement for patients with COVID.³⁶ Overall, studies seem to favor the use of both low and high dose dexamethasone, with the majority favoring low dose dexamethasone.

Studies did not favor the use of Interferon alpha, another agent initially attempted in hopes of having clinical improvement for COVID.²³ Colchine was also a therapeutic agent that was found to have little to no impact on the mortality or clinical progression of patients with COVID in comparison to use of a placebo.^{36, 37} Antiplatelet agents such as Aspirin was also found to have no difference in 28 day mortality as well as clinical course, with only a slight reduction noted in thrombotic events during the hospital course of COVID patients.^{38, 39}

Further research was also recommended for the use of Ribavirin.⁴⁰⁻⁴² There were some studies that mentioned an overall lower mortality and better clinical improvement with the use of this agent rather than a placebo.⁴³ In comparison with other agents such as corticosteroids, Lopinavir as well as Ritonavir, and Hydroxychloroquine, it was shown to have some additional benefit.⁴⁴⁻⁴⁷ However, due to the overall low quality of evidence, in most cases it appears there was not a clear conclusion able to be drawn for the recommendation of its' use for COVID.^{48, 49, 50}

Table 1: Therapeutic Agents Favored by Literature and Outcomes Noted

Therapeutic Agents Favored by the Literature	"Favorable" Outcome Per the Literature and Amount of Times Cited					Total Number of References Supporting Use
	Decreased Hospitalization	Faster Rate of Recovery	Decreasing Viral Load	Decreasing Cytokine Storm	Decreased Mortality	
Remdesivir	3	6				9
Hydroxychloroquine with Azithromycin		3	5			8
Tocilizumab				2	3	5
Dexamethasone (Low Dose)	3	2				5
Dexamethasone (High Dose)		3				3
Favipravir		3				3
Teicoplanin		1				3
Antibody Therapy	2					2
Methylprednisolone				2		2
Cell Therapy	1					1
Paxlovid	1					1
Sofosbuvir and Daclatasvir		1				1
Drinking Tea			1			1
Edaravone					1	1
IL1/IL6 Inhibitor	1					1
Ivermectin		1				1

Table 2: Therapeutic Agents Not Favored By Literature and Outcomes Noted

Therapeutic Agents Not Favored by the Literature	"Not Favorable" Outcome Per the Literature and Number of Times Cited			Total Number of References Not Supporting Use
	No Acceleration Clinical Course	Adverse Cardiac Effects	No Difference to Placebo	
Lopinavir-Ritonavir	7			7
Hydroxychloroquine with Azithromycin	3	2		5
Azithromycin Only	1			1
Umifenovir			1	1
Remdesivir	1			1
Interferon alpha with Ribavirin			1	1
Dexamethasone (High Dose)	1			1
Colchine	1			1
Antiplatelet Agents	1			1

4. Conclusions

Agents found to have an efficacious effect on treating COVID were antibody therapy, cell therapy, Paxlovid, Remdesivir, Hydroxychloroquine with Azithromycin, Favipravir, Sofosbuvir and Daclastavir, Tocilizumab, drinking tea, edaravone, IL1, IL6 inhibitors, teicoplanin, low and high dose dexamethasone, methylprednisolone, as well as ivermectin. There was most support for the use of remdesivir, followed by hydroxychloroquine, and then low dose dexamethasone. The efficacy of these agents was measured with overall lower mortality, decreased use of oxygen, and decreased hospital stay. There was evidence against the use of Umifenovir, lopinavir-ritonavir, azithromycin without hydroxychloroquine, interferon alpha with ribavirin, Colchine, and antiplatelet agents. The literature strongly

suggested against the use of LopinavirRitonavir. Further research is recommended for the use of Hydroxychloroquine with Azithromycin, though thus far the research has been generally supporting its use in the treatment of COVID. Further research is also suggested in the treatment of Ribavirin. Areas for further research and analysis also recommend incorporating details such as availability of these therapeutic options, route of administration, as well as cost since these details were often not included in the literature analyzed.

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