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A Review on Pharmacological Treatments for COVID -19

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ABSTRACT: The pandemic of coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus (SARS-COV-2) presents an unprecedented challenge to identify effective drugs for prevention and treatment. There are no proven treatments therapies exist currently for the virus. The rapidly expanding knowledge regarding SAR-COV-2 virology provides a significant number of potential drugs targets. The most promising therapy is Resdesivir. Though, it is not USDFA approved, it is potent against SARS-COV-2 and currently is being tested in ongoing randomized trials. There are no stopping evidences in using Angiotensin Converting Enzyme II (ACE-II) Inhibitors or angiotensin receptors blockers in patients with covid-19 convalescent plasma therapy has also been considered as one of the treatment methods. But no therapies have been shown effective to date.

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INTRODUCTION:

The global pandemic of novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome Coronavirus 2 began in Wuhanin, China, December 2019, and this viral infection spread worldwide. As of May 31, 2020 there have been more than 60 Lakhs reported cases and more than 3 Lakhs deaths in more than 200 countries. This novel Beta coronavirus is similar to severe acute respiratory syndrome coronavirus (SARS-COV) and Middle East respiratory syndrome (MERS-COV) based on it genetic proximity it is likely originated from bat derived coronavirus with spread via an unknown intermediate mammal host to humans. The viral genome of SARS-COV-2 was rapidly sequenced to enable diagnostic

testing epidemiologic tracking and development of preventive and therapeutic strategies [1,2].

Currently there is no evidence from randomized clinical trials that any potential therapy improves outcomes in COVID-19 patients. There are no clinical trials data supporting any prophylactic therapy. More than 350 active clinical treatment trails are underway. This narrative review summarizes current evidences regarding major proposed treatments repurposed or experimental for COVID-19 and provides a summary of current clinical experience and treatment guidance for this novel epidemic corona virus [3,4].

SARS-COV-2 Virology and Drug Targets:

SARS-COV-2 a single stranded RNA enveloped virus target cells through the viral structural spike protein that binds to the ACE II Receptor. Following receptor binding the virus's particle uses host cells receptors and endosomes to enter cells. A host type 2 transmembrane serine protease (TMPRSS2) facilitates cell entry via the Spike (S) protein. After entering into a cell viral poly proteins are synthesized that encode for the replicate transcriptase complex. The virus then synthesized RNA via its RNA dependent RNA polymerase. These viral lifecycle steps provide potential targets for drug therapy. Promising drug targets include nonstructural proteins (e.g. 3-chymotrypsin like protease, papain like protease RNA-dependent RNA polymerase), which share homology with other novel coronavirus (nCoVs). Additional drug targets include viral entry and immune regulation pathways [5,6].

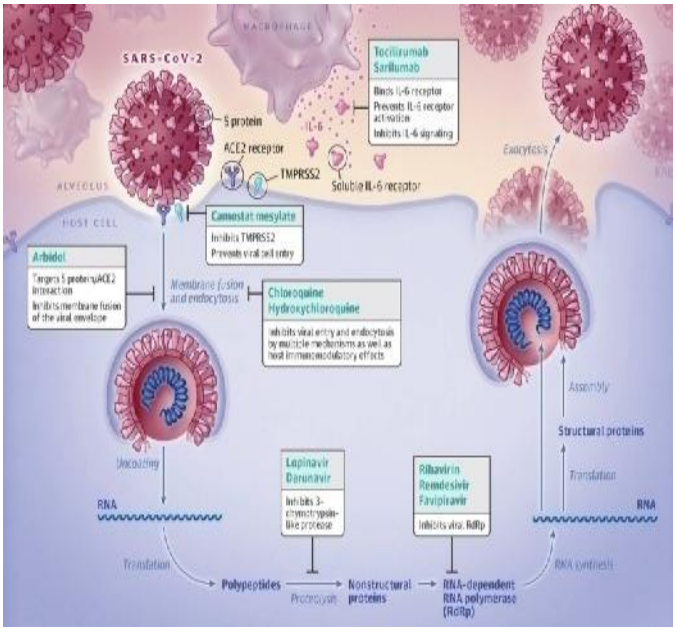

Fig 1. Medications used in treatment of Covid-19.

MEDICATION USED IN TREATMENT OF COVID-19:

Repurposed Drugs:

Agents previously used to treat SARS and MERS are potential candidates to treat COVID-19 [7]. Below *in vitro* activity and published clinical experiences of some of the most promising repurposed drugs for COVID-19 are presented below.

***Chloroquine and Hydroxychloroquine*:**

These are best in prevention and treatment of malaria and treatment of chronic inflammatory diseases. These drugs prevent viral entry of cells by inhibiting glycosylation of host receptors, proteolytic processing and endosomal acidification. No high quality evidence exists for the efficacy of chloroquine and hydroxychloroquine treatment of SARS and MERS. But when given in combination with Azithromycin, it has been considered as successful in treatment. It was reported that it is resulting in improved radiologic findings, enhanced viral clearance and reduced disease progression. Though these medications show some adverse effects, but are considered safe in pregnancy, randomized clinical trials are underway to report their efficacy [8,9].

***Lopinavir or Ritonavir and Other Antiretroviral*:**

There are USFDA approved oral combination agents for trending HIV. Demonstrated their activity via inhibition of 3-chymotrypsin like protest against other novel corona viruses but they are considered ineffective due to delayed treatment inhibition. These agents may cause gastro intestinal distress as adverse effect. The randomized clinical trials with these drugs are underway in China [10].

***Ribavirin*:**

A Guanine analogue inhibits RNA- dependent RNA polymerase. It inhibits viral replication and has been reported with its activity against other novel corona virus. But studies demonstrated that it causes harmful adverse effects include hematologic and liver toxicity. Ribavirin is also a known teratogen and contraindicated in pregnancy [11].

***Other Antivirals*:**

Oseltamivir is a neuraminidase inhibitor approved for the treatment of influenza has no documented in retro activity SARS-COV-2. But this has no role in management of COVID-19 once influenza is excluded and thus this drug is rarely using [12].

Umufenovir is a more promising repurposed antiviral agent with a unique mechanism of action targeting the S protein or ACE 2 interaction and inhibiting membrane fusion of the viral envelope. This agent is currently approved in Russia and China for the treatment of COVID-19 [13].

Investigational Drugs:

***Remdesivir*:**

Remdesvir, formally known as GS-5734, is a monophosphate prodrug that undergoes metabolism to an active C-adenosine nucleotide triphosphate analogue. This drug was discovered a screening process for antimicrobials with activity against RNA viruses, such as coronaviridae and flaviviridae. Currently it is a promising therapy for COVID-19 due to its activity against several nCOVs including SARS-COV-2. Remdesivir also has very fewer adverse effects compared to other agents [14].

***Favipiravir*:**

Previously known as T-705, is a prodrug of a purine nucleotide, favipiravir ribofuranosyl-5- triphosphate. This drug inhibits the RNA polymerase, halting viral replication. It has been reported with influenza and Ebola activity. It has also demonstrated broad activity against other RNA viruses. This agent has low profile adverse effects and clinical trials are ongoing [15].

Adjunctive Therapies:

***Corticosteroids*:**

The use of corticosteroids is to decrease the host inflammatory responses in the lungs and acute respiratory distress syndrome (ADRS). However, benefits are outweighed by adverse effects, including delayed viral clearance and increased risk of secondary infection. Their potential harms and lack of proven benefit cautions its use against COVID-19 [16].

Anticytokine or Immunomodulatory Agent:

Monoclonal antibodies directed against key inflammatory cytokines or other aspects of the innate immune response represent another potential class of adjunctive therapies of COVID-19. Tocilizumab, a monoclonal antibody IL-6 receptor antagonist, is FDA approved to treat Rheumatoid Arthritis and cytokine release syndrome following chimeric antigen receptor T-cell therapy. Sarilumab, another Interlukin (IL) 6 receptor antagonist approved for Rheumatoid Arthritis, is being studied against patients with severe COVID-19 and it can be suggested for therapeutic uses [17,18].

***Convalescent Plasma Transfusion (Immunoglobulin Therapy)*:**

Another potential adjunctive therapy for COVID-19 is the use of convalescent plasma or hyper immune immunoglobulin's. The plasma of recovered COVID-19 donors contains specific IgG and IgM anti-SARS-COV-19 antibodies, which can neutralize the virus. But this therapy has some drawback such as blood related issues because the donor plasma may be different from the plasma of the new recipient, COVID-19 patient [19,20].

CONCLUSIONS:

The COVID-19 pandemic represents the greatest global public health crisis of this generation and potentially, since the pandemic influenza outbreak of 1918. The speed and volume of clinical trials launched to investigate potential therapies for COVID-19 highlight both the need and capability to produce high quality evidence even in the middle of a pandemic. No therapies have been shown effective to date.

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REFERENCES:

1. Zhu N, Zhang D, Wang W, *et al*. China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in china, 2019. N Engl J Med, 2020; 328(8): 727-733.
2. Chen Y, Liu Q, Guo D. Emerging coronaviruses: genome structure, replication and pathogenesis. J Med Virol, 2020: 92(4): 418-423.
3. Kumagai Y, Murakawa Y, Hasunuma T, *et al*. Lack of effect of favipiravir, a novel Antiviral agent, on QT interval in healthy Japanese adults. Int J Clin Pharmacol Ther, 2015; 53(10): 866-874.
4. Sanders JM, Monogue ML, Jodlowski TZ, et al. Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19) - A Review. JAMA, 2020; 323(18):1824-1836.
5. Hoffmann M, Kleine-Weber H, Schroeder S, *et al*. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell, 2020; 181(2): 271-280.
6. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol, 2015; 1282: 1-23.

7. World Health Organization. WHO R&D blueprint: ad-hoc expert consultation on Clinical trials for Ebola therapeutics. Geneva: WHO; 2018.
8. Chloroquine. Hudson, OH: Lexicomp Inc.; 2016. http://online.lexi.com (Accessed March 17, 2020).
9. Hydroxychloroquine. Hudson, OH: Lexicomp Inc; 2016. http://online.lexi.com (Accessed March 17, 2020).
10. Lopinavir/ritonavir. Hudson, (OH): Lexicomp Inc; 2016. http://online.lexi.com (Accessed March 17, 2020).
11. Foolad F, Aitken SL, Shigle TL, *et al*. Oral versus aerosolized ribavirin for the treatment of respiratory syncytial virus infections in hematopoietic cell transplant recipients. Clin Infect Dis, 2019; 68(10):1641-1649.
12. Chinese Clinical Trials. http://www/chictr.org/enindex.aspx. Accessed March 31, 2020.
13. Chu CM, Cheng VC, Hung IF, *et al*. HKU/UCH SARS Study Group. Role of lopinavir/ ritonavir in the treatment of SARS: Initial virological and clinical findings. Thorax, 2004; 59(3): 252-256.
14. Foolad F, Aitken SL, Shigle TL, *et al*. Oral versus aerosolized ribavirin for the treatment of respiratory syncytial virus infections in hematopoietic cell transplant recipients. Clin Infect Dis, 2019; 68(10): 1641-1649.
15. Gao J, Tian Z, Yang X. Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Biosci Trends, 2020; 14(1):72-73.
16. Hayden FG, Shindo N. Influenza virus polymerase inhibitors in clinical development. Curr Opin Infect Dis, 2019; 32(2):176-186.
17. Mentre F, Taburet AM, Guedj J, *et al*. Dose regimen of favipiravir for Ebola virus disease. Lancet Infect Dis, 2015; 15(2): 150-151.
18. Fung TS, Liu DX. Coronavirus infection, ER stresses apoptosis and innate immunity. Front Microbiol, 2014; 5: 296-302.
19. US Food and Drug Administration. US Food and Drug Administration. Investigational COVID-19 Convalescent plasma: Emergency INDs. USA: US FDA; 2020.
20. Bossart KN , Wang LF, Flora MN, Chua KB , *et al*. Membrane fusion tropism and heterotypic functional activities of the Nipah virus and Hendra virus envelope glycoproteins. J Virol, 2002; 76: 11186-11198.

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