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Treatment of Covid-19/ SARS-COV 2- A Review

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ABSTRACT-

In the last month of 2019, i.e., December, COVID-19 hit Wuhan town in China. Since then, it's infected over 210 countries and nearly regarding 33.4 million individuals with 1,000,000 deaths globally. Coronavirus illness 2019 (COVID-19) is associate degree communicable disease caused by coronavirus-2 (SARS-CoV-2) that causes a severe acute metabolism syndrome. It is a infectious agent illness with flu-like symptoms; therefore,hindrance and management is that the most suitable choice to be adopted for its cure. Currently, no treatment will act specifically against the SARS-CoV-2 infection. supported the pathological options and totally different clinical phases of COVID-19, Notably in patients with moderate to severe COVID-19, the categories of medication used square measure antiviral agents, Ayurvedic, Allopathy and Homoeopathy to cure COVID-19

Keywords: COVID-19, Symptoms, Ayurveda, Allopathic, Homeopathy, MERS-CoV, SARS-CoV

Introduction:

In the last decade, completely different strains of coronaviruses have given difficult health issues to human society. The foremost fashionable viruses during this class are severe acute metabolic process syndrome coronavirus (SARS-CoV) and geographic area metabolic process syndrome coronavirus (MERS-CoV). As population, migration, and social life enlarged, these viruses showed enlarged rates of intraspecies and interspecies recombination, inflicting them to adapt to every recent host. The corona virus results in serious infections that were shortly a part of the human severe acute respiratory syndrome virus and has affected the complete world, leading to loss of business, business enterprise and human life [1]. CoVs are enveloped viruses with a positive-sense single-stranded RNA genome and contain at least four structural proteins: Spike (S) protein (trimeric), envelope (E) macromolecule, membrane (M) macromolecule, and nucleocapsid (N) macromolecule. Spike macromolecule promotes host attachment and virion-cell membrane fusion throughout infection. Spike proteins so play a key role in determinative host vary and tissue reaction. Zoonotic disease is common among CoVs and that they are often transmitted from one animal species to a different other animal to humans and humans to humans [2]. Since the happening, several agents are planned that might be effective against COVID-19. Numerous antiviral agents, together with Antiviral agent, Lopinavir/Ritonavir, Antimalarial drug phosphate, Ribavirin, and Arbidol, are enclosed within the most up-to-date National Health Commission recommendations. Angiotonin receptor blockerslike losartan have additionally been urged for the treatment of COVID-19.

Guidelines for treating COVID-19 vary from country to country. The World Health Organization tips are terribly general, recommending treatment of symptoms and recommending caution in medicine patients, pregnant women and patients with underlying comorbidities. There is no approved treatmentfor COVID-19; it's counseled to supply supportive treatment in keeping with the wants of every patient .

metabolic process distress). Additionally, World Health Organization recommendations counsel that in severe cases, empiric antimicrobial medical aid ought to lean with mechanical ventilation instituted, reckoning on the clinical standing of the patient. A number of the Asian directions (such because the Japanese instructions) weren't straight forward to interpret as a result of that they had not nevertheless been translated into English. However, treatment protocols in numerous countries are similar and embrace Plaquenil, Antimalarial drug phosphate, Remedesivir and Lopinavir/Ritonavir [3].

Symptoms:

1. Fever 2. Cough 3. Tiredness 4. Shortness of breath or difficulty breathing 5. Muscle aches 6. Chills 7. Sore throat 8. Runny nose 9. Headache 10. Chest pain 11. Pink eye (conjunctivitis) 12. Nausea 13. Vomiting 14. Diarrhea 15. Rash

Pathophysiology: Pathophysiology of COVID-19. SARS-CoV-2 enters host cells through interaction of its spike protein with the entry receptor ACE2 within the presence of TMPRSS2 (far left). Planned mechanisms for COVID-19 caused by infection with SARS-CoV-2 embrace-

Direct virus-mediated cell damage.

Dysregulation of the RAAS as a consequence of downregulation of ACE2 associated with infective agent entry, that ends up in reduced cleavage of Hypertensin and vasoconstrictor II.

Epithelial tissue cell injury and thrombo-inflammation.

Dysregulation of the immunologic response and hyperinflammation caused by inhibition of antiviral drug communication by the virus, lymph cell lymphodepletion, and therefore the production of unhealthy cytokines, notably IL-6 and TNFα. [4]

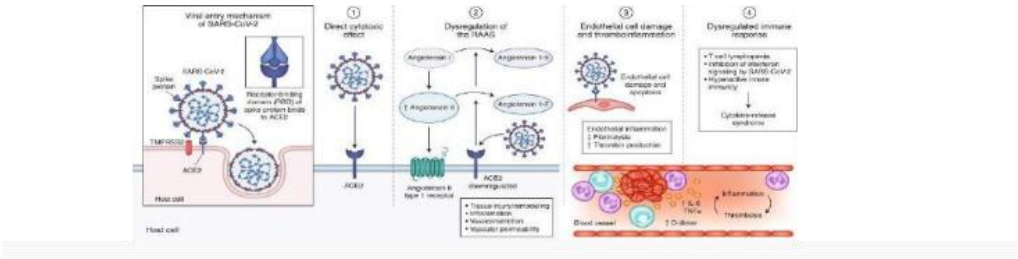

Fig. 1 Pathophysiology of COVID-19

Pharmacological Therapy:

Multiple pharmacotherapies have been tried on an experimental basis on COVID-19 patients across the globe.

Hydroxychloroquine/Chloroquine and Azithromycin:

Mechanism of action- Hydroxychloroquine and Antimalarial block entry of the virus into human cells by chemical action process, inhibiting glycosylation of host receptors, and natural process within endosomes. These agents could have immunomodulatory effects through blockage of autophagy and lysosomal activity in host cells, at the side of dissipating protein production and inhibition. Azithromycin is an antibacterial macrolide and works through binding to 50s ribosomal subunit and inhibition of messenger RNA directed polypeptide synthesis. Antiviral mechanism of macrolides is scarce and was hypothesized to inhibit metabolism syncytial virus through the reduced expression of fusion macromolecule receptor, activated isoform A of the Ras homologous (Rho) family, and therefore the inhibition of sequent Rho-kinase activation in human airway animal tissue cells. Azithromycin was shown to inhibit replication in Zika and haemorrhagic fever viruses.

Pros and cons:

Chloroquine and Anti-inflammatory drug are well tolerated and has been used for ages in patients with general LE (SLE) and protozoal infection. However, each agents will cause serious adverse effects (< 10%), like hypoglycaemia, retinopathy, medical specialty effects, QTc prolongation.

Proposed dose for COVID-19:

Hydroxychloroquine dose most used is 400 mg twice daily orally for two doses, then 400 mg daily orally for a total of 5 days. Chloroquine dose suggestedby FDA is 1 g on day 1, then 500 mg daily for 4 - 7 days total.

Remdesivir:

Mechanism of action - Remdesivir, or GS-5734, is an adenosine monophosphate prodrug that metabolizes to an active C-adenosine nucleoside triphosphate analogue, thereby interfering with the action of viral RNA-dependent RNA polymerase.

Pros and cons:

The agent was first discovered in 2015 in the process of finding antimicrobials with activity against RNA viruses. Accelerated the recovery time

by 31%, from 15 days to 11 days in patients who received treatment with it. Few case reports and series suggesting its effectiveness in the novel COVID-19 has been published. Notable side effects are nausea, vomiting, and reversible rise in aspartate aminotransferase and alanine transaminase.

Proposed dose for COVID-19:

The current dose under investigation is a single 200 mg loading dose, followed by 100 mg daily infusion.

Favipiravir:

Mechanism of action -Favipiravir inhibits contagious disease microorganism replications by targeting RNA enzyme, and this mechanism is additionally being applied to the novel coronavirus, which is a single-stranded RNA virus and requires RNA polymerase for replication.

Pros and cons:

Favipiravir is not available commercially in the USA. The safety and efficacy of the drug is not established as of now. Notable side effects include decreased neutrophil count, diarrhoea, increased uric acid levels, elevated transaminases.

Proposed dose for COVID-19:

Recommended dosing is 2,400 to 3,000 mg loading dose every 12 hr for two doses, followed by 1,200 to 1,800 mg twice a day as maintenance dose.

Lopinavir/Ritonavir:

Mechanism of action -The lopinavir part binds to the location of infectious agent peptidase activity and inhibits the cleavage of infectious agent Gag-Pol polyprotein precursors into individual practical proteins needed for infectious human immunological disorder virus (HIV). This ends up in the formation of immature, noncontagious infectious agent particles. The ritonavir component inhibits the cytochrome P450 3A (CYP3A) metabolism of lopinavir, allowing increased plasma levels of lopinavir.

Pros and cons:

Widely and successfully used in HIV management, this combination has been tried in the management of 2019 novel coronavirus (2019-nCoV). This drug has shown some effect in the in vitro model for MERS and SARS treatment. Adverse reactions should be kept in mind. The most frequently reported reactions in patients receiving lopinavir therapy are diarrhoea, nausea, elevated total bilirubin, hepatic enzyme levels, and triglycerides have also been reported.

Proposed dose for COVID-19:

Commonly studied lopinavir/ritonavir dosing in COVID-19 patients is 400 mg/100 mg twice daily for up to 14 days.

Histamine 2 receptor antagonist (H2RA):

Mechanism of action -Histamine has pleiotropic effects on the system from totally different natures of its receptors. one in all its effects being immunomodulation leading to infection was detected in diabetic mice. This happens through cut white corpuscle achievement and impaired aerophilic burst from elevated amine levels. H2RAs block these immunological disorder effects of amine and stimulate the functions of T and B white cells. The antiviral effects of this H2RA were demonstrated in patients with herpes zoster infection, herpes simplex virus (HSV), and

human papillomavirus (HPV). It was also shown that cimetidine, an H2RA, increased immunogenicity when given as an adjuvant along with HBV viral vaccines. It also decreased HIVreplication in vitro.

Pros and cons:

Although H2RA is a very commonly used medication that is even available over the counter, no conclusive data are supporting how H2RA helps againstCOVID-19.

Proposed dose for COVID-19:

Standard dose to treat gastroesophageal reflux disease.

Interferon (IFN) beta:

Mechanism of action-IFN-beta could be a subtype of sort I IFN secreted by several cell sorts, principally by plasma cytoid nerve fiber cells upon recognition of microorganism elements by pattern recognition receptors (PRR). IFN-stimulated genes (ISG) area unit concerned in inflammation and immunomodulation. ISGs interfere with microorganism replication and microorganism unfold through totally different pathways like protein secretion or delay of cell metabolism.

Pros and cons:

Data obtained from the experiments involving treatment of SARS-CoV and MERS-CoV and ISG's ability to disrupt the IFN signaling pathway would be valuable for selecting IFNbeta as a potential treatment option against SARS-CoV-2 . Type I (IFN-alpha and beta) IFNs were efficient in vitro and also in specific animal models but failed to control the disease in humans. It was hypothesized that SARS-CoV-2 induces an IFN-I mediated antiviral response, leading to tissue damage.

Proposed dose for COVID-19:

IFN-beta is that the most relevant IFN-I that ought to incline as early as doable to optimize antiviral medical care and avoid complications from the virus.No specific dose has been valid, particularly for COVID-19. the final dosing guideline is being followed.[5]

Ayurvedic:

From an Ayurvedic perspective, COVID-19 is a janapadodhwamsa vikara (epidemic disease). The concept of epidemic is described in the Charaka Samhita: Vimana Sthana even though there is a difference in the physical constitution of human beings, there are still such factors which are common to all individuals and the disturbance of these factors leads to the simultaneous manifestation of a disease having the same set of symptoms leading to the destruction of countries. The factors common to all inhabitants of the earth are air, water, location and season. Janapadodhwamsa is a situation where the environment-air, water, land and seasons - is damaged, causing simultaneous manifestation of disease among large populations (epidemic), destroying Human Habitations. In India, the treatment of Chikungunya virus epidemic using Ayurvedic and Siddha medicines is preferred. However, there is no attempt to use Ayurvedic medicines directly in India treatment of coronavirus disease. In this context, we provide this case study where a patient with coronavirus disease tested positive in New York was fully treated with Ayurvedic medicines to get complete relief from his symptoms. It is worth emphasizing here that all three drugs used in the treatment of COVID-19 are classic preparations. The modes of action of each according to the texts are as follows:Sudarsana Churna: Alleviates all three doshas; cures all types of fevers including Agantuja jwara, Sannipata jwara etc., Dhanvantara Gutika: cures Svasa, Kasa; Vaataanulomana (facilitates normal flow of vayu), Talisadi Churna: cures Jwara, svasa, kasa, aruchi (loss of taste); Deepanam (stimulates digestion).[6]

Allopathy and homeopathy:

Position of Homeopathy and Ayurveda in COVID-19:

From the ultimate two hundred years in the late 1700s, a German doctor named Dr. Samuel Hahnemann founded the homeopathy as a therapeutic remedy which helped to deal with many epidemics, frightened, and intense illnesses like cholera, fever, chikungunya, hepatitis, and malaria. The preventive measures of homeopathy are eminent and plain; as homeopathic medicines act remarkably on a fitness condition and therapy the illnesses. The medical literature related to homeopathy is exceptionally witnessed. there are various confirmations that inside the year 1918–1919, while Spanish flu emerged, homeopathy had proven outstanding consequences, all through which round about 21 million sufferers died around the world and approximately 5,00,000 in the america alone. A observe discovered that there was a distinction within the mortality rate the various patients which had been dealt with through homeopathy and physicians, i.e., 1–2% seemed in another way as they had been handled with the aid of homeopathy as examine to 50–60% of patients who had been treated with the aid of allopathic. In homeopathic treatment, each patient after being fully diagnosed and analyzed acquired drugs. The scientific grounds of homeopathy have a clean protocol of sanitation, antibiotics, and vaccinations to control the infections . In illnesses like dengue which reasons hemorrhagic fever, homeopathy has helped in enhancing the platelet matter and consequently there is a slowdown inside the medical center for approximately 2–three days. Likewise, there are many illnesses in which homeopathy has acted as a buffer or manage to decrease the mortality rate via approximately 15–16% conversely with the individuals who got certainly institutional management. So, by way of searching on the beyond history, it can be found that there are many times wherein homeopathy had proven notable outcomes and it may be equivalently used for the COVID sufferers but no have a look at has shown its results on Covid-19. The homeopathic medicines like Belladonna 3c, Eupatorium perfoliatum Q, Grindelia, Calcarea carb, Chinimum sulph, Bryonia, Gelsemium, Phosphorus, Thymulin, Camphora, Influenzinum, Antim tart, and a combination of few tinctures and homeopathic capsules show to have a high rate of frequency to lessen excessive ache, pain, and many greater ailments in viral diseases. There were numerous individuals who were infected by means of the virus and confirmed revolutionary circulation in their records in China's Wuhan village in December 2019. The name of the homeopathic therapies was previously reported to prevent viral infections that are presented henceforth. Arsenicum album is shaped whilst for continuously 2–3 days arsenic is heated with distilled water. On the premise of the fact sheet released via the CCRH **(**Central Council for research in Homeopathy), Arsenicum album 30 may be considered as "prophylactic medication" COVID-19. The inflammatory signs proven via COVID-19, Arsenic toxicity, and HIV infection are the same and there's a definite synergy between them and may have the correct capability to aggravate each other. Consequently, Arsenicum album can be taken into consideration as a suitable treatment for COVID-19 remedy. Arsenic is one of the ingredients in it which showed its enumerating effect on the exclusive macrophage cells as properly on tumor cells. Additionally, it confirmed reduced NF-κβ hyperactivity (nuclear factor kappa light-chain-enhancer of activated B cells; faded verbalization of reporter pleasant of inexperienced fluorescent protein (GFP) in transfect HT29 cells) and decreased TNF-α (tumor necrosis aspect-alpha) launch in macrophages. Arsenic album-30 turned into advised to be taken as soon as in an afternoon for 3 days. The tincture of album- 20 is arsenic trioxide that's enormously diluted and it really works to prevent disorder. The proposed mechanism of motion of Arsenicum is proven there's no clinical proof for homeopathy remedy as a drug for COVID19 remedy . moreover, for extra than 3000 years, Ayurveda, a Sanskrit phrase, originated in India. In recent times, it's far considered as a traditional gadget of drugs which helps in the management of infection and maintains the homeostasis of ailment. It additionally allows in building the strength of the thoughts and soul, and teaches the frame to combat in opposition to pressure. throughout COVID-19, Ayurveda is also playing a crucial role because it has enough possibilities and ability for the prevention of infection and remedy for corona victims. The asymptomatic cases in India assist in enforcing the position of Ayurveda, through the ordinary use of Ayurveda medicines and domestic remedies. However nonetheless, the affirmation imagined through traditional chinese remedy (TCM) can't be unnoticed in China . This is immediately understood that at the time of the pandemic, about 3100 TCM-associated employees had been passed directly to the Hubei district. TCM become officially regular with the aid of the chinese tenet on quit and used as a treatment for COVID-19. That is especially essential to look at that precise TCM wards have been installation, and quarantine facilities were evolved which had used chinese drugs for treatment using western medicinal drug. With the accomplishment of TCM in controlling an infectious pandemic, it changed into affordable and principal to look at how Ayurveda can assist in treating COVID-19. Via this time, it turned into the Ministry of AYUSH which created a standard to change Indian social safety and to reveal the electricity of AYUSH to build up prosperity. With this ultimate goal of AYUSH, Ayurveda throughout the COVID-19 pandemic, human beings were divided into four unique classifications along with characters and natural herbs for remedy that is tabulated. This category has huge important facts which turned into entire and properly controlled. Eventually, it is advised that proper data of factors which are critical must be accomplished on each case. These variables should incorporate age, sex, manifestations, topography and contact history which results in a clear prescription and should be recorded. On the other hand, TCM did not control COVID- 19 cases. Equivalent philosophy was also adopted and has been used in Ayurveda and it should pursue its own skill for finding and coming about remedies optional on roga and rogi bala.[1]

Role of Allopathic in COVID-19:

Inside the allopathic technique, treatment in coronavirus covered intravenous infusion of fluid, oxygen therapy, and lifestyles assist device in critical instances. It became recommended if all and sundry prevails signs and symptoms of the virus like flu, fever, and breathlessness, they should contact the health practitioner right now. This virus is much like the human immunodeficiency virus (HIV) in terms of virus replication and proteins. exclusive administrating capsules had been found to clear and handle in vitro movement in opposition to SARS-CoV and MERS-CoV.[1]

Treatment approach for child in critical conditions:

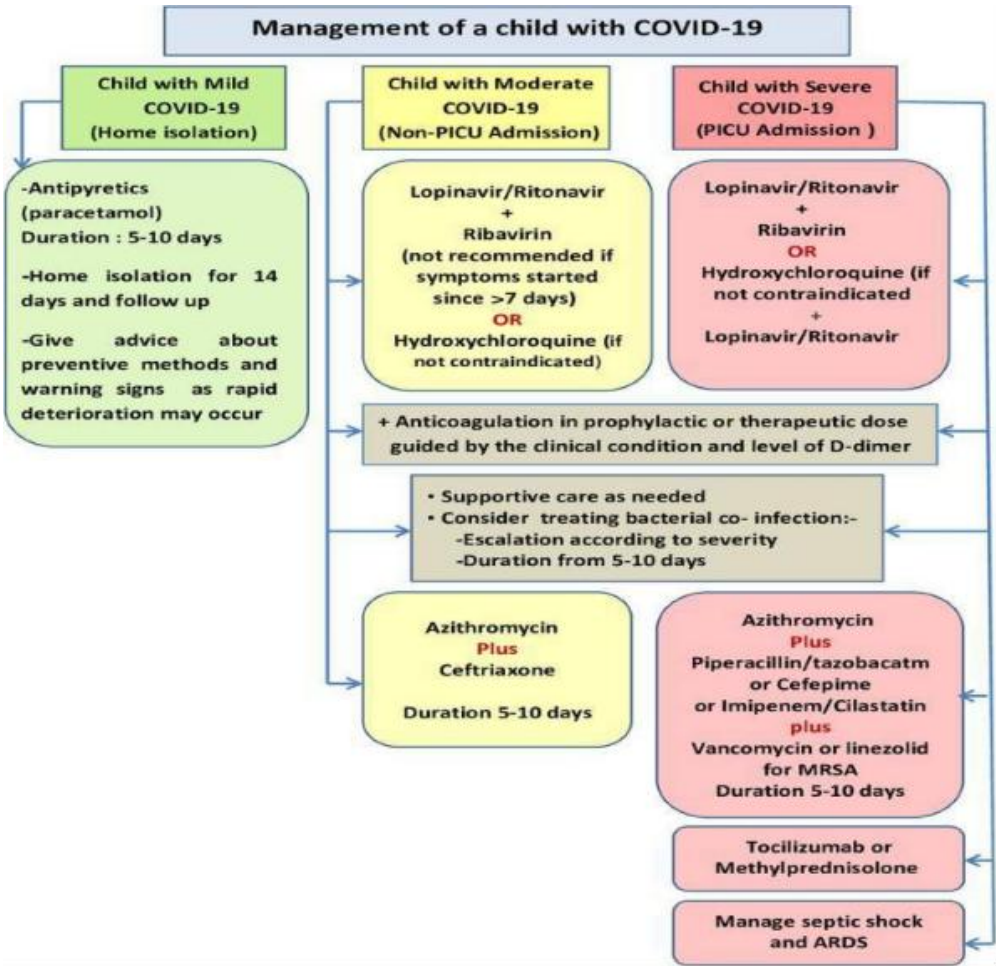

Fig. Treatment approach for child in critical conditions [7]

Conclusion:

Antiviral agents are helpful to inhibit the clinical progression and complications of COVID-19. Future studies are required to spot specific targets that inhibit the life cycle of SARS-COV-2 to forestall its replication which, if used early, might avoid the characteristic complications of COVID-19. COVID-19 is considered as pandemic worldwide and spreading at an alarming fee. therefore, it's been important to explore diverse techniques to overcome the impact of this dreadful viral sickness. This assessment summarizes the utility of presently opted treatment options for COVID-19. No appropriate remedy islocated to exist currently for this virus contamination. The hastily growing affected person's statistics of COVID-19 is triggering clinical groups to return forward to increase a few viable remedy. The maximum reassuring treatment is considered to be remdesivir. This drug is known to possess strong antiviral interest as confirmed by means of numerous in vitro studies. Alternatively, homeopathy and Ayurveda can be promising, however not applicable toward all styles of sufferers. consequently, the existing look at concludes that COVID-19 contamination may be averted throughfollowing authorities tips and opting immune-boosting Ayurveda routes.

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