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COVID-19 (NOVEL CORONA VIRUS) :- AN OVERVIEW OF DRUG THERAPIES USED TO TREAT COVID 19 GLOBALLY TILL NOW

Medicine

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ABSTRACT

Corona virus disease (Covid -19) – A challenging issue to health sector globally . First broke out in Wuhan, china in December 2019 & spread globally . Currently no specific medication or vaccine proven to be effective to prevent covid-19 infection. As a epidemic spread, scientist and doctors around the world are actively exploring drugs, that would be potential effective in treating Covid-19 infection . The efficacy and safety of the drugs in treatment of covid-19 infection need to be confirmed in further clinical trials. Each country is formulating there own guidelines for the management of covid -19 infection .we will have a gross outlook of few drugs which were used in treatment protocol by various countries to treat covid-19 infection.

KEYWORDS

Covid-19 , drugs, treatment , Vaccine, Trials , Protocols…

INTRODUCTION :

Corona Virus disease (Covid -19) is a new strain of corona virus discovered in Wuhan, china in 2019 and latter spread world wide. First case of Covid-19 was detected on Jan 30th 2020 in India. Common signs of infection include fever, running nose, cough, sore throat , shortness of breath . In severe cases infection may cause Pneumonia, SARS , Respiratory failure & Multi organ failure. It has been noticed that few of patients also having Gastrointestinal symptoms. Currently there are no specific medications or Vaccines proven to be effective to prevent Covid-19. The novel corona virus uses the same receptor – Angiotensin converting enzyme-2 /ACE 2 as that of SARS-Cov, and mainly spreads through respiratory tract. Elderly people and immuno compromised people like TB, HIV, Cancer, Transplant patients etc.. are most affected group. They may be associated with ARDS and Cytokine storm. In this paper we will discuss about the tentativedrugs used globally for the management of Covid -19 infection.(1)

Name of Drug	Dose	Route of Administration
Chloroquine / Hydroxy chloroquine (HCQ)	500mg / 400mg twice daily for 1 day followed by once a week	Oral route .
HCQ + Azithromycin	400mg / 500mg once daily	Oral route
Lopinavir / Ritonavir	200mg /50 mg - 2capsules each time / 2 times a day	Oral route
IFN-Alpha	5 million Units -2 times daily	Vapour inhalation
Ribavarin	500 mg each time- 2 to 3 times dailyin combination with IFN-Alpha or Lopinavair /Ritonavir	Intra Venous Infusion
Arbidol	200 mg each time , 3 times daily	Oral route

Newer drugs Therapies showing promising results are :-
1. Favipiravin
2. Remdesivir
3. Convalescent Plasma

1. Chloroquine :-

Chloroquine and Hydroxychloroquinine (HCQ) Receiving Intense attention because of positive results in small studies. Chloroquine has been sporadically used in treatment of SARS-Covid infections. HCQ Share same mechanism of action as chloroquine (2) , widely used in Rheumatology issues . As it is more tolerable, safety profile makes it preferable drug. The immunomodulatory effect of HCQ also usefull in controlling cytokine storm, that occurs in critically ill patients. In combination with other anti inflammatory functions , we predict that drug has a good potential to combat the disease .

Viruses are surrounded by lipid envelope which binds to plasma membranes of target cells , by attaching to specific protein on cell surface. These viruses are then internalized by receptor mediated endocytosis & delivered to lysosomes . At acidic PH membrane surrounding virus fuses with membrane of lysosome allowing nucleic acid of virus to cross lysosomal membrane and enters to cytoplasam , where virus replicates. Certain strains of Influenza virus can be prevented by Chloroquine. An agent that blocks the functions of Lysosomes. Chloroquine is a weak base that diffuse in to lysosomes and becomes protonated by raising the PH and Ionic strength of Lysosomes when PH raises lysosomal enzymes fail to function. Viruses that require Acid PH to fuse with cell membrane can no longer do so in presence of chloroquine and cells are protected from infection.

Based on the available evidence so far, However (Including Invivo&Invitro studies) considering the benefit risk ratio as well as cost effectiveness of Chloroquine / HCQ seems to have some promising role in management of Covid -19 infected patients. In India – Based on ICMR- Indian council of medical research prophylaxis guidelines(3) – prophylaxis can be taken by high risk exposure people like Medical and health care professional and Paramedic staff in following mentioned ways :-

1. Hydroxy Chloroquine 400 mg twice daily for 1st Day & then 400 mg once a week for 7 weeks.

Keep an eye on side effects :-

1. Hypoglycemia in Diabetic patients .
2. HCQ should not be used in combination with Lopinavir / Ritonavir & Remdisivr

Contra Indications of Prophylaxis :-

1. Children less than age of 15 yrs
2. Retinopathy , Hypersensitivity to HCQ
3.Role of Combination of HCQ + Azithromycin(4) :-

Synergistic combination of HCQ + Azithromycin shown to be active in Vitro against Zika , Ebola Viruses and prevented severe Respiratory Infection ,when administered to patients suffering viral infections .

This combination has to be furthur explored whether this combination is more effective especially in severe cases. This combination acts as both Anti Viral Therapy and prevents Bacterial super added infections.

Well controlled French clinical study conducted by Bidier Raoult MD / Phd etal in france published in International Journal of Anti microbial agents has found some early evidence , reveals that patient received combination of HCQ & Azithromycin , reduce the duration of viruses in patients . As it is a limited study and small sample size , yet results to be confirmed by the other big trials . One major drawback of this combination is – both drugs prolongs QT Interval in ECG , Which provokes Arrhytmia.

3 .Intereferon –Alpha(5) :-

- Vapour Inhalation used at dose of 5 million units – twice daily dose.

- Broad spectrum Anti viral used in Treatment of Hepatitis
- Reported to inhibit SARS-COVID Reproduction –Invitro

4.Lopinavir / Ritonavir(6) :-

- HIV Protease Inhibitor.
- Used in HIV. Has some Anti-SARS-COV Activity in vitro and shown to show some results in some clinical studies
- 200mg /50 mg capsule – 2 capsules each time / 2 times a day .
- This combination doesn't seems to be effective as per the latest published data in NEJM – March 2o2o.
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- **5 . Ribavirin(6) :-**
- Nucleoside analogue with broad spectrum of anti viral effects.
- A study shows that combination of Lopinavir / Ritonavir + Ribovarin has low risk of ARDS & Deaths, when compared to monotherapy.
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- **6. Arbidol(7) :-**
- Antiviral used to treat Influenza virus .
- Effectively inhibits SARS-Covid infection .(200 mg 3 times a day –Oral dose)

- **7. Favipiravin(8) :-**
- Drawing attention . Approved for treatment of Covid-19 from Feb 15th 2020 in china.
- New type RNA Dependent RNA Polymerase inhibitor. This drug is undergoing clinical trial in treatment of covid-19.
- Anti Influenza activity + Blocks Replication + Inhibits RNA Polymerase activity
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- **8.Remdesivir(9) :-**
- Clinical trial going on in china and USA & Its preliminary results may come out soon. SOLIDARITY Trial showing Remdesivir has best potentials.
- Nucleoside Analogue with Broad spectrum Anti viral activity
- 200 mg initial dose followed by 100 mg for 9 days –Intra Venous
- Yeilding promising results in treatment of patients with Covid 19 infections.
- It reduces the viral load in lung tissues & improves lung functions

9 .Convalescent Plasma:-

Experimental therapyin New York , United states going on for Covid - 19 infected patients . They uses blood from people who recover from disease . Takes advantages of virus fighting antibodies present in people blood after they recover from illness. For trial researchers they would collect plasma ,Liquid portion of blood. It do not include blood cells , platelets . These antibodies then be injected in to critically ill covid-19 infected patients. The study researchers then evaluate whether plasma improves any disease outcome.

No specific Anti viral Drug or Vaccine is available for covid -19 Infection. United states recently declared a vaccine by name M – RNA 1273, It is undergoing its Phase -1 clinical Trial in united states . In an era it may take around 12 -17 months for developing an effective vaccine against Covid-19 Infection.

Critically important studies emerging from china suggest that many patients who die of Covid-19 may be their own immune system rather than the virus itself , that deals the fatal blow . This is called Cytokine storm . During cytokine storm excessive immune response damages healthy lung tissue , leading to Acute Respiratory Distress leading to Multi organ Failure. Cheap , quick , readily available serum ferritin blood test can be done to screen for Cytokine storm syndrome in sick patients with fever. It can be treated with drugs Targeting Interlukin-1, 6 and eighteen / Interferon Gamma.

CONCLUSION :-

The current outbreak of covid-19 has globally spread all over world over a short period of time. Confirmed cases increasing day by day , inspite of strict rules imposed by the governments all over world. Mainly affecting Elderly people above 55 years with immuno compromised status .scientist all over the world are actively trying to explore new drugs that would be potentially effective in treatment of covid-19 infection. Till now unfortunately not even a single drug or vaccine is available for covid-19 infection, inspite of many efforts . The safety and efficacy of above mentioned drugs towards covid-19 has to be furthur confirmed in furthur clinical Trials.

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