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REVIEW ON WHO RECOMMENDED AND FDA AUTHORISED DRUGS FOR TREATMENT OF COVID 19

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ABSTRACT:

COVID19 which is caused by the virus that affects the respiratory system leading to difficulty in breathing, head ache, loss of smell and taste, fever, dry cough, fatigue to the affected person. It also infects the healthy individual through the droplets of infected person. No antiviral agents are effective against COVID 19. During first and second wave of COVID 19 Antivirals such as Ivermectin, Remdesivir, Ritonavir, Lopinavir and Antimalarials such as Hydroxychloroquine was administered for number of patients who are suffering with COVID 19 but these drugs does not decrease the replication of SARS COV virus and no relief to the patients from the symptoms and no decrease in mortality rate after use of Antivirals and Antimalarials. Still, clinical trails are going on for certain medications such as Janus kinase Inhibitors, Monoclonal antibodies, IL 6 inhibitors, Steroids which are recommended by WHO and drug (oral pills) Paxlovid, Molnupiravir (presently reviewed by Health Science Authority) which was authorised by US FDA. This review article contains the Medications, Mechanism of action, Dose, Dosage form, Frequency, Drug interaction of Paxlovid, Contraindications and Use of drugs based on severity of infection and Information on clinical trials of paxlovid. **No antiviral agents are effective against COVID 19.**

KEY WORDS:

COVID19, Janus kinase inhibitors, Monoclonal antibodies, IL6 Inhibitors, Steroids, Paxlovid, Molnupiravir

I. INTRODUCTION:

- **WHO Recommended drugs for COVID 19:**

1.JANUS KINASE INHIBITORS:

Mechanism of Action: Inhibits activity of Cytokines because over activity of cytokines causes potential death.

Name of Drug	Dose	Route of administration	frequency	Effect of drug
Baricitnib	4mg	Oral	OD	Strong
Ruxolitinib	5mg	Oral	BD	Weak
Tofacitinib	10mg	Oral	BD	Weak

Janus kinase Inhibitors are expensive and given for patients who are severely infected with corona virus given for 14 days. Tofacitinib which is having weak effect on virus and have shown Adverse events but is given when there is no availability of Baricitinib and IL 6 Receptor Inhibitors

2.INTERLEUKIN 6 INHIBITORS:

Mechanism of action: Inhibits the binding of IL 6 to IL6 receptors there by supressing the immune system because increase in IL6 levels causes respiratory failure and death

Name of drug	Dose	Route of administration	frequency	Effect of drug
Tocilizumab	800mg	IV (initial dose over 1 hr)	Second dose after 12-48 hrs of initial dose	Strong
Sarilumab	400mg	IV (initial dose over 1 hr)	Second dose after 12-48 hrs of initial dose	Strong

WHO recommends the arthritis drugs (Janus kinase inhibitors) such as Baricitinab for critical condition of COVID 19 that decrease the patient hospitalization and need for Mechanical ventilation but is expensive.

3.STEROIDS: Dexamethasone

Steroids recommended by Guideline Development Group (GDG) of WHO

Dexamethasone with a dose of 6mg given oral or IV with a frequency of OD for 7 to 10days having strong effect on Virus

Baricitinab(oral) along with corticosteroids(systemic) that supresses the immune system.

Baricitinab along with IL6 receptor blockers, on giving combination it may cause bacterial or fungal infection

4.MONOCLONAL ANTIBODIES: Casirivimab + Imdevimab Sotrovimab

Mechanism of action: Monoclonal antibodies show action against spike proteins of virus

Given to individual with mild to moderate symptoms of COVID 19 and can be administrated to patient if having any comorbidities.

- ✓ **CASIRIVIMAB+IMDEVIMAB:** 1200 to 2400mg of dose which is given IV/SC one off dose. If patient with serious condition dose is increased to 2400 to 4800mg, after drug administration patient is monitored for any allergic reactions.

The efficiency of monoclonal antibodies can be seen in patients with seronegative for antibodies of SARS COV2.

- ✓ **SOTROVIMAB:** 500mg of dose given IV infusion over 30 mins and patient was monitored for 1 hr after drug infusion. This drug has less adverse events

However monoclonal antibodies had shown less effect on virus but used as substitute in certain conditions

- After use of these medications the GDG of WHO had provided anevidence that JANUS KINASE INHIBITORS, IL6 RECEPTOR BLOCKERS, STEROIDS, MONOCLONAL ANTIBODIES has proven in decreasing the hospitalisation and mortality rate.

5.ANTIVIRALS such as **Remdesivir** with a dose of 200mg given IV for 1st day followed by 100mg IV daily for 3 days had shown severe adverse drug effects and Lopinavir which is used carefully in case of liver diseases, and not given to pregnant women and is having interaction with CYP3A inducers, given with a dose of 800mg combined with ritonavir of 200mg dose given orally in divided doses daily has shown side effects. Remdesivir is approved for use in COVID19 treatment for Children age group of more than 12yrs.

6.ANTIMALARIALS such as **Hydroxychloroquine** with a dose of 800 to 1600mg given orally for 1st day followed by the dose of 200 to 800mg for 5 to 21 days with 1 to 2 divided doses

- Antivirals and Antimalarials that are used in 1st and 2nd wave of COVID 19 had shown No or Mild improvement from the symptoms in hospitals and increased risk of adverse drug effects and now these agents are use as supportive care and is having weak effect

▪ **FDA Authorized Drugs for COVID19 Treatment:**

1.PAXLOVID:

Combination of Nirmatrevir and Ritonavir which is a ANTICOVID oral pill that had approved for use in Australia and Singapore. South Korea, Israel, Britain had started using the oral pill, WHO recommends the paxlovid and is authorized by US FDA for Emergency Use Authorisation (EUA)

Clinical Trails (randomised, Placebo-controlled study) conducted in 2085 patients who are suffering with mild to moderate symptoms of COVID 19 with age group of 18 to 88 years

Total of 1039 patients had taken paxlovid and 0.8% are hospitalized and no deaths Where as in placebo administrated patients of 1046, 6.3% are hospitalized and 12 deaths these results are given by Health Sciences Authority (HSA)

Mechanism of Action: Paxlovid targets at different site rather than on spike protein of virus. It is active against VOC such as delta and omicron

✓ **NIRMATRELVIR:** Blocks the activity of SARS-COV-2 (3CL), protease inhibitor, an enzyme which is responsible for replication.

✓ **RITONAVIR:** An HIV-1 Protease/CYP3A inhibitor that increases half-life of nirmatrelvir

Availability of paxlovid is from 21 April after DCGI approval to launch the drug

WHO recommends the Pfizer oral pill paxlovid that contains 3 tablets out of which 2 tablets are nirmatrelvir(150mg) and 1 tablet is ritonavir(100mg) given orally twice a day for 5 days, this medication will work on patients who are suffering with mild to moderate symptoms of COVID-19 and detection of virus within 5 days after its entry into the body and decrease the severity and hospitalization and is having strong effect on virus and is having mild side Effects

SIDE EFFECTS: Vomiting, Diarrhea, Hypertension, Muscle pain, Alteration in taste, Chills

DRUG INTERACTIONS:

- Anticonvulsants decreases the effectiveness of the paxlovid
- Antiarrhythmic agents, Anti hypercholesterolemic agents, migrane medication may increase the side effects

CONTRAINDICATIONS

- Pregnancy, Children, Breast feeding
- Paxlovid is not effective against severe infection, and as prophylaxis

2.LAGEVRIO:

Molnupiravir administered at a dose of 800mg given orally for 5 days having no Adverse effects and is having weak effect on virus. HSA is still reviewing on this medication regarding whether the drug decreases the hospitalization stay of patient and severity of virus

Mechanism of Action:

Lageviro stops the viral replication thus making the virus difficult to survive in the body, causing death of virus.

II. CONCLUSION:

It's better to get vaccinated even the mediation which are effective against the virus, as vaccines are effective against COVID 19. If vaccinated person infected with COVID 19 the symptoms are mild to moderate which can be cured with Monoclonal antibodies, IL 6 receptor blockers, Corticosteroids, Janus kinase inhibitors, Plaxovid are effective against mild to moderate symptoms of COVID 19 and recovery rate for the vaccinated patient is very high.

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