

Ivermectin



Introduction

Ivermectin is used to treat certain parasitic roundworm infections thus improving the quality of life.

It is a Food and Drug Administration (FDA)-approved antiparasitic drug that is used to treat several neglected tropical diseases, including onchocerciasis, helminthiases, and scabies.

Ivermectin is also being evaluated for its potential to reduce the rate of malaria transmission by killing mosquitoes that feed on treated humans and livestock.

For these purposes, Ivermectin has been widely used and is generally well tolerated.

Ivermectin is not approved by the FDA for the treatment of any viral infection

It is an extremely potent semisynthetic derivative of the antinematodal principle obtained from *streptomyces eremitish*.

Ivermectin is the **drug of choice** for single dose treatment of onchocerciasis and strongyloidiasis and is comparable to DEC for banfroftian and brugian filaria.

It is microfilaricidal but not macrofilaricidal.

It has been used as an add on drug to albendazole in heavy trichuriasis. Certain insects, notably scabies and head lice are killed by overreacting.

Classification

Antimicrobial- Antihelminthics-Antinematodal

Mechanism of action

Nematodes develop tonic paralysis when exposed to ivermectin. It acts through a special type of glutamate gated Cl⁻Channel found only in invertebrates .

Such channels are not involved in the motor control of flukes and tapeworms which are unaffected by ivermectin.

Potentiation of GABAergic transmission in the worm has also been observed.

The lack of GABA related actions in man could be due to its slow affinity for mammalian GABA receptors and its exclusion from brain by P-glycoprotein mediated efflux at the blood brain barrier.

Mechanism of Action and Rationale for Use in Patients With COVID-19(proposed)

Reports from in vitro studies have suggested that ivermectin acts by inhibiting the host importin alpha/beta-1 nuclear transport proteins, which forms the part of a key intracellular transport process that viruses hijack to enhance infection by suppressing the host's antiviral response.

In addition, ivermectin may interfere with the attachment of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein to the human cell membrane.

Ivermectin is thought to be a host-directed agent, which may be the basis for its broad-spectrum activity in vitro against the viruses that cause dengue, Zika, HIV, and yellow fever.

Despite this in vitro activity, no clinical trials have reported a clinical benefit for ivermectin in patients with these viruses. Some studies of ivermectin have also reported potential anti-inflammatory properties, which have been postulated to be beneficial in people with COVID-19.

Rationale for use in COVID-19

Ivermectin has been shown to inhibit the replication of SARS-CoV-2 in cell cultures.

However, pharmacokinetic and pharmacodynamic studies suggest that achieving the plasma concentrations necessary for the antiviral efficacy detected in vitro would require administration of doses up to 100-fold higher than those approved for use in humans.

Even though ivermectin appears to accumulate in the lung tissue, predicted systemic plasma and lung tissue concentrations are much lower than 2 μM , the half-maximal inhibitory

concentration (IC50) against SARS-CoV-2 in vitro.

Some clinical studies showed no benefits or worsening of disease after ivermectin use, whereas others reported shorter time to resolution of disease manifestations that were attributed to COVID-19 ,greater reduction in inflammatory marker levels, shorter time to viral clearance, or lower mortality rates in patients who received ivermectin than in patients who received comparator drugs or placebo.

However, most of these studies had incomplete information and significant methodological limitations, which make it difficult to exclude common causes of bias.

These limitations include:

- The sample size of most of the trials was small.
- Various doses and schedules of ivermectin were used.
- Some of the randomized controlled trials were open-label studies in which neither the participants nor the investigators were blinded to the treatment arms.
- Patients received various concomitant medications (e.g., doxycycline, hydroxychloroquine, azithromycin, zinc, corticosteroids) in addition to ivermectin or the comparator drug. This confounded the assessment of the efficacy or safety of ivermectin.
- The severity of COVID-19 in the study participants was not always well described.
- The study outcome measures were not always clearly defined.

Route of administration

This medication is taken per orally with a full glass of water (8 ounces or 240 milliliters) on an empty stomach at least 1 hour before a meal.

However administration of ivermectin with food increases its bioavailability

Dose

- 0.2 mg/kg single dose is highly effective in cutaneous larva migrans and ascariasis.
- For covid 19 -12 mg OD for 3 days

Side effects

- Diarrhea
- Headache
- Nausea
- Vomitting
- Dizziness
- Muscle pain

Precautions

- History of anaphylaxis
- The drug may make the person dizzy thus driving or operation of heavy machinery should be avoided

Interactions

Ivermectin is metabolised by CYP3A4 , but no drug interactions related to this isoenzyme are .

Ivermectin in pregnancy and children

Safety of ivermectin in pregnant women is not yet established.

Ivermectin is used in children weighing >15 kg for the treatment of helminthic infections, pediculosis, and scabies.

The safety of using ivermectin in children weighing <15 kg has not been well established.

Ivermectin is generally well tolerated in children, with a side effect profile similar to the one seen in adults. Currently, there are no available pediatric data from clinical trials to inform the use of ivermectin for the treatment or prevention of COVID-19 in children.

Missed Dose

If a dose is missed, it should be taken as soon as possible. If it is near the time of the next dose, skip the missed dose. Take your next dose at the regular time. Do not double the dose to catch up.

Storage

Store at room temperature below 86 degrees F (30 degrees C) away from light and moisture.

References

- KD Tripathi, textbook of medical pharmacology.
- <https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/ivermectin/>
- <https://www.webmd.com/drugs/2/index>