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Ivermectin

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Ivermectin is a Food and Drug Administration (FDA)-approved antiparasitic drug that is used to treat several neglected tropical diseases, including onchocerciasis, helminthiasis, and scabies.¹ It is also being evaluated for its potential to reduce the rate of malaria transmission by killing mosquitoes that feed on treated humans and livestock.² For these indications, ivermectin has been widely used and has demonstrated an excellent safety profile.¹

Proposed Mechanism of Action and Rationale for Use in Patients With COVID-19

Ivermectin acts by inhibiting the host importin alpha/beta-1 nuclear transport proteins, which are part of a key intracellular transport process that viruses hijack to enhance infection by suppressing the host antiviral response.³ Ivermectin is therefore a host-directed agent, which is the basis for its broad-spectrum activity *in vitro* against the viruses that cause dengue, Zika, HIV, and yellow fever.³⁻⁶

Recommendation

- The COVID-19 Treatment Guidelines Panel **recommends against** the use of **ivermectin** for the treatment of COVID-19, except in a clinical trial (**AIII**).

Rationale

Ivermectin has been shown to inhibit the replication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in cell cultures.⁷ However, pharmacokinetic and pharmacodynamic studies suggest that achieving the plasma concentrations necessary for the antiviral effect detected *in vitro* would require administration of doses up to 100-fold higher than those approved for use in humans.^{8,9} 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*.^{10,11}

Ivermectin is not approved for the treatment of any viral infection, including SARS-CoV-2 infection. The FDA issued a [warning](#) in April 2020 that ivermectin intended for use in animals should not be used to treat COVID-19 in humans.

Clinical Data in Patients With COVID-19

The available clinical data on the use of ivermectin to treat COVID-19 are limited.

Retrospective Analysis of Using Ivermectin in Patients With COVID-19

This study has not been peer reviewed.

This retrospective analysis of consecutive patients with confirmed SARS-CoV-2 infection (27% with severe COVID-19) who were admitted to Florida hospitals compared patients who received at least one dose of ivermectin (n = 173) to those who received "usual care" (n = 103). The primary outcome was all-cause, in-hospital mortality. The secondary outcomes included mortality in patients with severe disease (defined as "need for either FiO₂ \geq 50% or noninvasive or invasive mechanical ventilation") and extubation rates in those who were mechanically ventilated.

Results

- Ivermectin administration was reportedly consistent with hospital guidelines: a single dose of 200 $\mu\text{g}/\text{kg}$, with repeat dosing on Day 7 if the patient was still hospitalized (13 patients received a second dose). Ninety percent of the ivermectin group and 97% of the usual care group received hydroxychloroquine (the majority received hydroxychloroquine in conjunction with azithromycin).
- All-cause mortality was lower among the patients in the ivermectin group than among patients in the usual care group (OR 0.27; $P = 0.001$). The mortality benefit appeared to be limited to the subgroup of patients with severe disease.
- There was no difference between the groups for the median length of hospital stay (7 days in both groups) or the proportion of mechanically ventilated patients who were successfully extubated (36% in the ivermectin group vs. 15% in the usual care group; $P = 0.07$).

Limitations

- This was a retrospective analysis.

- The study included little or no information on oxygen saturation or radiographic findings. It was also unclear whether therapeutic interventions other than hydroxychloroquine, such as remdesivir or dexamethasone, were used in the study.
- The timing of therapeutic interventions was not standardized; if the timing is not accounted for, it can bias the survival comparison.
- The analyses of the durations of ventilation and hospitalization do not appear to account for death as a competing risk.
- No virologic assessments were performed.

Interpretation

The limitations of this retrospective analysis make it difficult to draw conclusions about the efficacy of using ivermectin to treat patients with COVID-19.

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