Opening a can of helminths: Ivermectin for COVID-19

CLINICAL QUESTION

Does ivermectin improve clinical outcomes in COVID-19?

BOTTOM LINE

The best available evidence does not show that ivermectin improves clinically important outcomes in COVID-19. Use in COVID-19 is discouraged.

EVIDENCE

- Focusing on quality randomized controlled trials (RCTs) and systematic reviews reporting patient-oriented outcomes and published in peer reviewed journals.
- Two large, well designed, double-blind, RCTs:
  - 400 patients with mild COVID-19 (at home or hospitalized without oxygen support) randomized to ivermectin or placebo for 5 days:\(^1\)
    - Time to symptom resolution:
      - Not statistically different: 10 days ivermectin, 12 days placebo.
  - 501 out-patients randomized to ivermectin or placebo for 2 days:\(^2\)
    - COVID-19 related hospitalization:
      - Not statistically different: Ivermectin 5.6% versus 8.4% placebo.
- High-quality living meta-analysis found no statistically significant impact of ivermectin on any clinical outcome.\(^3\)
19 RCTs with 2740 patients (outpatients and inpatients); primarily reported on surrogate outcomes (example viral load).

Clinical outcomes in outpatients at day 28:
- Clinical improvement: 2 trials (526 patients): No difference.
- All-cause mortality: 4 trials (1255 patients): No difference.

Formally published systematic review found similar.4

CONTEXT

- Most ivermectin trials are not published in peer reviewed journals, have small numbers of participants, are at high risk of bias, or only report on surrogate markers.3
  - One oft-cited “meta-analysis” which reported a benefit had no authors listed, included cohort studies, and had questionable conclusions regarding study quality.5
  - The study with the largest reported mortality effect (only available in pre-print), was retracted due to data integrity issues.6,7
- Of >14,000 COVID-19 pre-prints:
  - Only ~30% are published in peer reviewed journals one year later.8
  - Pre-print results and conclusions can change substantially when published as peer reviewed publication:
    - Example COLCORONA trial: Same results, different conclusions.
      - Preprint: “colchicine reduces the composite rate of death or hospitalization”.9
      - Publication: “effect of colchicine on COVID-19-related clinical events was not statistically significant”.10
- Despite the evidence, animal feed stores inundated with requests for ivermectin.11
- Poison control centers report increased calls for ivermectin toxicity.12
  - Toxicity symptoms may include nausea/vomiting, abdominal pain, diarrhea, headache, blurred vision, dizziness, and seizures.12

REFERENCES


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