IVERMECTIN IN THE PREVENTION AND TREATMENT OF COVID-19

A Summary Statement

By Rob Rennebohm, MD
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- History of IVM: In the late 1970s Dr. Omura, a Japanese microbiologist, discovered IVM. Its first use was as an anti-parasitic drug, starting in 1987 (36 years ago). IVM has nearly eliminated two terribly disfiguring and devastating diseases---river blindness and elephantiasis. 36 years of safety studies have shown IVM to be a remarkably safe medication. In 2015 Dr. Omura was awarded the Nobel Prize in Medicine for his discovery of IVM.
- Treatment of COVID-19 with IVM has been far more extensively and carefully studied than has treatment of COVID-19 with Paxlovid, Molnupiravir, or remdesivir.
    - More than 95 clinical trials (78 of which have been published in peer-reviewed journals)
    - More than 2 dozen RCTs showing benefit from IVM
    - Several Meta-analyses of RCTs showing benefit from IVM
    - Many OCTs (observational controlled trials) showing benefit from IVM
    - Many published reports of successful widespread government-sponsored IVM distribution programs (in Peru, Argentina, Paraguay, Brazil, Mexico, Honduras, India, and the Philippines, e.g.)
    - In vitro studies: for example, Caly et al, have demonstrated that a single addition of IVM to Vero-hSLAM cells 2 hours post infection with SARS-CoV-2 resulted in a 5000-fold reduction of viral RNA at 48 hours---i.e., completely eliminated the virus by 48 hoars, suggesting that it is virus-cidal. (See more details about the Caly study, including a diagram about its possible mechanism of action, at the end of this article.)
    - Since 2012 there have been at least a dozen published in vitro studies showing that IVM is a broad spectrum antiviral agent. It has been shown to stop replication of at least ten different viruses---e.g., influenza Zika, West Nile, influenza, HIV, now SC-2---all RNA viruses.
- In contrast, Paxlovid and remdesivir were granted Emergency Use Authorization (EUA) based on 1 RTC, each. The "rebound" phenomenon seen with Paxlovid suggests that it is probably virus-static, rather than virus-cidal. And prophylactic use of Paxlovid has been shown to be of no benefit (not to mention its impracticality and probably unsafe use as a

prophylactic agent for COVID-19). Whereas leaders of the prevailing COVID-19 narrative have heavily promoted Paxlovid for routine use in treatment of COVID-19, they have portrayed prescription of IVM as ridiculous and irresponsible use of a "horse dewormer."

- Studies of the efficacy of IVM treatment of COVID-19 (RCTs, meta-analyses, observational clinical trials, in vitro studies, animal studies, and analyses of widespread IVM distribution programs) have suggested that that, overall, the efficacy of IVM is at least comparable to the efficacy of alternative anti-viral therapies (Paxlovid, Molnupiravir, and remdesivir) and is more effective (and far more practical) than Paxlovid when used in the critically important prophylactic treatment of COVID-19. Unfortunately, no RCTs have been conducted to compare IVM with Paxlovid (or Molnupiravir or remdesivir) head-to-head. It is obvious that the leaders of the prevailing COVID-19 narrative should have and could have carefully and honestly conducted such head-to-head studies long ago, if they truly cared about treating COVID-19 in the best possible way. It is also unfortunate that the pro-Paxlovid studies and the anti-IVM studies that have been referenced by the promoters of the prevailing COVID-19 narrative have been rife with conflict of interest and have been of questionable quality.
- The efficacy of the widespread IVM distribution campaign noted in Uttar Pradesh deserves particular mention. Uttar Pradesh (UP) is a state in northern India with 231 million people. The Chief Minister of UP was a Hindu monk named Yogi Adityanath. In mid-2020 UP started treating all close contacts of COVID patients and all health workers with prophylactic IVM---as well as treating all COVID patients with early IVM treatment. They noted impressive results. Prior to launching this initiative, their state had the 16th lowest death rate in India. Three months later they had the 6th lowest death rate, and 2 months after that they were noticing almost no deaths.

  By the summer of 2021 COVID appeared to be eradicated from UP. Cases had become very rare. Only 0.004 % of tests for COVID were positive in UP. In contrast, in Kerala, where IVM had been rejected, 19.7% of tests were positive for COVID at that same time.

  WHO tried to attribute the UP success to vaccination and did not mention UP's use of IVM. But only 10% of UP citizens were fully vaccinated.

  Other states in India had started using prophylactic HCQ for health care workers, starting in March 2020. The Indian Council of Medical Research promptly conducted a trial and found that prophylactic HCQ reduced infection rates by up to 80% in these health care workers. This prompted an eventual visit to India by Bill Gates in September 2021. Perhaps, India was having too much success with HCQ and IVM? Two days after his visit both IVM and HCQ were dropped from India's national guidelines.

Similar IVM distribution programs in Mexico, Argentina, Brazil, Paraguay, Peru, and the Philippines have also appeared to show impressive success.

- The experience of widespread IVM distribution campaigns in Peru also warrants special mention. From April 1, 2020, until October 31, 2020, a mass IVM distribution program was initiated in 8 Peruvian states---but not in the highly populated city of Lima, whose city government rejected use of IVM. Peru's IVM distribution program was associated with a massive reduction in cases and deaths. The case fatality rate (CFR) plummeted in the 8 states that implemented use of IVM. The CFR in Lima was far worse.

  Specifically, excess deaths fell by a mean of 74% in the states that implemented a widespread IVM distribution program. Excess deaths decreased 14-fold during the IVM distribution program and then increased 13-fold after IVM distribution programs were discontinued when a new (anti-IVM) President took office in Peru.

- The safety of IVM has been established to a far greater extent (36 years of experience) than has the safety of Paxlovid, Molnupiravir, or remdesivir. IVM is extremely safe. In comparison, Paxlovid, Molnupiravir, and remdesivir are very new and far less safe.
- IVM is inexpensive. Paxlovid, Molnupiravir, and remdesivir are very expensive.
- The leaders of the prevailing COVID-19 narrative have deliberately, unscientifically, unethically, and wrongly demonized and ignored IVM, and, appallingly, have punished and even delicensed physicians who have sought to help patients by prescribing IVM.
- It is high time for physicians to stop being hesitant, defensive, and afraid to even mention IVM as a treatment option (out of fear of being ridiculed or punished by their colleagues, administrators, or friends). It is time for physicians to confidently state that IVM is our best, most scientifically-sound anti-viral option for COVID-19--- when safety, cost, practicality, availability, the extent of scientific study, quality of studies, honesty, and extent of conflict of interest are taken into account. It is the physicians who have been prescribing Paxlovid (and certainly remdesivir and Molnupiravir) who should be feeling hesitant and defensive about promoting use of Paxlovid, Molnupiravir, and remdesivir and embarrassed to have belittled, demonized and ignored IVM. Physicians who have refused to prescribe IVM and pharmacists who have refused to fill such prescriptions should think about the effects of that behavior on patient care---not only on an individual patient level, but also on a population level and a global level.
- At the same time we must realize that all of the available anti-viral therapies, including IVM, are of limited value. The relative risk reduction reported in studies with all of these anti-viral therapies, including IVM, has often been quite modest.
- It is noteworthy, however, that Dr. Omura, who was awarded the Nobel Prize for his discovery of IVM, strongly endorses the use and further study of IVM for COVID-19. In

fact, the people who have been most enthusiastic about the use of IVM for prophylaxis and early treatment of COVID-19 have been the physicians who have actually treated large numbers of COVID patients with IVM. There is still a place for clinical judgment in medicine. Thoughtful analysis of clinical experience needs to be honored.

FURTHER DETAILS ABOUT THE IN VITRO STUDY BY CALY ET AL:

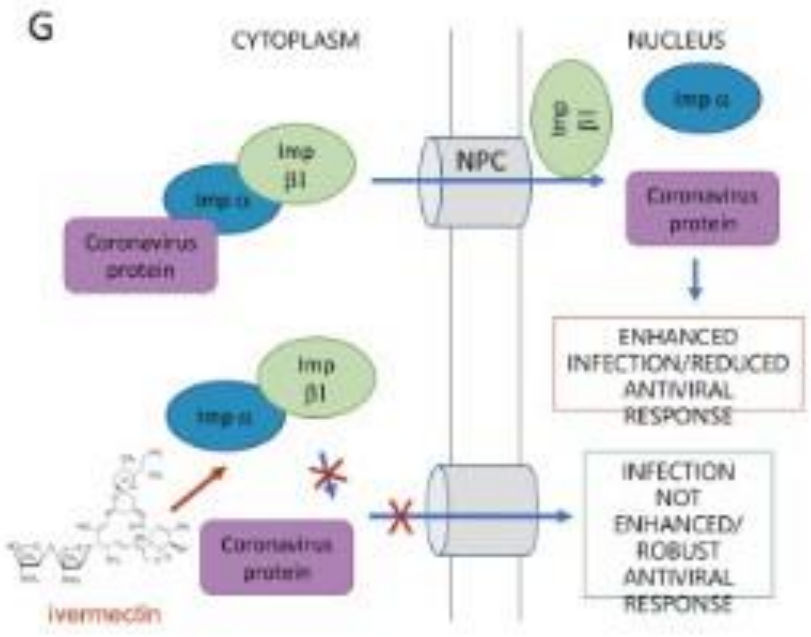
Leon Caly, Julian D. Druce, Mike G. Catton, David A. Jans, Kylie M. Wagstaff.
The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro.
Antiviral Research, Volume 178, 2020, 104787, ISSN 0166-3542,
https://doi.org/10.1016/j.antiviral.2020.104787.
(https://www.sciencedirect.com/science/article/pii/S0166354220302011)

Abstract: We report here that Ivermectin, an FDA-approved anti-parasitic previously shown to have broad-spectrum anti-viral activity in vitro, is an inhibitor of the causative virus (SARS-CoV-2), with a single addition to Vero-hSLAM cells 2 h post infection with SARS-CoV-2 able to effect ~5000-fold reduction in viral RNA at 48 h. Ivermectin therefore warrants further investigation for possible benefits in humans.

A single addition of IVM to Vero-hSLAM cells 2 hours post infection with SARS-CoV-2 resulted in a 5000 fold reduction of viral RNA at 48 hours---i.e., completely eliminated the virus by 48 hrs.

The authors propose that IVM to inhibits integrase protein (IN) and the Importin alpha/beta 1 heterodimer responsible for IN nuclear import.

As depicted in the drawing below, IMPα/β1 binds to the coronavirus cargo protein in the cytoplasm (top) and translocates it through the nuclear pore complex (NPC) into the nucleus where the complex falls apart and the viral cargo can reduce the host cell's antiviral response, leading to enhanced infection. Ivermectin binds to and destabilizes the Impα/β1 heterodimer thereby preventing Impα/β1 from binding to the viral protein (bottom) and preventing it from entering the nucleus. This likely results in reduced inhibition of the antiviral responses, leading to a normal, more efficient antiviral response.



The authors hypothesize that the beneficial effect of IVM is likely through inhibiting IMPα/β1-mediated nuclear import of viral proteins, as has been shown for other RNA viruses. This probably represents only one of several possible mechanisms by which IVM inhibits SARS-CoV-2.

FURTHER READING:

Please see the extensive discussion of IVM on the FLCCC website:
https://covid19criticalcare.com/treatment-protocols/

Also, see:

Pierre Kory's important book, ***The War on Ivermectin***.

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