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INCONCLUSIVE ROLE OF IVERMECTIN IN THE TREATMENT OF COVID -19 MANAGEMENT

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ABSTRACT

From 2019 till 2022 the world is facing a unwanted pandemic corona or SARS, Covid-19 from starting of this disease doctors are doing their best to fix this virus. In this connection they use different types of medication to treat the patients. Ivermectin recently draws an attention internationally as a potential management of Covid -19.WHO recommend that the drug only be used within clinical trials and then recommendation which applies to patient with covid-19 of any disease severity is now part of WHO guidelines on Covid-19 treatment. There are insufficient data for the Covid 19 treatment guidelines panels to recommend either for or against the use of Ivermectin for the treatment of corona. Ivermectin is a drug which is known as broad spectrum, antiparasitic agent included in WHO essential medicine list for several parasitic disease it is used in treatment of 'Onchoceraciasis'(river blindness), strongyloides and other disease caused by soil transmitted helminthiasis. It is also used to treat scabes.

KEYWORDS: Ivermectin, broad spectrum, onchocerciasis, anti- parasitic agent.

INTRODUCTION

Ivermectin is a semi synthetic macrocyclic lactone,it is derived from streptomyces avermutilis a soil actinomycetes. It is a drug of choice for onchocerasis It acts by increasing the release and binding of gama amino butyricacid (GABA), thereby producing paralysis. Some gastrointestinal nematodes infecting man are also susceptible to ivermectin.thus it also appears to be highly effective in strongyloidasis, ascariasis, trichuriasis and enterobiasis it is less effective against hookworms.

Ivermectin is a semi synthetic derivative of avermectin B and consist of 80:20 mixture of the equipotent homologon 22,23 dehydro B 1a and B1b.This anti parasitic agent developed by Merck and Co. is frequently use under veterinary medicine due to its broad spectrum of activity, high efficacy and wide margin of safety.

The 1st formulation designed for human was launched in 1987 when Merck lab had enough data to register ivermectin for use against onchocerciasis. the company announced that the drug would be provided at no cost to treat onchocerciasis anywhere in the world for as long as it was needed. Ivermectin is used as repurposed medicine by a panel of doctors .An independent group which has international panel of experts clinical case experts in multiple specialities and also include ethicist and potential partner.

The group reviewed pooled data from 16 randomised controlled trials (total enrolled 2407) including both in patient and out patients with Covid -19.They determined that the evidence on whether Ivermectin reduces mortality, need mechanical ventilation, need for hospital admission and time to clinical improvement in Covid- 19 patients is of very low certainty, dye to small size and methodological limitations of available trials data including small number of events. The panel did not look at use of Ivermectin to prevent covid- 19 which is outside of scope if the current guidelines.

METHODOLOGY

Since the start of the covid- 19 pandemic both observational and randomized studies have evaluated that Ivermectin as treatment for and as prophylaxis against covid -19 infection concluding that Ivermectin" demonstrate a study signal of therapeutic efficacy "against covid -19.

Tracking

1. Gender distribution
2. Age distribution
3. Percentage of patients accompanying disease e.g. diabetes, B.P., Heart problems, COPD, Immunodeficiency, malignancy.
4. Percentage of patients with baseline clinical symptoms.

OBSERVATIONS

1. Change in SpO_2 value 0- 5 days Baseline, Primary end point 5th day reading
2. Change in serum lymphocytes countsBaseline. 1,3,5th day
3. Change in ratio of polymorphonuclear leukocyte count (PNL/L)
4. Serum ferritin level
5. Change in serum D-dimer level
6. Treatment related adverse events assessed by (TCAV4.0).*

Adverse effects of Ivermectin and other drugs are noted.
*NIH -national Library of medium clinical trials.gov.

Baseline Characteristics
Control group is that group which consists of patients who were hospitalized with a prediagnosis of severe Covid 19 pneumonia and thereafter diagnosis of Covid-19 was also confirmed microbiology Cally with PCR positivity in respiratory tract samples were included into the study.

They were randomized to the control and study group respectively hydroxychloroquine, favipiravir and azithromycene (HFA) standard treatment protocol were given to as recommend in the covid- 19 (SARS- COV -2) patients guide.

Study Group
In addition to HFA treatment, Ivermectin 200 micrograms .9mg/wt 36-50 kg,12mg

B/w 51 -65kg ,15 mg 66-79 kg & 20 mg to more than 80kg in the form of solution prepared for the external use was added HFA+I to the treatment protocol for five days to the study group. Blood sample was taken with the 1st 3rd and 5th dose of Ivermectin.

36 patients are included in the study group but 6 patient s from the study group were excluded from the study and analyse because ivermectin treatment were terminated due to detection of a mutation that impaired ivermectin metabolism as a result overall.

There is insufficient evidence for the use of ivermectin in covid -19 managment as reported from various studies.

Reports from in vitro studies suggest that ivermectin act by inhibiting the host importin alpha /beta -1 nuclear transport proteins which are part of a key intra cellular transport process that viruses hijack to enhance infection by suppressing the host 's antiviral response. In addition Ivermectin docking may interface with the attachment of the severe acute respiratory syndrome coronavirus -2 Spike protein to the human cell membrane. ivermctin is thought to be a host directed agent, which may be basis for the broad spectrum activity in vitro against the viruses that cause dengue, zila, HIV, and yellow fever .Despite this in vitro activity no clinical trials have reported a clinical benifits for ivermectin in patient s with these viruses. Some studies of ivermectin have also reported potential anti -inflamatory properties which have been postulated to be beneficial in people with covid -19.

Monitoring Adverse Effect and Drug Drug Interaction Ivermectin is generally well tolerated.adverse effects may include dizziness (itching) pruritis nausea or diarrhoea.

Neurological adverse effects have been reported with the the case of ivermectin for the treatment of onchocerciasis and other parasitic disease but it is not clear whether these adverse effects were caused by Ivermectin or the underlying conditions.

Ivermectin is a minor cytochrome P3 A4 substrate and a para glycoproteins substrate. Ivermectin is generally given by an empty stomach with water however administering ivermectin with food increase its bioavailability.

The FDA issued a warning in April 2020 that ivermectin intended for use in animal should not be used to treat covid-19 in human.

CONCLUSIONS
There is insufficient evidence for the covid-19 treatment guidelines panel to recommend either for or against the use of ivermectin for the treatment of covid-19. Result from adequately powered well designed and well conducted clinical trials needs to provide more specific evidence-based guidance on the role of Ivermectin in the treatment of covid-19. The panel did not look at the use of Ivermectin to prevent covid-19 which is outside the scope of the urgent guidelines so we see that the current evidence on the use of Ivermectin to treat covid-19 patient is inconclusive until more data to available WHO requirements that the drug may be used within clinical trials.

SUGGESTED READINGS

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