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RESEARCH ARTICLE

ROLE OF IVERMECTIN IN THE TREATMENT OF COVID 19

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Abstract

In vitro, ivermectin, an anti-parasitic drug licenced by the US Food and Drug Administration, was found to limit the replication of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).The three groups had similar clinical symptoms of fever, cough, and sore throat. When compared to the placebo group, virological clearance was faster in the 5-day ivermectin treatment arm (9.7 days vs 12.7 days; p = 0.02), but not in the ivermectin Plus doxycycline arm (11.5 days; p = 0.27). In the research, there were no serious adverse medication reactions. Adult patients with mild COVID-19 were treated with a 5-day course of ivermectin, which was proven to be both safe and efficacious. To corroborate these early findings, larger trials will be required.

Introduction:-

Ivermectin awell knownanti-parasitic agent, approved by US FDA which causes stimulation of gamma amino butyric acid(GABA)-gated-Cl−channels, leading to hyperpolarization, and resulting in paralysis of the infesting organism[1,2] In vitro Ivermectinhas shown its potent antiviral effects against several RNA viruses, such as Zika virus, Influenza A virus, Newcastle disease virus, Chikungunya virus, Yellow fever virus, Dengue virus etc[3]. It has been used to treat ecto and enteroparasitosis in children as young as 5 years old. In humans orally it does not cross the blood-brain barrier and It is contraindicated in pregnancy[4].Furthermore Ivermectin has shown promising benefits in the treatment of COVID-19 patients with a modest degree of severity in several national and international observational studies[5].

Sars-CoV-2

A single-stranded RNA virus known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes severe acute respiratory syndrome. SARS-CoV-2 which was later renamed COVID-19 and declared a global health emergency by the World Health Organization. The first known instance of illness was discovered in early December 2019 and has since spread to several continents, including the United States [6]

Ivermectin in the treatment of covid:

Ivermectin's anti-SARS-CoV-2 activity is thought to be based on its binding to the Imp/1 heterodimer, which causes it to destabilise and prevents Imp/1 from attaching to viral proteins. This inhibits viral proteins from entering the nucleus, lowering antiviral response inhibition and resulting in an effective antiviral response. After 2 hours of SARS-CoV-2 infection, Vero-hSLAM cells were treated with ivermectin, resulting in a 5000-fold reduction in viral RNA after 48 hours, according to Caly et al.The antiviral spectrum of ivermectin has been expanded by its in vitro

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antiviral efficacy against SARS-CoV-2.[7]combination therapy of hydroxychloroquine along with ivermectin is shown to have a synergistic inhibitory effect on SARS-CoV-2. In this combination, hydroxychloroquine acts by preventing the entry of SARS-CoV-2 into the host cells, whereas ivermectin further enhances the antiviral activity by preventing viral replication[7].Guzzo et al. showed that higher doses of ivermectin 120 mg (up to 2,000 μg/kg) given once or 180 mg (up to 3,000 μg/kg) given in split doses over 1 week are well-tolerated and safe[8]

Pharmacokinetics

Moderately well absorbed. Improved absorption with high fat meal.The volume of distribution is 3 to 3.5 L/kg and it does not cross the blood-brain barrier.Primarily hepatic. Ivermectin and/or its metabolites are excreted almost exclusively in the feces over an estimated 12 days, with less than 1 % of the administered dose excreted in the urine.Following oral administration, the half-life of ivermectin is approximately 18 hours.

Resistance

Resistance to ivermectin has become a major issue in many regions of the world, and it is expected to worsen as the use of anthelmintics in animals and humans increases. The expression of P-glycoproteins may provide resistance to ivermectin. P-gp, as it's popularly known, is a membrane protein that transports aromatic, hydrophobic medicines through cell membranes and into the cytoplasm. Drug resistance is thought to be caused by these proteins in mammalian tumour cells and parasites like Plasmodium falciparum.

P-glycoproteins may play a role in ivermectin resistance by binding to and transporting ivermectin out of cells. This notion is supported by research on Haemonchus contortus (a type of sheep worm). Many populations of H. contortus have been discovered to be resistant in the wild. In one study, ivermectin treatment resulted in greater amounts of P-glycoprotein mRNA in H. contortus strains compared to unselected strains. The structure of the P-glycoprotein gene was also altered in the therapy group. (Xu, Molento, and others, 1998)

Changes in the structure of the glutamate-gated chloride channel itself could be another way to confer resistance. Treatment with Ivermectin causes selection pressures on the gene for the alpha-subunit of the glutamate channel in H. contortus, according to at least one study.

Conclusion:-

Ivermectin exhibits broad-spectrum antiviral activity against, a variety of animal and human viruses, including both RNA and DNA viruses. As SARS-CoV-2 is an RNA virus. Ivermectin antiviral activity is mediated through the inhibition of importin α/β-mediated nuclear transport of viral proteins. Ivermecin's clinical efficacy against SARS-CoV-2-infected patients isunpredictable.

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