Clofazimine: another potential magic bullet for the treatment of COVID-19?

As of March 2020, the novel COVID-19 caused by SARS-CoV-2 was declared a pandemic. The novelty of the virus is the driving force for numerous clinical trials taking place in an attempt to discover appropriate therapeutic agents.[1] Many pharmacological agents have shown promising results, including clofazimine.[2 3] More recently, a prospective open-label randomised controlled clinical trial of dual therapy with interferon beta-1b and clofazimine for patients infected with COVID-19 is being conducted.

Clofazimine is licensed for use against mycobacterial infection and as an adjunct agent for the treatment of multibacillary leprosy. However, it has also proven to comprise immunosuppressive properties.[2] Therefore, we would like to outline a potential use for clofazimine in COVID-19 infections, where it could be a potential prophylactic and therapeutic agent in the management of critically ill patients.

The most important cause of mortality postinfection with COVID-19 is a cytokine storm leading to end organ damage from inflammation.[2] Thus, one of the main therapeutic treatments being used to increase survival, reduce inflammatory sequelae and decrease hospitalisation following COVID-19 pneumonia are anti-inflammatory drugs. Clofazimine is an antibiotic with anti-inflammatory properties, which can potentially be used for the treatment of COVID-19.[2 3]

In patients with severe infection leading to cytokine storm, the use of immunosuppressive agents has proven beneficial.[2 3] Indeed, clofazimine can inhibit the proliferation and activation of T-lymphocytes through inhibition of the sodium–potassium ATPase.[3 4] This immunomodulatory effect of clofazimine has proven beneficial in the treatment of autoimmune disorders such as psoriasis and multiple sclerosis.[4] Yuan *et al* reported significant decrease in the mRNA expression of interleukin 6 (p=0.0001), Tumor necrosis factor-alpha (TNF-α) (p=0.0006) and C-C chemokine receptor type 4 (CCR4) (p=0.0029) in the hamsters treated with clofazimine.[2]

Interestingly, antiviral synergistic effects have been reported when clofazimine is coadministered with remdesivir.[2] The coapplication of clofazimine and remdesivir in an in vitro cellular assay with a 10% concentration of fetal bovine serum resulted in a nearly 20-fold reduction in the concentrations of remdesivir required to inhibit viral replication by 90%. This synergistic pharmacological effect did not elicit detectable cytotoxic changes. However, to further narrow the in vivo side effects profile, clofazimine can be administered via inhalation reducing its systemic side effects such as skin discoloration and gastrointestinal discomfort.[5]

In summary, clofazimine with its anti-inflammatory and immunomodulatory effect with minimal side effects could increase survival in critically ill patients infected with the COVID-19 virus.

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