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Clofazimine: Can it be Useful in COVID 19?

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Authors' contributions

This work was carried out in collaboration among all authors. Author AC wrote the manuscript. Authors EC and AP revised the manuscript. All authors read and approved the final manuscript.

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Short Communication

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ABSTRACT

Clofazimine is a riminophenazine dye originally used as an antitubercular agent after its first synthesis in 1954, just few years after it was administered as a treatment for leprosy by YT Chang. In the following years, also an anti-inflammatory effectiveness on erythema nodosum leprosum was recognized [1]. In the '70s, its therapeutic activity on discoid lupus erythematosus and pyoderma gangrenosum was documented [2]. The safety of Clofazimine is good with a median frequency of the most reported adverse event (skin discoloration and gastrointestinal events) of 5.1% and a requiring discontinuation of the treatment in 0.1% of cases [3].

Keywords: Clofazimine; COVID-19; treatment.

1. INTRODUCTION

Recent papers suggest interesting properties of this drug as a modulator of the immune response, a sit blocksKv 1.3 potassium channel [4], a voltage dependent transmembrane domain identified outside of electrically excitable tissues in macrophages and T lymphocytes and it plays a critical role on the subset of "effector memory" (CD4+ CD62L, CD44) when blocked,

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downgrading particular functions in severe, inflammatory diseases. On the other hand, it expands “central memory” T population (CD4+ CD62L, CD44). In fact it is known that CD62L+ memory cells increase with time after infection [5].

2. DISCUSSION

The induction of long living, antigen specific “central memory” T cells is supportive of an efficient and long lasting action against bacterial and viral infections, whereas a quick overload of T cells “effector memory” may be detrimental for the organism because it may cause a more severe inflammation during an infectious disease, like tuberculosis, HIV [6] and severe acute respiratory syndrome (SARS). Clofazimine is electively accumulated in macrophages, forming crystal-like inclusions, this effect results in a reduction of bacterial replication [7]. It has also an inhibitory action on acid sphingomyelinase, preventing the ceramide accumulation induced by intracellular pathogens and restoring the autophagic clearance of intracellular pathogens. On the other hand, in models of bacterial pathogen killing an apoptotic inducing activity in macrophages may be recognized [8]. Inside these cells, the drug alters immune signaling response pathways, like to Toll like receptor binding, NF-kB activation and Tumor necrosis factor (TNF) production. Clofazimine might be able to promote antigen specific Th17 cascade in lymphocytes “central memory”, acting as a “self-propelled vaccine” in infection and cancer. In HIV/AIDS it may provide some benefits by enhancing T cell mediated immunity against HIV and also contrasting the well documented neurotoxicity of viral proteins, as the envelope glycoprotein 120 against microglia. Additionally, it influences the immune reconstitution following antiretroviral therapy, thus preventing the development of immune reconstitution inflammatory syndrome (IRIS) and preserving the integrity of HIV specific effector T-cell responses. The vast majority of since infectious diseases and cancers induce inflammation and inflammatory responses play a central role in protecting immune responses, hence profound inflammation can exacerbate a disease and thus can be detrimental, as in viral SARS. Patients infected by SARS COV-2, who have a severe disease, show high leukocytes count, lymphocytopenia and thrombocytopenia, abnormal respiratory findings, cardiovascular and haemocoagulative alterations, increased serum levels of blood C-reactive protein, erythrocyte sedimentation rate, D-dimer, pro-inflammatory cytokines, such as TNF-alpha, IL-1 and IL-6, and chemokines, such as IL-8, compared to individuals with mild disease or healthy controls. A cytokine storm, with vascular inflammation/endothelial damage, could play a role in the hyper-coagulativestate observed in SARS COV2 leading to thrombotic events in lungs, myocardium and kidneys. An exuberant host inflammatory response is not always correlated with the amount of viral load.

3. CONCLUSION

Due to the combination of an antiviral and anti-inflammatory property, clofazimine, an inexpensive, well tolerated, lipid soluble, orally administrated drug with good bioavailibility, could be used in the treatment of COVID 19, to reduce the excessive and detrimental inflammatory “fire”.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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