Cyclosporine: hope for severe COVID-19?

To the editor,

We are in the midst of the COVID-19 pandemic from the SARS CoV-2. This has taken at the time of writing 0.8 million lives which has put the medical fraternity under extreme challenge to find an effective treatment. Numerous promising antiviral therapies against SARS-CoV-2 are under investigation to prevent both interindividual transmission and severe disease complications. In COVID-19 mortality is thought to be related to both direct viral pathogenicity and a dysregulated inflammatory host response. Unfortunately, current treatment remains only supportive and symptomatic. An affordable drug would help resource poor countries against this challenge. Cyclosporine may have potential for severe COVID-19.

Cyclosporine was discovered more than four decades ago in the search for new antifungal agents. It is used to prevent organ rejection and treat autoimmune diseases like rheumatoid arthritis, systemic lupus erythematosus and dermatological diseases. It has immunosuppressive and anti-inflammatory effects by decreasing interleukin-2 (IL-2) production through prevention of the nuclear factor of activated T cell (NF-AT) activation. SARS-CoV non-structural protein 1 may induce expression of IL-2 via NF-AT activation, so cyclosporine can help to prevent the cytokine storm in severe COVID-19.[1]

Despite it being an immunosuppressive, infections are not commonly as an adverse event.[2] It has also been found that cyclosporine has potent antiviral activity, at low micromolar concentration it blocks the replication of all coronavirus genera (including SARS-CoV-1) in cell cultures.[3] Cyclosporine also binds to cyclophilin-D, which inhibits opening of the mitochondrial permeability transition pore, which prevents oxidative stress injury, hypoxia and which may improve cell function and survival. It also inhibits cyclophilin-D which has the potential to block viral replication.[3 4] Thus, cyclosporine might be a good candidate in severe COVID-19 to prevent the cytokine storm (or hyperinflammation) and inactivate viral replication.

Side effects of cyclosporine like hypertension and nephrotoxicity must be monitored carefully. Clinical trials are underway of cyclosporine in COVID-19. It can be used at lower dosages (usual dosage 3–5 mg/kg/day) in SARS-CoV-2-induced cytokine storm. Moreover, cyclosporine is not expensive and can be afforded worldwide, including in those countries where the COVID-19 health crisis continues to grow at pace with little or no access to expensive drugs. In conclusion, cyclosporine use in COVID-19 should be considered based on its antiviral properties and the alleviation of the cytokine storm.

Yashdeep Singh Pathania

Department of Dermatology, Venereology and Leprology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India

Correspondence to Dr Yashdeep Singh Pathania, Department of Dermatology, Venereology and Leprology, All India Institute of Medical Sciences Jodhpur, Jodhpur 342005, Rajasthan, India; yashdeepsinghpathania@gmail.com

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ORCID iD
Yashdeep Singh Pathania http://orcid.org/0000-0003-3462-1625

REFERENCES

1 Sanders JM, Monogue ML, Jodlowski TZ, *et al*. Pharmacologic treatments for coronavirus disease 2019 (COVID-19). *JAMA*;323.
2 Colombo D, Chimenti S, Grossi P, *et al*. Prevalence of past and reactivated viral infections and efficacy of cyclosporine A as monotherapy or in combination in patients with psoriatic arthritis--synergy study: a longitudinal observational study. *Biomed Res Int* 2014;2014:1–7.
3 de Wilde AH, Pham U, Posthuma CC, *et al*. Cyclophilins and cyclophilin inhibitors in nidovirus replication. *Virology* 2018;522:46–55.
4 Hausenloy DJ, Boston-Griffiths EA, Yellon DM. Cyclosporin A and cardioprotection: from investigative tool to therapeutic agent. *Br J Pharmacol* 2012;165:1235–45.