Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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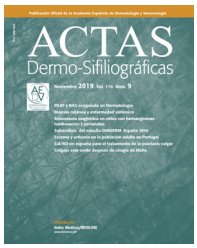

OPINION ARTICLE

Use of Cyclosporine Therapy in Dermatology During COVID-19 Pandemic

Uso de ciclosporina en dermatología durante la pandemia de COVID-19

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Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has engulfed more than 227 countries in the world with its menace since more than 20 months. Dermatologists are striving for clear evidences for the use of the immunosuppressive agents which form an important part of their treatment armamentarium. Generally, immunosuppressive use has been prohibited during COVID-19, hence, this has posed restrictions and difficulty on the part of dermatologist to treat patients with severe or flare of diseases. Therefore, robust research is underway to find a suitable immunosuppressive agent which would treat the disease flare and simultaneously, does not pose higher chances of contracting the SARS-CoV-2 infection or worsen COVID-19 patient condition. Cyclosporine has emerged out to be an agent which has shown a ray of hope in such crucial times. Apart from immunosuppressive and anti-inflammatory effect, it has potent antiviral activity by inhibiting SARS-CoV replication at very low and non-toxic doses.[1] Cyclosporine role has been speculated in severe COVID-19 patients by abating cytokine storm. The cytokine storm clinical findings are attributed to the action of proinflammatory cytokines like IL-1, IL-6, IL-18, IFN-γ, and TNF-α.[2] Cyclosporine has been considered an appropriate option in the treatment of secondary hemophagocytic lymphohistiocytosis as a cause of cytokine storm in SARS-Cov-2.[3] Few authors have advocated low dose cyclosporine use in SARS-CoV induced cytokine storm.[4] In a recent report by Kemmner et al.,[5] cyclosporine-based immunosuppression represented a therapeutic option in the case of COVID-19 following kidney transplantation. Vito Di Lernia et al.[6] observed there are no evidences that support a preventative discontinuation of cyclosporine during COVID-19 outbreak in patients with psoriasis and atopic dermatitis.

The duration of cyclosporine effects on the immune system is currently not known, however, in vivo animal models it was demonstrated through cytokine expression that there was progressive return of T-cell function after cyclosporine cessation, with full recovery seen by day 4 of the recovery period.[7] Therefore, it can be extrapolated that discontinuing cyclosporine in the patients can rapidly regain their immunocompetency. None of the patients in a study of 225 patients, receiving cyclosporine for 12 months experienced the reactivation or new onset viral infections like herpes simplex 1 & 2, cytomegalovirus, Ebstein-Barr virus and HIV in a study.[8] Azathioprine, cyclophosphamide and methotrexate do not possess anti-viral activity unlike cyclosporine. However, mycophenolate mofetil (MMF) has also some amount of anti-viral activity besides immunosuppression. It interferes with the early stage of the viral replication, before the protein synthesis.[9] In a study by c. Fotiadis et al.,[10] it was found that immunosuppression induced by MMF in maintaining graft function was median 2 days more than

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induced by cyclosporine. Therefore, MMF has a longer lasting immunosuppressive activity than cyclosporine and moreover, cyclosporine is better afforded than MMF. We have not encountered any COVID-19 infection in patients of acute flare of psoriasis, atopic dermatitis and Steven-Johnson syndrome who were administered cyclosporine therapy. A meta-analysis showed that cyclosporine had a beneficial effect on mortality for Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) where rapid onset of treatment response as in Covid-19 is warranted.[11] Therefore, cyclosporine can be used in present scenario in patients presenting with dermatological emergencies like SJS, TEN, erythroderma secondary to psoriasis or atopic dermatitis. It can however, also be used in flares of diseases for a shorter period with better outcome.

Moreover, a recent comment supports the idea that cyclosporine might be the drug of choice during the COVID-19 pandemic for renal transplant recipient due to the in vitro evidence.[12] The results of randomized controlled trials on cyclosporine in COVID-19 are lacking and till then, its use in dermatology should be undertaken with guarded approach in the most suitable and essential cases along with strict monitoring of the blood levels to avert toxicity and side-effects. Therefore, the decision making of initiation and cessation of cyclosporine should be made on a ''case to case'' basis.

In conclusion, using cyclosporine at lower dosage (3 mg/kg/day) for a shorter period in dermatological emergencies or severe disease flares along with regular monitoring and counselling of the patient may be undertaken during COVID-19 scenario.

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