Intervirology

Letter to the Editor

Intervirology
DOI: 10.1159/000512134

Received: April 9, 2020
Accepted: September 22, 2020
Published online: December 11, 2020

Available Antiretrovirals in the Treatment and Pre-Exposure Prophylaxis of SARS-CoV-2: Quo Vadis?

Miguel Alpalhão[a, b, c] Paulo Filipe[a, b, c]

[a]Dermatology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte EPE, Lisbon, Portugal; [b]Dermatology Universitary Clinic, Faculty of Medicine, University of Lisbon, Lisbon, Portugal; [c]Dermatology Research Unit, iMM João Lobo Antunes, University of Lisbon, Lisbon, Portugal

Dear Sir,

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has put severe strain on global economies, healthcare systems, and public health. The coronavirus disease 2019 (COVID-19) seems to carry significantly higher mortality compared to the viral respiratory infections we were accustomed to.

Nevertheless, severe COVID-19 in individuals infected with the human immunodeficiency virus (HIV) has been seldomly described, which is unexpected. An article has been published describing no increased incidence of COVID-19 or increased severity in HIV-infected individuals (indeed, in some instances, the incidence of severe disease may be even lower in the presence of HIV infection) and limited evidence showed that under certain antiretroviral therapeutic schemes, namely the ones including lopinavir/ritonavir, no cases of SARS-CoV-2 were detected [1].

This contrasts with the results of Cao et al. [2], where lopinavir/ritonavir showed no significant improvement in the outcomes of a sample of COVID-19 patients. We must note this population had a higher mortality than that usually seen for COVID-19 infection, which may imply that the treatment was offered only to those most severely ill. We cannot ignore that while the disease initiator is a virus, and much of the lung damage seen in severe disease is an inflammatory response. It is plausible that antiviral drugs may be of interest either to prevent or to treat recent onset infections, but fails to add benefit after significant inflammatory response takes place. We hypothesize that antiretroviral therapy in the context of HIV infection or Pre-Exposure Prophylaxis (PrEP) against HIV infection may offer some degree of protection against, at least, severe forms of SARS-CoV-2 infection.

This could be explained by the fundamental role of proteases to viral replication such as C30 endopeptidase (3CLpro), which is inhibited by protease inhibitors used in the treatment of HIV infection [3]. Moreover, Furin, a protein convertase expressed by the host shown to promote SARS-CoV-2 binding to ACE2 receptor [4], could be inhibited by tenofovir disoproxil (TDF) [5], widely used both in the treatment and PrEP of HIV infection, but these data are yet to be peer-reviewed or replicated.

This hypothesis seems to be supported by recent evidence that viral loads of SARS-CoV-2 seem to be lower in ferrets when TDF + emtricitabine (TDF/FTC) is administered [6]. Furthermore, a recent article where 77,950

karger@karger.com
www.karger.com/int

Miguel Alpalhão
Dermatology Department, Hospital de Santa Maria
Centro Hospitalar Universitário Lisboa Norte EPE
Ave. Prof. Egas Moniz, PT–1649 035 Lisbon (Portugal)
migueldbalpalhao@campus.ul.pt

HIV-positive individuals were followed found reduced incidence of SARS-CoV-2 infection in individuals under TDF/FTC compared to other antiretroviral regimens, and no cases of severe COVID-19 requiring intensive care unit admission or deaths were seen in this subset of patients [7]. Of note, patients under the novel Tenofovir alafenamide + FTC (TAF/FTC) treatment seem to have a higher risk compared to those under TDF/FTC. Considering that the major difference between TDF and TAF pertains to pharmacokinetics, where TAF allows for a higher intracellular concentration of tenofovir with lower plasmatic concentration than TDF [8], if this difference in effect on SARS-CoV-2 infection proves to be true, one may hypothesize that the higher concentrations of plasmatic tenofovir observed after the administration of TDF may play a more significant biological role against SARS-CoV-2 than the higher intracellular concentrations of tenofovir that are reached with TAF. Such a conclusion would further support the hypothesis that TDF effects on SARS-CoV-2 infection may be mostly due to Furin inhibition (or of other yet unknown extracellular host protein) rather than through direct inhibition of intracellular viral replication, which should be most affected by the intracellular concentration of the drug. Even in a reference article where caution is advised when considering HIV-infected individuals to have lower risk of severe COVID-19, we can see that the patients undergoing antiretroviral treatment with TDF/FTC did not present poor outcomes [9].

We, thus, propose that further investigation should be carried to investigate the potential merits of common antiretrovirals in the treatment of early COVID-19 infection, or even as PrEP for this infection. It would be fundamental for centers with high number of patients under HIV PrEP to analyze the epidemiology of SARS-CoV-2 in their patients. SARS-CoV-2 PrEP would be invaluable in reducing morbidity and mortality in the most vulnerable populations, until an effective vaccine is available.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding to declare.

Author Contributions

Miguel Alpalhão and Paulo Filipe contributed equally to the conception, writing, revision, and final approval of this manuscript. All contributing authors have been listed.

References

1 Guo W, Ming F, Dong Y, Zhang Q, Zhang X, Mo P, et al. A survey for COVID-19 among HIV/AIDS patients in two districts of Wuhan, China. SSRN Electron J. 2020 Mar.

2 Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A trial of Lopinavir-Ritonavir in adults hospitalized with severe Covid-19. N Engl J Med. 2020 Mar;382(19):1787–99.

3 Dayer MR, Taleb-Gassabi S, Dayer MS. Lopinavir; a potent drug against coronavirus infection: Insight from molecular docking study. Arch Clin Infect Dis. 2017 Oct;12(4).

4 Walls AC, Park Y-J, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell. 2020 Apr 16;181(2):281–92.e6.

5 Li H, Wu C, Yang Y, Liu Y, Zhang P, Wang Y, et al. Furin, a potential therapeutic target for COVID-19. ChinaXiv. 2020.

6 Park SJ, Yu KM, Kim YI, Kim SM, Kim EH, Kim SG, et al. Antiviral efficacies of FDA-approved drugs against SARS-COV-2 infection in ferrets. MBio. 2020 May;11(3).

7 del Amo J, Polo R, Moreno S, Díaz A, Martínez E, Arribas JR, et al. Incidence and severity of COVID-19 in HIV-positive persons receiving antiretroviral therapy. Ann Intern Med. 2020 Oct 6;173(7):536–41.

8 Podany AT, Bares SH, Havens J, Dyavar SR, O'Neill J, Lee S, et al. Plasma and intracellular pharmacokinetics of tenofovir in patients switched from tenofovir disoproxil fumarate to tenofovir alafenamide. AIDS. 2018 Mar;32(6):761–5.

9 Vizcarra P, Pérez-Elías MJ, Quereda C, Moreno A, Vivancos MJ, Dronda F, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. Lancet HIV. 2020 Aug;7(8):e554–64.