Is sitagliptin effective for the treatment of COVID-19?

Cluster of differantiation 26 (CD26) plays an important role in chronic graft versus host disease (GVHD), psoriasis, diabetes, haematological and solid cancers. In addition, S1, the spike protein of Middle East respiratory syndrome coronavirus, has been shown to enter human host cells using CD26, also known as dipeptidyl peptidase-4 (DPP-4), as a functional receptor.[1] In a molecular docking study, it was determined that the S1 domain of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike protein could potentially interact with CD26, an important immunoregulatory factor for hijacking and virulence.[2]

In a retrospective observational case-control study, 338 patients with type 2 diabetes and coronavirus disease 2019 (COVID-19) were matched 1:1 for age and gender. One hundred and sixty nine patients received 50–100 mg sitagliptin, a DPP-4 inhibitor, in addition to standard care, while the other 169 patients received standard care only. Although the initial C-reactive protein and respiratory rate of the patients in the standard care group were higher than in the sitagliptin group, other characteristics (such as age, gender, comorbidities, ferritin, interleukin-6) of the groups were similar. The mortality rate was 18% in the sitagliptin group, while it was 37% in the standard care group ($p=0.0001$). In addition, sitagliptin reduced the risk of mechanical ventilation and intensive care admission ($p<0.05$).[3]

A very recent phase II study conducted by Farag and colleagues investigated the efficacy and safety of 600 mg of sitagliptin twice daily in acute GVHD prophylaxis. The daily dose of sitagliptin used in this study was 12 times the daily dose used in the treatment of type 2 diabetes, and sitagliptin was administered to patients from the pre-transplant day to the 14th post-transplant day. As a result of this study, it was found that the combination of sitagliptin with tacrolimus and sirolimus caused a very low incidence of acute GVHD (5%) and 1 year non-relapse mortality in patients, and did not cause any significant additional toxicity.[4]

The anti-inflammatory effects of DPP-4 inhibitors are known. DPP-4 inhibitors are thought to slow the progression of COVID-19 and prevent the formation of cytokine storm inflammation by suppressing nuclear factor κB, which plays an important role in the pathogenesis of SARS-CoV-2 infection.[5] Based on all these data, randomised controlled trials have been started to determine the efficacy of sitagliptin in patients with COVID-19. The use of high dose sitagliptin (2×600 mg), as in the study conducted by Farag and colleagues, could be considered in randomised trials of patients with COVID-19 . The use of high-dose sitagliptin causes greater inhibition of DPP-4, and could result in less entry of SARS-CoV-2 into the host cell, and a decrease in the likelihood of cytokine storm by nuclear factor κB inhibition.

In conclusion, sitagliptin could have beneficial effects in patients with COVID-19, but this needs to be confirmed in randomised controlled trials.

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Contributors All authors contributed equally to the writing of the letter.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

To cite Memiş H, Çakır A, DURMUŞ M, *et al*. *Eur J Hosp Pharm* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/ejhpharm-2021-002702

Eur J Hosp Pharm 2021;**0**:1. doi:10.1136/ejhpharm-2021-002702

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