Received: 24 August 2021 | Accepted: 27 August 2021

DOI: 10.1111/bcpt.13650

LETTER TO THE EDITOR

BCPT Basic & Clinical Pharmacology & Toxicology

Home therapy of COVID-19 at the earliest may greatly prevent hospitalization

Dear Editor,

The wise use of pharmaceuticals to treat SARS-CoV2 infection and thereby drastically reduce hospital overload of patients affected by COVID-19 represents a fundamental bottleneck to prevent an exacerbation of the sickness and should encourage physicians to retrieve the most suitable therapy protocol for these patients. The recent contribution by Naveed Nazir Shah and coworkers on the emerging therapeutics to combat COVID-19 is a noteworthy synopsis of the developing strategy in fighting the SARS-CoV2 pandemic, but these weapons are ordinarily adopted in a hospitalization context.[1] Treating patients undergoing the initial symptomatology of SARS-CoV2 infection with the proper therapy protocol to prevent further hospitalization is the challenge.

A recent paper by Suter et al. reported that a recommended therapy protocol with selective cyclo-oxygenase (COX2) inhibitors, such as nimesulide, celecoxib, etoricoxib and other non-steroidal anti-inflammatory drugs (NSAIDs), reduced drastically the impact of hospitalization caused by COVID-19 with respect to patients prevalently treated with paracetamol.[2] We previously addressed the warning about acetaminophen,[3] despite the majority of physicians are still recommending this pharmaceutical to relieve pain and discomfort related to fever in subjects undergoing the early symptoms of COVID-19.

Following the evidence that the COVID-19 ethiopathogenesis is closely related to impairment in the endothelial-platelet crosstalk, causing immuno-thrombosis,[4] NSAIDs should have the ability to target this issue. Actually, the role of these drugs in targeting the COX-1 and COX-2 activity is considered of utmost importance to highlight their ability in suppressing platelet activation and prevent thrombosis in microcirculation.[5] However, during SARS-CoV2 infection, the expression of COX-2 is completely altered by viral targeting,[6] and the activity of selective COX-2 inhibitors, such as nimesulide, cannot be inferred from studies on healthy subjects.[5] The earliest activity to be targeted is preventing the impaired endothelial-platelet crosstalk triggered by SARS-CoV2 and which may rapidly lead to thrombotic events in microcirculation.

The persistence of viral particles is highly deleterious for platelets. SARS-CoV2 induces platelet apoptosis, which may generate fragments known as platelet microparticles (PMPs), particularly active in triggering thrombotic and disseminated coagulation events.[7] The antiviral property of NSAIDs, such as indomethacin, may serve in greatly reducing viral load in these districts and inhibiting the ability of coronavirus to initiate a programmed cell death in platelets.[7] Viral enhancement of COX-2 may disturb many activities promoted for SARS-CoV2 clearance; for example, the expression of COX-2-PGE_2 inhibits natural killer cell (NK) migration, cytotoxic effect and interferon production and also dendritic cell maturation and expression of MHC class II molecules, and so on.[8]

The anti-inflammatory therapy, therefore, should target the complex milieu made by innate immunity and endothelial-platelet interplay in order to rapidly reduce the impact of the pro-thrombotic damage elicited by SARS-CoV2.

As a matter of fact, the huge complexity of the mechanisms involved in the prompt pharmacological response to SARS-CoV2 is asking for an urgent Consent Guideline and the formulation of a reliable and feasible therapy protocol for treating home-residing patients with COVID-19 at the earliest.[8] Reducing fever cannot be the priority; extinguishing the burning infection is the decision to take as early as possible. A plethora of anti-inflammatory drugs is recommended often without focusing on the immuno-thrombotic ethiopathogenesis of COVID-19, or, when occurring, by formulating empirical associations of NSAIDs with antioxidants, vitamins or anti-coagulants, anyway without referring to any purported Consensus Panel able to address COVID-19 early symptoms in the most successful way. The need for a globally agreed on protocol is therefore crucial.

Emerging pharmaceuticals are strategic to address the pandemic with encouraging results,[1] yet, in the meantime, current better availability of NSAIDs prompts physicians and practitioners to recommend primarily and more

frequently these pharmaceuticals, with respect to affordable novelties. This consideration has put spotlight on the urgency to reach a commonly shared protocol rather than referring to one's own empiricism and medical practice.

People referring to their family doctor may use phones or other multimedia devices to avoid physical contact, and medical recommendations should be much more standardized to prevent misleading messages and comprehension. The first stages of COVID-19 infection are particularly crucial to forecast any development of the sickness.

In this respect, to reduce the burdensome overload of hospitalization, the topic of COVID-19 early home treatment should be taken into consideration very seriously.

ACKNOWLEDGEMENT

A special thank to Dr Wilbur Ghersley for his kind assistance with references.

CONFLICT OF INTEREST

The authors state they have no conflict of interest.

KEYWORDS

COVID-19, COX-2, home therapy, ibuprofen, NSAIDs

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