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## Opinion on double strategy to fight against COVID-19: Vaccination and home treatment with non-steroidal anti-inflammatory drugs

Serafino Fazio, Flora Affuso

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### Abstract

The goals of global vaccination are to control, eliminate, or eradicate infectious diseases in a sustainable way that strengthens public health systems. Although the use of vaccines is essential for the control of epidemics, the vaccines against coronavirus disease 2019 (COVID-19) proved to be inadequate to end the pandemic and thus are considered incomplete. These vaccines failed to prevent infection, so their primary purpose has been shifted to prevent severe disease and reduce hospitalizations and deaths. Therefore, we believe that all the strategies available to reduce transmission, hospitalizations and deaths due to COVID-19 will be put in place. It is reported that uncontrolled inflammation and thrombosis are the principal mechanisms for aggravation and death in patients with COVID-19. Unlike corticosteroids that should not be administered at the beginning of the symptoms for their immunosuppressive action, which could worsen the evolution of the disease, the usefulness of non-steroidal anti-inflammatory drugs in the early at-home treatment of the disease is becoming evident.

**Key Words:** Vaccination; Non-steroidal anti-inflammatory drugs; COVID-19; Early Treatment; Indomethacin; Hospitalizations

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**Core Tip:** The goals of global vaccination are to control, eliminate, or eradicate infectious diseases in a sustainable way that strengthens public health systems. Although the use of vaccines is essential for the control of epidemics, the vaccines against coronavirus disease 2019 (COVID-19) proved to be inadequate to end the pandemic and thus are considered incomplete. These vaccines failed to prevent infection, so their primary purpose now has been shifted to prevent severe disease and reduce hospitalizations and deaths. Therefore, we believe that all the strategies available to reduce transmission, hospitalizations and deaths due to COVID-19 will be put in place. In this regard, many observational studies have constantly shown beneficial effects of non-steroidal anti-inflammatory drugs (NSAIDs) in patients with low to moderate degree of COVID-19, in particular when administered within the first 72 h of symptom onset. Randomized controlled studies with NSAIDs should be carried out as soon as possible to confirm these results.

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## INTRODUCTION

In a recent article regarding coronavirus disease 2019 (COVID-19) vaccinations, the authors stated that “current vaccines provide only modest protection against infection and transmission with omicron variant, even at peak immunity after boosting”, that “boosting every 4 to 6 mo to maintain high serum neutralizing antibody titers may not be a practical or desirable long-term strategy” and that “boosting with mRNA vaccines is not risk free”[1].

The goals of global vaccination are to control, eliminate, or eradicate infectious diseases in a sustainable way that strengthens public health systems. Although the use of vaccines is essential for the control of epidemics, the vaccines against COVID-19 proved to be inadequate to end the pandemic and thus are considered incomplete. These vaccines failed to prevent infection, so their primary purpose has been shifted to prevent severe disease and reduce hospitalizations and deaths. Therefore, we suggest that all the strategies available to reduce transmission, hospitalizations and deaths due to COVID-19 should be put in place.

## AT-HOME EARLY TREATMENT WITH NSAIDS

At the beginning of pandemic, we proposed that it is not ethical to leave the patients with COVID-19 without any treatment, waiting certainties to be established by evidence-based medicine, and, among the various drugs that we could have used, we have proposed the use of indomethacin for its peculiar mechanisms[2]. At present we suggest that vaccination and early at-home pharmacologic treatment should be used together to fight against severe acute respiratory syndrome coronavirus 2 infection. Pharmacologic treatment is simple and cheap, and should be carried out promptly at home worldwide, especially for the population with no access to vaccines and the expensive approved antivirals. It has been reported that uncontrolled inflammation and thrombosis are the principal mechanisms for aggravation and death in patients with COVID-19[3]. Unlike corticosteroids that should not be administered at the beginning of the symptoms for their immunosuppressive action, which could worsen the evolution of the disease, non-steroidal anti-inflammatory drugs (NSAIDs) are now indicated for the early at-home treatment of the disease. Unfortunately, at the beginning of pandemic, NSAIDs were discouraged because of fears that they would result in a worsened disease [4], but recently Perico *et al*[5], in their review published in *Lancet Infectious Diseases* have reported that NSAIDs, in particular selective anti-Cox2 drugs and indomethacin may be useful in the treatment of COVID-19. Indomethacin has anti-inflammatory, antiviral and anti-platelet properties[6]. It has shown a better efficacy in a randomized controlled study in comparison with paracetamol, by greatly reducing the percentage of patients with desaturation (Spo<sub>2</sub> ≤ 93) in the course of the disease from 20% in the paracetamol group to 0% in the indomethacin group[7]. In addition, our group showed that treatment of COVID-19 patients with indomethacin plus cardioaspirin, started within the first 3 days of onset of symptoms led to a zero hospitalization, and reduced significantly the symptom duration and the number of patients who had increased D-dimer after polymerase chain reaction negativization and complete recovery in comparison with a group of patients who started the same treatment after 3 d[8].

In a further retrospective observational study, we confirmed the significant reduction of hospitalizations not only with indomethacin, but also with other NSAIDs, in a group of over 50 years old patients

**Table 1 Characteristics of published manuscripts on early at home treatment of coronavirus disease 2019 with non-steroidal anti-inflammatory drugs**

Ref.	NSAID	Study design
Fazio <i>et al</i> [8], 2021	Indomethacin	Retrospective-observational
Perico <i>et al</i> [5], 2022	Various	Review
Fazio <i>et al</i> [9], 2022	Various	Retrospective-observational
Consolaro <i>et al</i> [10], 2022	Various	Matched cohort
Ravichandran <i>et al</i> [7], 2022	Indomethacin	Open label-randomized
Cosentino <i>et al</i> [11],2022	Various	Retrospective-observational

NSAID: Non-steroidal anti-inflammatory drug.

(mean age  $60 \pm 9$  years) treated early at home for COVID-19[9].

Consolaro *et al*[10] have shown that a home-treatment algorithm based on anti-inflammatory drugs prevented hospitalization of patients with early COVID-19[10].

Another recent study by Cosentino *et al*[11], reporting the results of a retrospective analysis of 392 cases of COVID-19 in Italy, treated early at home mainly with NSAIDs, shows a very low number of hospitalizations (5.8%) and lethality (0.2%).

Taken together, these studies (Table 1), although most of them with an observational design, consistently indicate that prompt therapy at home with NSAIDs may be very beneficial in patients with mild to moderate COVID-19[5,7-11]. While several observational studies consistently showed the same beneficial result, prompt randomized controlled trials should be performed to validate the result. However, inexplicably, this was not done.

## CONCLUSION

We hope that prospective randomized controlled trials on the efficacy of early at-home treatment with NSAIDs in patients with mild to moderate COVID-19, with a design of non-inferiority compared to the antiviral drugs currently authorized for treatment, will start as soon as possible. The demonstration of NSAIDs' efficacy in the therapy of COVID-19 would make an extended use of these drugs which are easily accessible and cheap, thus greatly saving health care costs.

## FOOTNOTES

**Author contributions:** Affuso F, and Fazio S contributed equally to this work; both authors have read and approved the final manuscript.

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