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Letter to the Editor

## Prescribing COVID-19 treatments: what we should never forget ☆

SARS-CoV-2 pandemics is challenging health care systems worldwide. Governments are investing a huge amount of financial resources both to support health facilities and to prevent economic collapse. Half of the humanity is currently confined at home in order to stop COVID-19 transmission. Health care workers are multiplying their efforts while they are struggling to cope with the shortage of personal protective equipment (PPE) globally.

Respiratory support appears to be the gold standard of treatment in severe forms of SARS-CoV-2.[1] However, multiple efforts were done to find a possible medical treatment. Since the beginning of the epidemics, many drugs were used despite the lack of strong scientific evidence.

COVID-19-induced proinflammatory status looks to trigger most severe SARS-CoV-2 forms.[2] Based on this assessment, many antinflammatory drugs have been proposed and used off randomized trials due to the epidemics spreading. Despite the hope and the first evidences, a real clinical utility of these molecules which mostly act on IL-6 and IL-1 (such as tocilizumab and anakinra) is still to be demonstrated, while their potential side effects are well known.[3]

Similarly, corticosteroids (CS) have been proposed and largely used worldwide to tackle the proinflammatory status. Despite some encouraging preliminary data, there is still no evidence of a reduction of mortality in patients receiving CS, and standard side effects, including septic shock, have been reported.[4]

Many drugs have been hypothesized to be directly active against COVID-19 only because of a supposed antiviral activity: remdesivir, a molecule originally tested against Ebola virus, shows in vivo activity against MERS-CoV[5] but there is actually no real evidence of in vivo activity against COVID-19; lopinavir/ritonavir, a well-known protease inhibitor used in HIV treatment, has been widely used before randomized clinical trials showed his inefficacy in mortality reduction[6]; chloroquine and hydroxychloroquine, which are largely used in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) treatment, show modest antiviral effects, but mortality due to QT elongation-related cardiac events is a matter of concern.[7]

Shifting drugs with proven activity against other diseases to SARS-CoV-2 empiric treatment is leading to a drug global shortage, that can significantly impact on the quality of life of those patients, such as those affected by SLE and AR, who could face hydroxychloroquine stock exhaustion.[8] Conversely, preliminary data about a potential role of ACE inhibitors in favouring the onset of severe forms of SARS-CoV-2 infection induced a massive change in antihypertensive drugs prescription that caused the onset of severe cardiovascular events.[9]

In conclusion, SARS-CoV-2 spreading requires strong and emergency medical actions to face the first global pandemics since EBM approach was established. Nevertheless, this is not the time to encourage clinical practices that can lead to severe adverse events in both COVID-19 and non COVID-19 patients. The basic motto that must drive clinical decision remains "*Primum non nocere*", even during this global emergency.

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