

The COVID-19 war and the battles of rheumatologists

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From the beginning of 2020, the SARS-CoV-2 infection upset our daily routine with a new disease, COVID-19, that challenged our lives and our work.^{1,2}

The disease had several implications for our clinical activity as rheumatologists in our daily practice.

As emerged immediately, COVID-19 had extremely variable clinical manifestation, from the asymptomatic disease to the systemic form with multi-organ involvement that can lead to interstitial pneumonia, respiratory failure, and patient's death.³

A dual approach was used for therapy: on one hand, the analogies with other retroviruses led to the use of antiviral drugs already tested for HIV and Ebolaviruses.^{4,5} On the other hand, given the systemic inflammatory response, blocking the inflammatory cytokines became a therapeutic option like in many rheumatic diseases.⁶⁻⁸ As a result, rheumatological drugs, which we usually administer to treat rheumatological patients, became known to the general population and of common use for this new disease, with the consequent shortage of supplies for the treatment of rheumatological patients.^{9,10}

Four strategic weapons are needed to win the war with COVID-19: firstly, a test to detect the virus, which is rapid and therefore allows to identify and confirm the infection swiftly; secondly, the prevention of contagions through vaccination, and for this reason an effective vaccine is needed; thirdly, a specific antiretroviral for SARS-CoV-2; and, finally, the development of a biotechnological monoclonal antibody, specific for the virus, that mimics the activity of the convalescent plasma. Unfortunately, none of these tools are currently available and all scientific research is and must be committed to achieving these strategic objectives.¹¹⁻¹³

Within this framework the medical community is forced to use drugs which are currently registered and approved by EMA and

FDA for other indications to treat COVID-19. These drugs offer the advantage that we know their safety profile, but they have the disadvantage of being used off label. Therefore, new randomized controlled trials are needed, but at present only case series, isolated experiences, or more or less extensive cohort studies are available. So, in this situation, some of the drugs that have been in use for some time in the rheumatological field have been proposed or used for the treatment of COVID-19.¹⁴⁻¹⁶

On the one hand, these are non-specific drugs, but they can help manage some stages of the disease. One of the most important challenges is to understand in which phase of the disease they could be used most successfully to obtain the best result, exploiting a potential *window of opportunity*, a time and clinical space in which the effect of these products could be maximum.

Therefore, for instance, hydroxychloroquine (an antimalarial drug that was then borrowed from the rheumatological field for the treatment of some connective diseases) is now used to fight against COVID-19 especially in the initial stages and in combination with antibiotics, such as azithromycin, which has also a partial antiviral effect.^{16,17}

IL-6 inhibitor tocilizumab and other products that inhibit or decrease IL-6 levels are also in use in the treatment of COVID-19. However, it was recently seen that the inhibition of IL-6 does not reduce mortality or the rate of transition to intensive care, if used at an early stage.¹⁸ Meanwhile, a study is still ongoing on patients treated at a more advanced stage, when the cytokine storm arises, immediately or before the need to intubate the patient. Rheumatologists seem to converge towards this latter approach to the treatment of COVID-19 based on their expertise in these drugs in agreement with both infectious disease specialists and resuscitators.^{14,19}

On the other front the other battle, which rheumatologists are expected to fight is the protection of rheumatic patients from infection. On this front, the situation is clearer. The scientific associations of American and European rheumatologists confirmed that immunosuppressive treatments must not be stopped²⁰⁻²¹ and that rheumatological patients must be vaccinated against common flu and bacterial pneumonia to prevent these diseases and to better identify any possible onset of COVID-19. Therefore, rheumatologist will have to take on the commitment of spreading greater awareness about the need for vaccination in rheumatic patients.²²

Vice versa, the commitment of rheumatologists in the use of antirheumatic drugs for the treatment of COVID-19, such as chloroquine, hydroxychloroquine, JAK-inhibitors, IL-6 inhibitors, will diminish with the development of the above-mentioned specific weapons (*i.e.*, vaccine, specific antiretroviral drugs, specific monoclonal antibodies).

Moreover, a new management of rheumatic patients must be adopted as an alternative to the conventional face-to-face approach. Over these months of lockdown, the inability to access hospitals and outpatient units, in order to protect the health of the general population, led to the use of a different way of managing chronic

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rheumatic patients by using remote systems. In this regard, scientific societies elaborated recommendations or guides for patient management remotely. Different approaches have been used, from telephone call evaluations to the video call visits, up to e-mail contacts. This has enhanced the use of telemedicine, a branch that we have often overlooked in the past, but that has proven extremely helpful in the recent months to identify early the patients who needed changes in the therapeutic strategy, minimizing the risk of contagion without forgetting the importance of patient treatment, resorting live patient assessments solely for urgent cases.²³⁻²⁶

In conclusion, this year we faced a war for which we were not prepared. With the use of the most suitable therapeutic and management approaches, our goal is to manage this new disease, and to take care of rheumatic patients. We hope that, in spite of the new measures to be taken, we hope that, once vaccination is widespread and an adequate therapy for this infection is developed, we will be able to return to our previous management, which is certainly enriched by this new cultural and managerial background.

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