Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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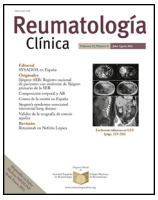

Editorial

COVID-19 with pulmonary involvement. An autoimmune disease of known cause☆

COVID-19 con afectación pulmonar. Una enfermedad autoinmune de causa conocida

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RNA viruses, such as influenza or COVID-19 coronavirus, are able to trigger devastating effects. They achieve this result with fewer than 12 genes, using strategies to evade the immune system of the host. In a variable percentage of cases they trigger an immune response that harms the host more than it does they themselves.

The antiviral response is triggered when the host pathogen recognition receptors bind to the molecular patterns associated with the pathogen and present in viral proteins and nucleic acids. The pathogen recognition receptors which take part in viral recognition include double-stranded RNA cytosolic helicases, MDA-5 or certain Toll-type receptors present on the cellular surface.

When the pathogen recognition receptors interact with molecular patterns associated with the pathogen, cellular activation is triggered that includes the activation of transcription factors such as factor 3 interferon regulator and nuclear kappa B factor, leading to a transcription of genes associated with type 1 interferons (IFN-1). These IFN-1 proteins may bind to the receptor that IFN-1 presents on the cellular surface and create a feedback loop that activates genes associated with inflammation, such as IL-8, interferon-gamma, tumour necrosis factor or IL-12. These inflammatory cytokines recruit macrophages, neutrophils and dendritic cells which connect with adaptive cellular immunity (lymphocytes) and humoral immunity (antibodies) which will control viral replication in an ideal scenario.

In scenarios where the IFN-1 response triggered by the virus is suppressed, the adaptive response will be reduced or delayed, giving rise to chronic viral infection or inflammation that destroys host tissue. The same result may occur if the IFN-1 response is excessive and/or is prolonged over time.

The ideal scenario is a moderate IFN-1 response that restricts viral replication and stimulates powerful induction of the adaptive system; theoretically this is the scenario that would be created by an effective vaccine.[1]

Our proposal is to inhibit the response to the virus in such a way that a scenario with a moderate IFN-1 response is created that induces a robust adaptive response.

How can this scenario be achieved?

Our proposal involves the early inhibition of the response to the virus using “mild” immunosuppressor/immunomodulating drugs that achieve a moderate IFN-1 response with hardly any side effects. These drugs would include:

- Corticoids at low/moderate doses.
- Hydroxychloroquine/chloroquine at moderate doses.
- Sulfasalazine at moderate doses.
- Methotrexate at low doses.
- Cyclosporine at low doses.
- Colchicine at low doses.
- Azithromycin at low doses.
- Baricitinib at low doses.

In case of progression and/or poor evolution:

- Corticoids at high doses.
- IL-6 tocilizumab/sarilumab inhibition.
- IL-1 anakinra inhibition.
- Mesenchymal stem cells.

The moment of administration and which of these measures are the most effective is debatable. Adaptive trials must be promoted to evaluate the highest possible number of these options, alone or combined, in as short a time as possible.

We believe that once the disease has been diagnosed and minor symptoms are present, these drugs can be used before the cytokine storm starts, and even before the not-very-well characterised autoimmune/autoinflammatory syndrome is triggered.

We also believe that some type of this kind of action would be recommendable in elderly people’s homes, where mortality is very high. In particular we believe that preventive colchicine, a

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very useful drug in autoinflammatory conditions similar to those triggered by COVID-19, may be useful in this context.

These simple measures may help to reduce, practically without side effects, poor evolution of the disease, as well as the need for subsequent respiratory support measures.

Reference

1. Katze MG, Fornek JL, Palermo RE, Walters KA, Korth MJ. Innate immune modulation by RNA viruses: emerging insights from functional genomics. Nat Rev Immunol. 2008;8:644–54.