ACADÉMIE NATIONALE DE MÉDECINE

Anti-SARS-CoV-2 hyperimmune immunoglobulins, an urgent strategic choice

Press release from the National Academy of Medicine

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No antiviral therapy has yet been clearly demonstrated to be effective in the treatment of COVID-19. Spontaneous improvement in most patients reflects the protective immune response, particularly related to neutralizing antibodies. Serotherapy, the principle of which is very old, has been used in recent epidemics by the Chikungunya and Ebola viruses but also SARS-CoV-1, MERS-CoV and A/H1N1. In COVID-19, two preliminary publications, one on 10 patients [1] and the other on 5 patients [2], showed that the use of plasma from convalescent patients was well tolerated and could improve the clinical course of severe forms of COVID-19 by neutralizing the viral load and rapidly decreasing the CRP. Also, although the interpretation of these preliminary results is debatable in the absence of a control group and due to the very small size of the study population, the Food and Drug Administration has recently approved the principle of this treatment and numerous trials have begun or will begin in the United States and France to evaluate its benefits and risks.

While the use of whole plasma is an emergency response to clinical situations of concern, it has a number of disadvantages: the nature, titer and neutralizing power of antibodies vary greatly from one donor to another. In addition, the risks associated with the presence of citrate, the volume infused in fragile patients, the possible transmission of infectious agents and the transfer of pro-inflammatory molecules are not negligible.

The French National Academy of Medicine recommends that pools of plasma from immunized (convalescent or cured) subjects with high antibody titers should now be established in order to prepare hyperimmune immunoglobulins (HIGI) in accordance with the rules of the art. The advantages are obvious: reduced risk of viral transmission thanks to the inactivation processes, better qualification of the product, improved scientific quality and level of proof of the studies to be carried out due to the standardisation of batches, provision of pneumococcal and anti-influenza immunoglobulins in subjects at risk of superinfection.

IGHI could be used not only in the treatment of severe forms, as reported in the 2 Chinese publications, but above all at the time of release from containment, in association with serological screening, in prevention among seronegative relatives of patients infected with CoV2-SARS, particularly in HPAE. They could also be used from the very beginning of the infection in fragile subjects (very old, cancerous, immunocompromised, etc.) at risk of developing a serious form.

France has the scientific and industrial means to initiate therapeutic trials and a production programme as soon as possible, which could have a rapid and significant impact in the

treatment and prevention of this infection. This is an emergency because the industrial production and marketing of recombinant monoclonal antibodies, which are necessary for the future, will take longer.

1] K Duan et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. PNAS in press.

[2] C Chen et al Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA (online March 27, 2020).