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Monoclonal antibody therapy in COVID-19 induced by SARS-CoV-2

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Abstract

Acute severe respiratory syndrome coronavirus-2 (SARS-CoV-2) infection causes coronavirus disease-2019 (COVID-19) which is associated with inflammation, thrombosis edema, hemorrhage, intra-alveolar fibrin deposition, and vascular and pulmonary damage. In COVID-19, the coronavirus activates macrophages by inducing the generation of pro-inflammatory cytokines [interleukin (IL)-1, IL-6, IL-18 and TNF] that can damage endothelial cells, activate platelets and neutrophils to produce thromboxane A2 (TxA2), and mediate thrombus generation. In severe cases, all these phenomena can lead to patient death. The binding of SARS-CoV-2 to the Toll Like Receptor (TLR) results in the release of pro-IL-1β that is cleaved by caspase-1, followed by the production of active mature IL-1β which is the most important cytokine in causing fever and inflammation. Its activation in COVID-19 can cause a "cytokine storm" with serious biological and clinical consequences. Blockade of IL-1 with inhibitory and anti-inflammatory cytokines represents a new therapeutic strategy also for COVID-19. Recently, very rare allergic reactions to vaccines have been reported, with phenomena of pulmonary thrombosis. These side effects have raised substantial concern in the population. Highly allergic subjects should therefore be vaccinated under strict medical supervision. COVID-19 has accelerated vaccine therapy but also the use of drugs and monoclonal antibodies (mABs) which have been used in COVID-19 therapy. They are primarily adopted to treat high-risk mild-to-moderate non-hospitalized patients, and it has been noted that the administration of two mABs gave better results. mABs, other than polyclonal plasma antibodies from infected subjects with SARS-CoV-2, are produced in the laboratory and are intended to fight SARS-CoV-2. They bind specifically to the antigenic determinant of the spike protein, inhibiting the pathogenicity of the virus. The most suitable individuals for mAB therapy are people at particular risk, such as the elderly and those with serious chronic diseases including diabetics, hypertension and obesity, including subjects suffering from cardiovascular diseases. These antibodies have a well-predetermined target, they bind mainly to the protein S (formed by the S1A, B, C and D subtypes), located on the viral surface, and to the S2 protein that acts as a fuser between the virus and the cell membrane. Since mABs are derived from a single splenic immune cell, they are identical and form a cell clone which can neutralize SARS-CoV-2 by binding to the epitope of the virus. However, this COVID-19 therapy may cause several side effects such as mild pain, bleeding, bruising of the skin, soreness, swelling, thrombotic-type episodes, arterial hypertension, changes in heart activity, slowed bone marrow activity, impaired renal function, diarrhea, fatigue, nausea, vomiting, allergic reaction, fever, and possible subsequent infection may occur at the site of injection. In conclusion, the studies promoting mAB therapy in COVID-19 are very promising but the results are not yet definitive and more investigations are needed to certify both their good neutralizing effects of SARS-CoV-2, and to eliminate, or at least mitigate, the harmful side effects.

Keywords: COVID-19; IL-1 family; SARS-CoV-2; anti-phospholipid antibodies; pro-inflammatory cytokines.