

Nebulized Therapy with Plasma-Platelet Growth Factors in Control of Cytokine Storm Hyperimmune Phenomenon in Lungs of Patients Affected by Covid-19

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In Regenerative Medicine, application of Plasma Growth Factors (PRP) represents a great scientific advance that opens a new knowledge in the functioning of platelets and their function on the immune system, intervening not only in bactericidal processes, but in complex mechanisms to regulate processes related to inflammation and cellular immunity through a large number of cytokines and interleukins [3,4].

The scarcity of adequately structured and designed clinical trials together with a proliferation of processes for obtaining PRP not tested in the scientific literature, means that this Biotechnology has been relegated to the background in Cell Therapy, fostered by a lucrative desire fierce for the different clinical applications that it is intended to give; losing the true essence of it, which is none other than being an economic procedure, simple to carry out with adequate training and with a potential for application in different fields of medicine thanks to its direct effect on the mechanisms that regulate apoptosis or perpetuation in survival, differentiation and multiplication within the cell cycle and on the immune system [2,3].

On the other hand, today it is known that these proteins have an extraordinary diffusion capacity through the tissues, in such a way that can obtain maximum pharmacokinetic levels within 30 - 40 minutes of their local application and stable for 5 - 6 hours in tissue. This allows its administration by different routes: infiltration, intravenous infusion, in the form of eye drops or even nebulized [4].

The existence of automated software for obtaining high concentration platelet plasma growth factors (between 1,500,000 - 3,000,000 platelets/mm³) could be a great scientific advance in having a useful, reliable and reproducible tool by any scientific working group to test its benefit for various clinical applications in the form of randomized clinical trials [4].

Unfortunately, these days we have had to experience the scourge of a pandemic caused by COVID-19 that is reaping tens of thousands of lives, especially those patients with a more compromised immune system, such as elderly patients or patients with various comorbidities, reaching figures of case fatality around 20% in these risk groups; and although every day we know more about its mechanisms of infection and symptom development, we currently do not have a specific treatment or vaccine that can confront it safely and efficiently.

It is known that an immunological effect occurs between the 5th and 7th day of infection, which has become known as "CYTOKIN STORM", which radically worsens the prognosis of patients, developing a phenomenon of lethal pneumonitis. In up to 35% of patients with pneumonia as a consequence of viral infection. This Fact is defined by the activation of the pulmonary monocyte-macrophage system, mediated by a series of interleukins, the best known being Interleukina-6 (IL-6).

Until this moment, therapeutic options have been considered like immunomodulators-immunosuppressants, such as certain monoclonal antibodies or high doses of corticosteroids.

From the point of view of regenerative medicine, the organism itself has means of regulating these phenomena of immune and inflammatory hyperreactivity. And at this point platelets have been shown to play a crucial role in controlling this inflammatory response in various murine and even human models. This explains that in histological samples of patients with bronchial and pulmonary hyperreactivity, a multitude of platelet aggregates has been observed in the affected areas; and recently it has been possible to objectify as two of the growth factors found in platelet alpha granules, known as Platelet-derived growth factor (PDGF), as well as Transforming Factor alpha/beta (TGF a/b), would improve the phagocytosis capacity of both dendritic cells and lung macrophages locally, inducing a suppression of

IL-6 secretion, which would reduce the phenomena of inflammation, hemorrhage and necrosis at the lung tissue level (Figure 1). Similarly, it has been observed *in vitro* that approximate levels around 10 ng/ml of TGF (a/b) or 15 ng/ml of PDGF, would induce overexpression of IL-13, which in turn would decrease CD-4 + T lymphocytic population in lung owing to an apoptotic effect, favoring an attenuation of cellular immunosuppression [1,2].

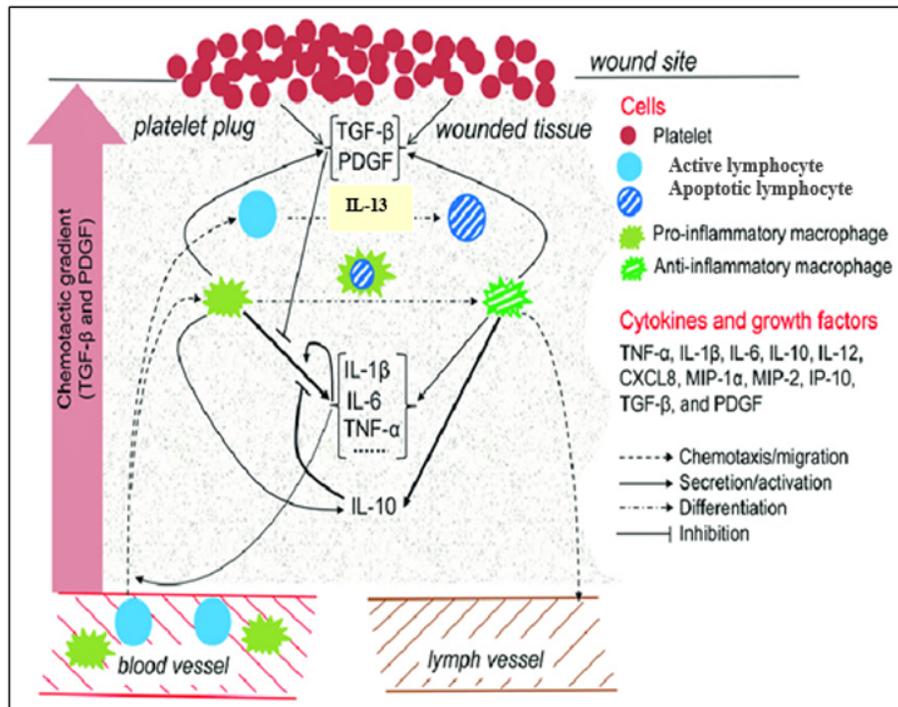


Figure 1

This phenomenon would provide a useful tool so that high concentrations of platelet growth factors in a nebulized form can be used in the early stages of pneumonitis of patients infected with COVID-19 in order to minimize the devastating evolution of the hyperimmune phenomenon that the “storm of cytokines” would produce on the diseased lung [1,2].

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