Residência Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 09/14/2020
Approved on: 09/18/2020

POINT OF VIEW

Contribution of pediatric rheumatology in the treatment of COVID-19

Sheila Knupp Feitosa de-Oliveira[1]

Keywords:
Coronavirus Infections, Biological Treatment, Rheumatology, Inflammation.

Abstract

The advance in the treatment of COVID-19 was based on the recognition of manifestations common to certain diseases that the pediatric rheumatologist is used to treating. The use of biological drugs that act on the mechanisms of the inflammatory state characterized by the storm of cytokines has helped to save lives.

[1] Federal University of Rio de Janeiro, Pediatrics Department - Rio de Janeiro - Rio de Janeiro - Brazil.

Correspondence to:
Sheila Knupp Feitosa de Oliveira.
Universidade Federal do Rio de Janeiro. Avenida Pedro Calmon, nº 550, Reitoria - Cidade Universitária da Universidade - Federal do Rio de Janeiro.
Rio de Janeiro - RJ. Brazil. CEP: 21941-901. E-mail: sheila_knupp@hotmail.com

DOI: 10.25060/residpediatr-2021.v11n1-473

This work is licensed under a Creative Commons Attribution 4.0 International License.

Large volumes of knowledge have been amassed since the start of the pandemic. If we had then the knowledge that we have today, and if we had started offering treatments to timely address pathophysiological manifestations, many deaths and sequelae resulting from organ involvement would have probably been avoided. When I write of early treatment, I am not referring to experimental therapies offered during the early stages of the disease that supposedly act directly against the virus to diminish viral load and/or the presence of the virus in one's body. In this stage of the disease, most patients (90%) have a functioning immune system that neutralizes the virus. Patients may have no symptoms or develop mild or more pronounced symptoms for a period of time, without facing the risk of death. The innate immune system signals the presence of danger and organizes to fight the replication of the virus and reduce viral loads. Subsequently, adaptive immunity produces specific antibodies against the virus, activates cytotoxic T-cells to kill cells infected by the virus and diminish the spread of the virus to other cells. In order for the immune system to work efficiently and safely, there must be a balance between the intensity and the time for which the immune system is activated.

Severe cases of COVID-19 affect a smaller group of patients in whom immune response is insufficient (or delayed) or excessive. In reality, very few cases of severe disease are due to difficulty eliminating the virus. In most circumstances, severity is tied to exaggerated immune response to the virus, in which a "hyperinflammatory state" develops with excessive macrophage activation, intense cytokine release (cytokine storm), cytotoxic T-cell production, complement activation, and involvement of the coagulation cascade. These multiple activations strengthen each other, creating a vicious circle. Cytokine storm leads to systemic inflammation with immune-mediated lesions affecting multiple organs, while the activation of coagulation produces micro and macro thrombi that may affect blood vessels. If patients are not promptly offered proper therapy to control the hyperinflammatory state, they are at risk of progressing to respiratory failure, heart failure, multiple organ failure, stroke, and death. This kind of hyperinflammatory response, known as "cytokine storm", has not been associated exclusively with COVID 19; it may occur in cases of bacterial infection and other viral infections, including the ones caused by the influenza virus.

Pediatric Rheumatology has significantly contributed to the development of treatments for COVID-19 by realizing the similarities that exist between immune-mediated phenomena stemming from cytokine storm in the secondary stage of COVID-19 and macrophage-activation syndrome (MAS) – a complication observed in a number of diseases in Pediatric Rheumatology. The most common cause of MAS is systemic-onset juvenile idiopathic arthritis (SoJIA). Ten percent of the children with SoJIA may develop MAS, a fatal complication in 10% of the cases if not recognized and treated early on. MAS is also observed, albeit less frequently, in individuals with juvenile-onset systemic lupus erythematosus and rarely in subjects with Kawasaki disease, dermatomyositis, and some autoinflammatory diseases. In recent decades, the experience accumulated by pediatric rheumatologists has driven the organization of international multicenter studies that helped establish the classification criteria for MAS used in the early diagnosis of the condition, since specific biomarkers for MAS are yet to be identified. The classification criteria used in the identification of cases of MAS in febrile patients with SoJIA are ferritin > 684 ng/ml and two of the following parameters: platelet count ≤ 181,000/mm^3, GOT > 48 U/l, triglycerides > 156 mg/dl, or fibrinogen < 360 mg/dl.[1] Other relevant workup findings include increased C-reactive protein, D-dimer, and IL-6 levels, low platelet count, and decreased levels of lymphocytes and albumin. Treatment protocols in use for MAS resort basically to glucocorticoids and anti-cytokine (anti-IL1 and anti-IL6). Medication dosage adjustments and patient condition monitoring must be performed continuously based on clinical and workup findings.[2]

Unfortunately, in the first months of the pandemic only a few patients with severe COVID-19 were offered protocols of this type in a timely manner, since very little was known about the disease at the time. Since COVID-19 is an infection, it is important to note that immunomodulators should be prescribed with caution. The addition of antiviral therapies under investigation might be needed and immunosuppressants, in less aggressive regimens, must be adjusted based on patient assessment.

Multisystem inflammatory syndrome in children (MIS-C) is a condition that often presents as complete or incomplete Kawasaki disease. MIS-C responds well to therapies similar to the ones prescribed to individuals with Kawasaki disease.[3]

The use of corticosteroids (dexamethasone) is now established in treatments offered to subjects with COVID-19. Pulse therapy with methylprednisolone, intravenous immunoglobulin, aspirin and heparin used Kawasaki disease as a basis, and therapies with anti-cytokine agents derived from the experience with MAS. Therefore, treatment must be individualized based on the specific characteristics of each patient.[4]

We cannot know how many deaths might have been avoided if suck knowledge had been incorporated to the therapies for COVID-19 since the start of the pandemic. Therapeutic approaches stemming from rheumatology are realistic and based on years of experience. Despite their inherent risks, they should be used to save lives.

REFERENCES

1. Henderson LA, Cron RQ. Macrophage activation syndrome and secondary hemophagocytic lymphohistiocytosis in childhood inflammatory disorders: diagnosis and management. Paediatr Drugs. 2020 Fev;22(1):29-44.
2. Dulek DE, Fuhlbrigge RC, Tribble AC, Connelly JA, Loi MM, Chebib HE, et al. Multidisciplinary guidance regarding the use of immunomodulatory therapies for acute COVID-19 in pediatric patients. J Pediatric Infect Dis Soc. 2020 Dez;9(6):716-37.

3. Rodríguez Y, Novelli L, Rojas M, De Santis M, Acosta-Ampudia Y, Monsalve DM, Ramírez-Santana C, et al. Autoinflammatory and autoimmune conditions at the crossroad of COVID-19. J Autoimmun. 2020 Nov;114:102506.

4. Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of Rheumatology Clinical Guidance for Pediatric Patients with Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2 and Hyperinflammation in COVID-19: version 1. Arthritis Rheumatol. 2020 Jul;72(11):1791-805.