

Glucocorticoids and COVID-19: A Multifaceted Relationship

Viktor I Goudochnikov*

Latin-American Chapter of International Society for DOHaD, Santa Maria RS, Brazil

***Corresponding Author:** Viktor I Goudochnikov, Latin-American Chapter of International Society for DOHaD, Santa Maria RS, Brazil.

Received: October 20, 2020; **Published:** December 31, 2020

Introduction

An outbreak of novel coronavirus disease at the end of 2019 (COVID-19) in Wuhan, China has resulted in rapid spreading of pandemics caused by this coronavirus type 2, provoking severe acute respiratory syndrome (SARS-CoV-2), all over the world, including Latin America and Brazil. One of synthetic glucocorticoids (GC), dexamethasone was appointed recently as the first successful treatment of COVID-19 pneumonia (See discussion in [1]). However, many doubts concerning the use of GC for this indication still remain. Therefore, the aim of this short commentary was to perform an overview in preliminary form of a variety of topics associated with COVID-19 and GC relationship. Earlier we have discussed other aspects of GC use in the treatment of some respiratory and other disorders [2].

The main part

First of all, a meta-analysis [3] has confirmed that systemic GC did not reduce mortality or the duration of lung inflammation, although they were able to cause a reduction in the duration of fever in adults with COVID-19. Unfortunately, the use of systemic GC prolonged the duration of hospital stay in patients. In addition, GC use increased the risk of bacterial or fungal co-infections and of multiple organ dysfunction syndrome.

A recent Italian study [4] has outlined the important role of GC in controlling cytokine secretion storm - one of the principal pathogenic mechanisms of COVID-19 pneumonia, especially in critical patients. Among such cytokines interleukin-6 (IL-6) appears to have an outstanding place, therefore a Dutch study [5] has used successfully methylprednisolone (MP), together with tocilizumab, an antagonist blocking IL-6 receptor, for treatment of COVID-19. However, the authors mention that because of the high cost of tocilizumab, MP can be employed alone.

Recent Chinese study [6] has explored another possible pathogenic mechanism of COVID-19 related to GC. In fact, some data show the role of GC in regulation of angiotensin-converting enzyme type 2 (ACE2). It is important that SARS-Cov-2 uses this enzyme as a target for infecting human cells. Nevertheless, from our point of view, there remain a lot of unclear aspects in this molecular mechanism that require much more detailed studies, in spite of endorsement of such work by some other researchers [7].

A quite special issue of GC use in the treatment of COVID-19 is their employment in patients with adrenal insufficiency [8]. Although at the first glance this issue appears to have limited importance, we should remember here that at least partial adrenal insufficiency may take place even in some cases of the treatment of asthma and other respiratory disorders with inhaled GC, particularly when there occurs abrupt interruption of corticotherapy without tapering. In COVID-19 patients with adrenal insufficiency the principal difficulty is to tailor proper dosage and period of exposure to substitution corticotherapy, usually with hydrocortisone. Another problem related to the long-term use of GC before coronavirus infection may be atypically long incubation period and associated with it extra-transmission of COVID-19 [9].

Finally, recent hypothesis tries to explain higher incidence of COVID-19 in minority ethnic groups by means of GC resistance [10]. As a matter of fact, IL-6 and other pro-inflammatory cytokines released in huge quantities during the critical phase of COVID-19 can really provoke GC resistance (see discussion in [11]). On the other hand, it appears that chronic stressful conditions of low socio-economic status, characteristic for several ethnic groups living in poverty, including some regions of Brazil, may provoke GC resistance, due to relative hypercortisolism and subsequent down-regulation of GC receptors. In fact, previously, by means of the analysis of epidemiologic data extracted from Brazilian national database called Data Sus, we were able to confirm partially an inverse gradient of total mortality, according to the number of years spent for education, which serves as one of indicators of socio-economic status [12].

Final Comments

There are two worrying topics that necessitate special attention for the relationship between GC, COVID-19 and other respiratory disorders. First of all, a situation in Indonesia, where the announcement of successful treatment of coronavirus infection with dexamethasone has resulted in rapid disappearance of synthetic GC from local pharmacies [13] clearly shows an extremely important role of health care professionals (especially those employing drugs - physicians, nurses and pharmacists) in educating lay public about the dangers of automedication with any drugs and particularly with GC.

In the second place, not negating the first positive results of GC use for the treatment of COVID-19, we should not forget previous alarming data showing that early use of GC for fever reduction and pneumonia prevention may increase the risk for critical disorder or death from another viral disease, influenza A (pH1N1) infection [14]. Earlier we have also tried to call for prudence in GC use, especially in perinatal period [15] and in childhood, because of the risk of pharmacotoxicologic programming/imprinting and embedding phenomena that may be caused by these potent drugs [16]. By the way, the employment of GC in the treatment of various respiratory illnesses needs careful re-evaluation, possibly paving way to more adequate use of these drugs in COVID-19 and other emerging respiratory infections.

Bibliography

1. Lockey RF and Hudey SN. "Coronavirus disease 2019 – associated urticaria with angioedema in a morbidly obese man successfully treated with glucocorticoids". *Annals of Allergy Asthma and Immunology* 125 (2020): 359-360.
2. Goudochnikov VI. "Use of corticosteroids for the treatment of respiratory and other disorders: Estimating benefit to risk relationship". *Lungs and Breathing Journal* 2.3 (2018): 1-3.
3. Lu S., et al. "Effectiveness and safety of glucocorticoids to treat COVID-19: a rapid review and meta-analysis". *Annals of Translational Medicine* 8.10 (2020): 627.
4. Solinas C., et al. "A critical evaluation of glucocorticoids in the management of severe COVID-19". *Cytokine and Growth Factor Reviews* 54 (2020): 8-23.
5. Ramiro S., et al. "Historically controlled comparison of glucocorticoids with or without tocilizumab versus supportive care only in patients with COVID-19 – associated cytokine storm syndrome: Results of the CHIC study". *Annals of Rheumatic Diseases* 79 (2020): 1143-1151.
6. Xiang Z., et al. "Glucocorticoids improve severe or critical COVID-19 by activating ACE2 and reducing IL-6 levels". *International Journal of Biological Sciences* 16.13 (2020): 2382-2391.
7. Deng C-X. "Glucocorticoids save lives in COVID-19 patients". *International Journal of Biological Sciences* 16.13 (2020): 2477-2478.
8. Isidori AM, et al. "COVID-19 infection and glucocorticoids: Update from the Italian Society of Endocrinology Expert Opinion on steroid replacement in adrenal insufficiency". *Journal of Endocrinological Investigation* 43 (2020): 1141-1147.

9. Han Y, *et al.* "COVID-19 in a patient with long-term use of glucocorticoids: A study of a familial cluster". *Clinical Immunology* 214 (2020): 108413.
10. Karan A, *et al.* "COVID-19 and ethnicity: Does reduced responsiveness to glucocorticoids explain the more aggressive nature of disease among minorities?" *Medical Hypotheses* 144 (2020): 110220.
11. Goudochnikov VI. "The contribution of stress and its mediators to the ontopathogeny of infections: A focus on the interactions of cytokines and glucocorticoids". *Advances in Gerontology* 7.1 (2017): 25-28.
12. Goudochnikov VI. "Partial gradients of total mortality in the south of Brazil, indicating psychosocial stress". In: *Annals of 22. SEPE. Santa Maria: Unifra* (2018).
13. Lin MA and Pranata R. "Worrying situation regarding the use of dexamethasone for COVID-19". *Therapeutic Advances in Respiratory Disease* 14 (2020): 1-3.
14. Han K, *et al.* "Early use of glucocorticoids was a risk factor for critical disease and death from pH1N1 infection". *Clinical Infectious Diseases* 53.4 (2011): 326-333.
15. Goudochnikov VI. "Perinatal treatment of some respiratory disorders with glucocorticoids in relation to prematurity". *EC Pulmonology and Respiratory Medicine* 6.1 (2017): 23-27.
16. Goudochnikov VI. "Emerging terms and concepts of pharmacotoxicologic programming/imprinting and embedding, as related to the ontopathogeny of respiratory and other disorders". *EC Pulmonology and Respiratory Medicine* 7.6 (2018): 413-415.

Volume 10 Issue 1 January 2021

©All rights reserved by Viktor I Goudochnikov.