



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Can dexamethasone prevent the seizures induced by SARS-CoV-2 infection?

Adriana Fernanda K. Vizuete^{a,b,*}, Carlos-Alberto Gonçalves^{a,b}

^a *Laboratory of Calcium Binding Proteins in CNS, Department of Biochemistry, Instituto de Ciências Básicas da Saúde, Universidade Federal do Rio Grande do Sul (UFRGS), Ramiro Barcelos, 2600-Anexo, Porto Alegre, RS, 90035-003, Brazil*

^b *Graduate Program in Biochemistry, Institute of Basic Health Sciences, UFRGS, Porto Alegre, Brazil*

1. Summary

A recent article published by Nikbakht et al. in this journal discussed potential mechanisms of seizure and epilepsy in Sars-CoV-2 infection (Mult Scler Relat Disord, 2020;102535). In addition, a recent study reported that dexamethasone was able to reduce the mortality in COVID-19 patients. Considering that dexamethasone abrogated neuroinflammation and improved astrocyte function in a refractory animal model of epilepsy and reduced seizures in refractory patients, it may be speculated that this steroid, in addition to reducing mortality, could prevent and/or mitigate convulsive and other neurological manifestations in COVID-19 patients.

2. Commentary

A recent article published by Nikbakht et al. in this journal discussed potential mechanisms of seizure and epilepsy in COVID-19 patients (Nikbakht et al., 2020). In fact, COVID-19 affects many systems other than the respiratory system, including the cardiovascular, renal and nervous systems. Neurological manifestations are varied, ranging from a headache and anosmia to convulsion and stroke (Wu et al., 2020; Yachou et al., 2020; Whittaker et al., 2020). These manifestations can be provoked either by a direct viral invasion, since neurons and astrocytes have membrane proteases such as ACE-2 and TMPRSS2 that anchor the entry of Sars-CoV-2, as well as by an inflammatory disorder caused by the cytokine storm described in the disease, as pointed out by Nikbakht et al (Nikbakht et al., 2020).

These data reinforce the idea that an active neuroinflammatory process may be at the basis of epileptic diseases, particularly those resistant to antiepileptic drugs. The cytokine storm has been associated with severe and lethal cases of COVID-19 (Hu et al., 2020), where IL-6 could mediate an exacerbated acute phase response by liver, that in turn could explain, in part, the incidence of atypical coagulopathy in these cases (Gonçalves and Sesterheim, 2020).

Based on such evidence, the use of immunomodulators has been proposed to control the severity of the disease (COVID-19, 2020). A recent trial suggested that dexamethasone reduces mortality in these patients (Group, RC, 2020). Interestingly, in a refractory model of epilepsy, dexamethasone was able to abrogate neuroinflammatory signs and improve astrocyte function (Vizuete et al., 2018); in fact, this anti-inflammatory steroid has been proposed as an adjuvant therapy in cases of refractory epilepsy (Ramos et al., 2019). Therefore, we speculate that dexamethasone, beyond reducing mortality, could be useful for preventing or mitigating convulsive manifestations in COVID-19 patients. Current investigations of the use of dexamethasone in COVID-19 patients will clarify this question and may be able to evaluate the outcome of other neurological manifestations during and post-COVID-19.

Declaration of Competing Interest

The authors declare no conflicts of interest.

Acknowledgements

The authors gratefully acknowledge to public funding agencies in Brazil: National Council for Scientific and Technological Development (CNPq) and Coordination for the Improvement of Higher Education Personnel (CAPES)

References

- Nikbakht, F., Mohammadkhanizadeh, A., Mohammadi, E., 2020. How does the COVID-19 cause seizure and epilepsy in patients? The potential mechanisms. *Mult. Scler. Relat. Disord.*, 102535
- Wu, Y., Xu, X., Chen, Z., Duan, J., Hashimoto, K., Yang, L., 2020. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav. Immun.* [Internet] 18–22. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146689/pdf/main.pdf>.

* Corresponding author.

E-mail address: adrianavizuete@gmail.com (A.F.K. Vizuete).

- Yachou, Y., El Idrissi, A., Belapasov, V., Ait Benali, S., 2020. Neuroinvasion, neurotropic, and neuroinflammatory events of SARS-CoV-2: understanding the neurological manifestations in COVID-19 patients. *Neurol. Sci. Neurol. Sci.* 41, 2657–2669.
- Whittaker, A., Anson, M., Harky, A., 2020. Neurological manifestations of COVID-19: a systematic review and current update. *Acta Neurol. Scand.* 142, 14–22.
- Hu, B., Huang, S., Yin, L., 2020. The cytokine storm and COVID-19. *J Med Virol.* 1–24. Internet John Wiley & Sons, Ltd Available from. <https://doi.org/10.1002/jmv.26232>.
- Gonçalves, C.A., Sesterheim, P., 2020. Serum amyloid a protein has been undervalued as a biomarker of COVID-19. *Diabetes Metab. Res. Rev.* e3376.
- Magro, G., 2020. COVID-19: review on latest available drugs and therapies against SARS-CoV-2. Coagulation and inflammation cross-talking. *Virus Res.*, 198070
- Group. RC, 2020. Dexamethasone in hospitalized patients with COVID-19 — preliminary report. *N Engl. J. Med.* 1–11.
- Vizuete Hansen, F., Negri, E., Leite, M., de Oliveira, D., Gonçalves, C., 2018. Effects of dexamethasone on the Li-pilocarpine model of epilepsy: protection against hippocampal inflammation and astrogliosis. *J. Neuroinflammation.* 15.
- Ramos, A.B., Cruz, R.A., Villemarette-Pittman, N.R., Olejniczak, P.W., Mader, E.C., 2019. Dexamethasone as abortive treatment for refractory seizures or status epilepticus in the inpatient setting. *J. Investig. Med. High Impact Case Rep.* 7, 1–12.