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Letter to the Editor

Is melatonin deficiency a unifying pathomechanism of high risk patients with COVID-19?

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An article by Zhang et al. [1] published in the March issue of Life Sciences suggested melatonin as a potential adjuvant treatment for COVID-19. Besides the antioxidative and immunomodulatory actions of melatonin, there is another reason supporting melatonin's use as a rational approach to COVID-19 treatment. The population with the greatest susceptibility to becoming infected and developing a severe SARS-CoV-2 infection involve the elderly and patients with hypertension, diabetes and various cardiovascular pathologies. The question arises, what unifying condition accounts for the increased sensitivity to and risk of poor prognosis of COVID-19 in these groups?

One feature common to these cohorts is their depressed night-time melatonin rise. The production of melatonin progressively decreases with increased age, the lowest levels being in the elderly [2]. Impaired nocturnal melatonin secretion is also observed in non-dipper hypertensive patients [3]. Experimental pinealectomy or continuous light exposure in rats is associated with reduced levels of melatonin and hypertension development [4]. Circadian rhythms of melatonin secretion are blunted in type 2 diabetic patients and low melatonin secretion at night is associated with autonomic neuropathy [5]. Decreased levels of serum melatonin predict adverse left ventricular remodelling during the chronic phase after myocardial infarction [6]. Based on these findings, we suggest that insufficient melatonin production may have an important role in the increased susceptibility of these patients to SARS-CoV-2 infection and to its negative prognosis. This pathophysiological association supports using melatonin both in prophylaxis and as a therapy in COVID-19 especially considering its high safety profile.

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Author contribution statement

FS - drafting the article, FS and RJR - the design of the study, data analysis and interpretation, critical revision of the manuscript, final approval of the version to be submitted.

References

- [1] R. Zhang, X. Wang, L. Ni, X. Di, B. Ma, S. Niu, C. Liu, R.J. Reiter, COVID-19: melatonin as a potential adjuvant treatment, *Life Sci.* 250 (2020), <https://doi.org/10.1016/j.lfs.2020.117583> 117583.
- [2] R. Hardeland, Melatonin in aging and disease —multiple consequences of reduced secretion, options and limits of treatment, *Aging Dis* 3 (2012) 194–225.
- [3] M. Jonas, D. Garfinkel, N. Zisapel, M. Laudon, E. Grossman, Impaired nocturnal melatonin secretion in non-dipper hypertensive patients, *Blood Press* 12 (2003) 19–24.
- [4] F. Simko, R.J. Reiter, O. Pechanova, L. Paulis, Experimental models of melatonin-deficient hypertension, *Front. Biosci. (Landmark Ed.)* 18 (2013) 616–625.
- [5] N.B. Tutuncu, M.K. Batur, A. Yildirim, et al., Melatonin levels decrease in type 2 diabetic patients with cardiac autonomic neuropathy, *J. Pineal Res.* 39 (2005) 43–49.
- [6] A. Dominguez-Rodriguez, P. Abreu-Gonzalez, E. Arroyo-Ucar, R.J. Reiter, Decreased level of melatonin in serum predicts left ventricular remodelling after acute myocardial infarction, *J. Pineal Res.* 53 (2012) 319–323.

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