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Editorial

Melatonin as a Potential Adjuvant for Treating Severe Cases of COVID-19

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The story began in December 2019 when a new coronavirus was isolated from some febrile patients presenting with dry cough and myalgia in Wuhan, China. With a significant similarity with SARS and MERS coronaviruses, the novel coronavirus was named as SARS-CoV-2 and the disease caused as COVID-19. Highly contagious, the virus infected the people across the planet in no time and the WHO declare the outbreak as a global pandemic on 11th March 2020 [1].

Infection spreads with close contact particularly in crowded places. Primarily, the virus affects the respiratory system but also the gastrointestinal and the central nervous system (CNS). Symptoms like fever, dry cough, myalgia, fatigue, dyspnea, and diarrhea appear within 2 - 14 days and as the disease progresses, there is Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS), respiratory failure, sepsis and cardiac arrest. It is an inflammatory disease with dysregulation of immune inflammatory responses and altered immunomodulatory functions. With increased pro-inflammatory cytokines, COVID-19 causes a severe cytokine storm - an exaggerated immune response leading to lung damage and possibly death [2].

The virus invades the CNS through olfactory mucosa and causes loss of smell. Because of viral infection there occurs acute necrotizing hemorrhagic encephalopathy, brain dysfunction and mental disorientation. Peripheral nerve terminals and blood circulation are other routes for the virus to reach the CNS - nucleus solitarius, which receives taste information and coordinates gastrointestinal and respiratory network. Anosmia, cognitive and attention deficits, new-onset anxiety, depression, psychosis, seizures, and suicidal behaviour are the commonly occurring neuropsychiatric conditions. These conditions are unrelated to respiratory insufficiency suggesting independent brain pathology. Patients with family history of suicide and major depression have been found to have increased proinflammatory and decreased neurogenesis markers in post-mortem brain studies [3,4].

More than 173 million people have been infected and as many as 3.73 million people died till date across the globe since the timed first cases of COVID-19 were reported. This highly infectious condition continues to ravage the world population and has yet to reach it peak infective rate in some countries [5]. Though we have succeeded in developing a vaccine against the disease, its large-scale availability to vaccinate everyone is many months away. Moreover, vaccination does not ensure full protection as it is difficult to immunize against the coronavirus. There has never been a successful human vaccine against any member of the coronavirus family.

It is a daunting task for the scientists to lower the mortality. Effective medication is urgently needed. Many conventional drugs including hydroxychloroquine/chloroquine, lopinavir, remdesivir, etc., have been repurposed as treatments, but there is no specifically-designed effective drug available; also, the drugs mentioned have significant side effects and their efficacy is not clearly understood. Established anti-viral drugs such as remdesivir, an anti-Ebola virus drug is tried in COVID-19 cases with only limited success. Frequently occurring mutations of the virus defeat the search for an ideal medicine and the vaccine developed may require repeated adaptation to the actually appearing viral subtypes [6,7].

The available drugs can only mitigate the mild to moderate symptoms if used in the early stage. Their efficacy is reduced with severe symptoms and associated co-morbidities. Severe conditions involving massive tissue damage need to be prevented to save lives. The severe symptoms in COVID-19 are beyond viral cytotoxicity and result from the overreaction of the innate immune response causing destructive inflammation. This is one of the reasons why antiviral drugs have poor efficacy in severely ill patients [8,9].

A more generalized and less virus-specific treatment for the severe symptoms is required. Melatonin, owing to its multiple actions may have beneficial effects in preventing or attenuating the cytokine storm and reducing morbidity and mortality. Melatonin has antioxidative and anti-inflammatory qualities and balances the overshooting innate immune response while promoting the adaptive immunity.

Melatonin (N-acetyl-5-methoxytryptamine) is a neuro-hormone secreted by pineal gland especially at nights, through the blood stream it reaches the cerebrospinal fluid (CSF). It is also secreted directly into the third ventricle. From CSF melatonin diffuses with the neural tissue and protects neurons and glial tissue from damage.

Melatonin is used in the treatment of sleep disorders, delirium, atherosclerosis respiratory disease and viral infection. It alleviates acute respiratory stress induced by virus, bacteria and radiation. It retards the process of degeneration with several neuro-protective actions because of following properties:

- Anti-viral, it reduces or lowers the new progeny production of the virus in the target cells.
- Anti-oxidant, it limits the lipid peroxidation and reduces oxidative stress.
- Anti-apoptotic, it protects against virus induced apoptotic cell death
- Regulatory effect on autophagy pathway
- Immuno-modulatory action
- Anti-inflammatory effect
- Reducing and delaying the severity of the disease.

Old age is a poor prognostic factor in COVID-19 because of decreased immune response and declining physiological functions; older people are more likely to develop severe pneumonia due to COVID-19. High levels of melatonin in the blood play a positive role against aging [10].

Obesity and Diabetes are risk factors for cardiovascular disease. Melatonin has anti-obesity properties since it regulates energy reserves. There is a functional interaction between insulin and melatonin; diabetic subjects have a lower concentration of melatonin. In insulin resistant patients there is decreased blood melatonin level. Low melatonin production is associated with an increased risk of cardiovascular disease [11].

To prevent cell damage, a higher dose supplementation of exogenous melatonin is needed which is generally safe in the dosage of 1–20 mg. Only a few minor side effects like fatigue, and drowsiness are reported.

In elderly COVID-19 patients and those associated with co-morbid psychiatric conditions, melatonin strengthens the immune response and a daily dose of 3 - 10 mg, 30 - 60 min before bed-time is helpful to simulate the normal physiological circadian rhythm. In high risk individuals like healthcare workers, a daily dose of 40 mg or higher may be required [12]. Melatonin is clinically useful in sepsis as well. It has been demonstrated to relieve many of the symptoms of other viral infections.

Melatonin's multiple actions make it a reasonable choice for use. It is readily available, can be easily synthesized in large quantities, is inexpensive, has a very high safety profile and can be easily self-administered. With a high pharmacological safety profile its efficacy in the treatment of COVID-19 is evidence-based. It is a useful supplement with other treatments such as remdesivir. Under the current critical conditions, the use of large doses of melatonin alone or in combination with currently-recommended drugs, appears justified.

Bibliography

1. Jilohas RC. "COVID-19 and Mental Health". *Epidemiology International* 5.1 (2020): 7-9.
2. Dun-Xian Tan and Ruediger Hardeland. "Estimated doses of melatonin for treating deadly virus infections: focus on COVID-19". *Melatonin Research* 3.3 (2020): 276-296.
3. Wadhawan A., *et al*. "Traumatic brain injury and suicidal behavior". *Journal of Alzheimer's Disease* 68.4 (2019): 1339-1370.
4. WooMS., *et al*. "Frequent neurocognitive deficits after recovery from mild COVID-19". *Brain Communications* 2.2 (2020): 205.
5. Russel J Reiter., *et al*. "Therapeutic Algorithm for Use of Melatonin in Patients With COVID-19 (2021).
6. Guan WJ., *et al*. "Clinical characteristics of coronavirus disease 2019 in China". *The New England Journal of Medicine* 382 (2020): 1708-1720.
7. Zou L., *et al*. "SARS-CoV-2 viral load in upper respiratory specimens of infected patients". *The New England Journal of Medicine* 382 (2020): 1177-1179.
8. Alhazzani W., *et al*. "Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19)". *Intensive Care Medicine* (2020).
9. Mahase E. "Covid19: what treatments are being investigated?" *British Medical Journal* 368 (2020): m1252.
10. Duffy JF., *et al*. "Aging and circadian rhythms". *Sleep Medicine Clinics* 10 (2015): 423-434.
11. Pandi-Perumal SR., *et al*. "Melatonin antioxidative defense: therapeutical implications for aging and neurodegenerative processes". *Neurotoxicity Research* 23 (2013): 267-300.
12. Wu J., *et al*. "Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19)". *Journal of Internal Medicine* (2020).

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