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CAN MELATONIN BE CONSIDERED AS A POTENTIAL EFFECTIVE ANTIVIRAL REMEDY AMID THE CORONAVIRUS PANDEMIC?

Abstract. *Corona virus or Covid-19, a well-known trending crisis, is inflicting many countries and causing as a potential genocide. Still after causing ravage worldwide, it has yet to reach peak.*

Melatonin can be a potential therapeutic solution in aiding Covid19 treatment, but considering the current scenario we need a medication that would be multi-beneficial, versatile and ready to use for any type of patients, be it young or old, strong or weak, having some normal or terminal illness and so on. We need to constantly evolve ourselves and our medical tech with the changing times. New innovations should be encouraged, potential ancient medicine such as Ayurveda should be re-explored and we must rationalize ourselves to think outside the box, because Corona virus has been evolving still, and so should we.

Key words: *Covid-19, melatonin, pandemic, patients.*

Introduction. While the safety of melatonin has been verified in many human studies, its effect when given to COVID-19 patients should be carefully monitored despite the very high safety profile of melatonin.

Corona virus or Covid-19, a well-known trending crisis, is inflicting many countries and causing as a potential genocide. Still after causing ravage worldwide, it has yet to reach peak [1]. Basically, Covid-19 is described as a contagious disease caused by a virus known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). This infection is observed in patient approximately after fourteen days of being infected. Symptoms include cough, fever, shortness of breath, fatigue, in some cases loss of smell and taste. But sometimes it remains asymptomatic. In severe cases, breathlessness is observed that can get severe and patients are put on ventilators. Recently, studies have shown that melatonin, a hormone, which is naturally synthesized and released in our body by the pineal gland, could be a potent solution.

Melatonin is a hormone which regulates our body's sleep-wake cycle. Also, it has many secondary functions which are quite essential in terms of Covid19 treatment. Melatonin can be used for treating various factors or symptoms of

Covid-19 like sleeplessness, inflammation of bronchioles or alveoli, mental health and can act as an antioxidant. The physiological actions of melatonin are exerted via G-protein coupled seven transmembrane receptors (subtypes of melatonin receptors (MT1) and (MT2) and non-receptor-dependent mechanisms. The MT1 receptor has been associated with mammalian brain function, while the MT2 receptor is known to be involved in the body's circadian rhythms [2]. Therefore, this review will summarize and showcase some of the research and results for melatonin, whether a potent therapeutic solution for Covid-19 or not.

Discussion

How was melatonin investigated to be a solution for such a serious crisis?

Melatonin is a hormone secreted by pineal gland in the body and is contemplated as a solution for the deadly virus, SARS CoV-2. Covid-19 is a disease which manifests inflammation of bronchioles and alveoli and in severe situations, fills the lung alveoli with fluid, making it difficult for gaseous exchange leading to difficulty in breathing. Other than this, it indirectly affects the mental health of patients, due to public restrictions such as lockdown, quarantine and social distancing which changed the lifestyle by

limiting physical interactions. People are more into gadgets, work from home, locked within four walls for months and developing an emotional turmoil within themselves. Hypothetically, melatonin is being considered as a boon. It can exhibit anti-inflammatory properties, build immunity and give strength to overcome these physical as well as mental illnesses. Recently, drug-disease outcome relationships for melatonin using a large-scale COVID-19 patient registry database was performed. It was revealed that among individuals who received testing for SARS-CoV-2, melatonin usage was associated with a 28% of less likely outcome of a positive laboratory test result, among a combined population and that of 52% among African-American population [3]. Using a user active comparator design, it was found that melatonin usage was associated with a reduced likelihood of a positive laboratory test result for SARS-CoV-2 compared to use of ARBs (Angiotensin II receptors blockers) and ACEIs (Angiotensin-converting enzyme inhibitors), which are cardiac medications that help manage blood pressure, as well. Conventional exogenous form of melatonin medications such as gummies and tablets might be a benefit for older patients with COVID-19, due to age-related reduction of endogenous melatonin and the greater vulnerability of older individuals to SARS-CoV-2 infection [4], the latter potentially due to declining immunity, i.e., immuno-senescence [5]. Moreover, melatonin also suppresses NLRP3 inflammasome (a critical component of the innate immune system involved in regulating certain crucial elements in response to microbial infection and cellular damage) activation which is induced by cigarette smoking and attenuates pulmonary inflammation [6], not only via reduction of NF- κ B p65 and tumour necrosis factor- α (TNF- α) expression, but also via increase in anti-inflammatory cytokines such as IL-10 or IL-6, which can also have anti-inflammatory effects [7,8]. Thus, large-scale observational studies and randomized controlled trials are needed to validate the clinical benefit of melatonin for patients with COVID-19. It is important, that the trials be designed, with the understanding of the mechanism of the drug to be repurposed.

Melatonin, Mental Health and Covid-19

There is always a key to every problem, we can overcome this crisis which would definitely take a lot of hard-work and dedication to come up with a cure. Progress is already seen in the prevention, that is vaccine [9]. Some willpower from our side is also a must, which helps in fighting Covid to the fullest. But according to studies, sleep pattern affects our thoughts. It is completely under the influence of melatonin.

Therefore, sleep is very important for our physical, mental and immune health. Since the SARS CoV2 outbreak, things have changed, online mode of studies, work from home, and so on, has affected people's sleep patterns, which in turn could affect their immunity. Studies have shown that administration of melatonin prior vaccination could improve sleep patterns to optimal conditions which is therefore essential during vaccination, and its application after vaccination increases its potency and efficiency [10].

Melatonin and Age

Melatonin levels decrease with age. Children have high levels of melatonin as compared to the elderly and are therefore more immune to the virus infection [1, 11].

This shows the power of melatonin as an armor from being infected with coronavirus, but still there are no concrete answers as for melatonin to be the perfect solution for the treatment of Covid19 and there are reasons. Some studies have shown that melatonin suppresses the immune response and inflammation to help fight Covid, which is quite actually opposite of vaccination purpose and therefore, intake of melatonin during vaccination might be a bane rather than a boon. [3, 12]. Currently melatonin is considered as a good choice of supplement for short term usage under a physician's advice, but its long-term usage can exhibit side effects such as sleepiness, headache, dizziness and can tamper with other medications, thus producing various complications. This would lead to emotional stress such as anxiety, confusion, short term depression, and so on [13].

Melatonin, Bats and Humans

If we take a look at Bat species, especially of the genus *Rhinolophus* which are the natural carriers of coronaviruses, they possess high levels of melatonin both during night and day as they have aversion to lights, they spend most of their

lifetime in darkness and hence have supreme immunity [1]. Therefore, Bats do not succumb to coronaviruses and the virus gets a suitable host and thus bats act as the carriers.

And not just bats, some other mammals that reside in high altitudes are known to possess pineal glands of larger size, with high melatonin activity [14].

However, it is impossible for humans to achieve the biochemistry of bats within them. However, even if we had the technology and the possibility to do so, there is a possibility that we humans ourselves could become a reservoir host for Coronavirus and though we would not succumb to it but can spread the infection virally and also act to serve as the best factory for the virus to mutate and evolve.

Therefore, we need the right formulation of melatonin for our body type and that is why a lot of efforts are needed in researching this matter to come up with a perfect solution.

Hope with Melatonin for Covid-19

Recently melatonin application at a molecular level has been studied. Melatonin is found to be closely associated with mitochondria, which is the energy generating factory of the cell. Melatonin maintains mitochondrial functions such as bioenergetics and redox homeostasis through the regulation of mitochondrial dynamics, which in turn is known to modulate antigen specific activation and immune responses [15].

It is found that COVID19 mortality rates increase with the age of the patient, which is related to mitochondrial dysfunction accompanied by drop in melatonin production. Therefore, the usage of melatonin as a nanocarrier is being studied. For many years nanoplateforms for melatonin delivery were developed as it would improve efficacy as an antioxidant agent due to its characteristic enhanced cellular uptake and better protection from oxidation as compared to the use of conventional melatonin. Its dosage requires significantly less amount of drug as compared to the conventional formulations, thus reducing the level of toxicity and side-effects that would otherwise be a challenge in conventional formulations. Therefore nano-formulations are found to be much advanced and effective way in administration of melatonin [16].

Conclusion

Melatonin can be a potential therapeutic solution in aiding Covid19 treatment, but considering the current scenario we need a medication that would be multi-beneficial, versatile and ready to use for any type of patients, be it young or old, strong or weak, having some normal or terminal illness and so on. We need to constantly evolve ourselves and our medical tech with the changing times. New innovations should be encouraged, potential ancient medicine such as Ayurveda should be re-explored and we must rationalize ourselves to think outside the box, because Corona virus has been evolving still, and so should we.

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