Review of: "Melatonin drugs inhibit SARS-CoV-2 entry into the brain and virus-induced damage of cerebral small vessels"

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It is a large and excellent study evaluating the effects of melatonin (MLT) and melatonin-derved drugs on the SARS-CoV-2.entry into the brain and the virus-induced cerebral vessels damage during the experimenatal model of Covid-19 .The study was performed on the K-18 hACE2 mouse model, which expresses the human ACE2 protein. It is well-known that ACE2 , an enzyme involved in the degradation of angiotensin II, is also the entry receptor of SARS-CoV-2. Studying this animal model of Covid-19 infection, It was shown that administration of MLT and melatonin-derived drugs (agomelatine and ramelteon) improved the scores of the infection clinical course .The viral load was detected in 100% of the vehicle-treated specimens while the treatment with higher dose of MLT (50 mg) significantly diminished cortical viral load. Interestingly, the viral-load is not diminished by the applied drugs in lungs. The possible explication is that in the case of lungs, the virus invasion is to massive to be counter-acted by MLT and MLT- derived substances. In cerebral cortical samples of SARS-CoV-2 –infected mice, higher dose of MLT (50 mg), and to some degree also the other drugs applied, decreased the virus –induced mRNA of the inflammation –linked cytokines,TNF, IL-1b, and IL-6. It is also found, that MLT and MLT-derived dtugs prevent the rarefication of cerebral cortical blood vessels and suppress the formation of so-called „string vessels , characteistic for the blood vessels that die. The further investigations showed that MLT,specially at high dose directly interferes with ACE2-dependent SARS-CoV-2 entry into the brain. Numerous previous studies suggested that melatonin may be an adjuvant drug useful in the acute phase of Covid-19 infection. The present paper shows the possible usefulness in protecrting the late phase of the Covid-19 disease, connected with the viral brain invasion.The further clinical studies on the prevention and/or treatment of the prolonged post-Covid-19 symptoms are urgently needed.