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RETROSPECTIVE REVIEW OF MELATONIN IN PATIENTS WITH COVID-19

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PURPOSE: Melatonin is a hormone released by the pineal gland that is responsible for the sleep-awake cycle in humans and has also been found to be in the mitochondria of all cells. Reducing mitochondrial oxidative stress has been the rationale for describing melatonin as having antioxidant and anti-inflammatory properties. A review of published reports for the treatment of other viruses found to have a specific role in the Ebola virus. While it was not found to be a viricidal, it reduced the degree of severity in those affected through the production of pro-inflammatory cytokines and scavenging free radicals. Based on what we know about COVID-19, its resultant “cytokine storm,” the chemical properties of melatonin, and the support of literature advocating the use of melatonin as an adjuvant treatment for COVID-19, we chose to identify whether there was any statistical difference in 30-day mortality, length of stay, inflammatory marker change between admission and during the course of hospitalization amongst those who were given melatonin, stratified by dose strength during their hospital course vs. those without melatonin use.

METHODS: A retrospective analysis was done of all inpatient adults >/= 18 years of age admitted to the Internal Medicine/Medical Critical Care service between February 21, 2020- August 31, 2020 with a confirmed diagnosis of COVID-19. We conducted multivariable direct logistic regression and multifactorial analysis of variance (ANOVA), respectively, to determine the independent contribution of melatonin dosage (none, 3mg, 6mg or 9mg) after adjusting for demographic and clinical variables. To ascertain model goodness of fit, we reported the omnibus chi square statistic and the Hosmer-Lemeshow goodness-of-fit statistic. For each covariate, we present adjusted odds ratios (AOR), and 95% confidence intervals (CIs).

RESULTS: There were 706 patients in our sample [mean age ± standard deviation = 65.1 years ± 16.1], predominantly male (57.5%); 355 with BMI > 30 (52.1%); with a white and non-Hispanic predominance (52.7%). There were 348 patients who received melatonin, amongst which 26.5% received 6mg. The other 358 patients did not receive melatonin. Treatment with 3 mg of melatonin was associated with reduced mortality, but this relationship was not statistically significant (AOR = .69, p = .24), while treatment with 6 mg or 9 mg of melatonin was associated with increased mortality, but this relationship was also not statistically significant (AOR = 1.30, p = .36). The hospital length of stay was significantly longer for patients receiving 6 mg or 9 mg of melatonin (p < .001). The melatonin group had no significant change in its CRP, Ferritin, and Lymphocyte count while those who received any dose of melatonin had values that nearly doubled during their admission.

CONCLUSIONS: There is supported evidence of melatonin reducing severity of mice models inflicted with various viruses, molecular mechanisms for use as an adjunct to COVID-19 treatment, and in patients with severe sepsis. Although melatonin was associated with a longer length of stay and no significant difference in mortality, this may be reflective of the severity of disease and further prospective and larger size studies would better assess these outcomes.

CLINICAL IMPLICATIONS: While no significant differences in mortality were found with melatonin, we encourage use for its primary effect in restoration of the circadian rhythm.

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