The Spectrum of COVID-19 Infection

In severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, there are marked inflammatory and immune responses leading to cytokine storm. This is because of the imbalance between the pro-inflammatory and anti-inflammatory mediators in the lung parenchyma. This eventually leads to apoptosis of epithelial cells and endothelial cells; subsequently, vascular leakage, abnormal T cell, and macrophages responses ensue and induce acute lung injury (ALI), acute respiratory distress syndrome (ARDS), multi-organ dysfunction, shock, and thrombosis thus contributing to significant morbidity and mortality. Several agents like steroids, ascorbic acid, vitamins (C, D, E), glutathione, N-acetylcysteine have been used and several studies are underway to identify its efficacy in addressing undesirable effects due to COVID-19 illness. Among several experimental modalities based on expert opinion and anecdotal data, melatonin is one molecule that appears promising. Owing to its anti-inflammatory, anti-oxidant, and immunomodulatory properties, melatonin can be an important agent used as a component of multimodal analgesia in COVID-19 patients, suspected patients, and patients with exposure to positive patients undergoing emergency or urgent surgeries. Further research is required to know the optimal time of initiation, dose, and duration of melatonin as an adjunct.

Key words: anesthesia; antioxidants; COVID-19; cytokine; inflammation; melatonin; multimodal analgesia; perioperative; surgery

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Cytokine storm in coronavirus disease 2019 (COVID-19) patients leads to acute lung injury, acute respiratory distress syndrome, multi-organ dysfunction, shock, and thrombosis thus contributing to significant morbidity and mortality. Several agents like steroids, ascorbic acid, vitamins (C, D, E), glutathione, N-acetylcysteine have been used and several studies are underway to identify its efficacy in addressing undesirable effects due to COVID-19 illness. Among several experimental modalities based on expert opinion and anecdotal data, melatonin is one molecule that appears promising. Owing to its anti-inflammatory, anti-oxidant, and immunomodulatory properties, melatonin can be an important agent used as a component of multimodal analgesia in COVID-19 patients, suspected patients, and patients with exposure to positive patients undergoing emergency or urgent surgeries. Further research is required to know the optimal time of initiation, dose, and duration of melatonin as an adjunct.

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CD147 and Its Implication in COVID-19

CD147 is a type I transmembrane protein that is implicated with unfavorable outcomes during viral infections including SARS-CoV-2. This is mediated through pro-inflammatory cytokines like interleukin-6, interferon-λ, tumor necrosis factor-α, and monocyte chemo-attractant protein-1. CD147 has also been found responsible for conditions like multiple sclerosis, myocardial infarction, and cancer proliferation. In SARS-CoV-2 infections, CD147, along with angiotensin-
Melatonin as Adjuvant in COVID-19 Treatment

Reducing inflammation and enhancing immunity is important in COVID-19 patients to prevent mortality and morbidity. The use of antiviral drugs in early stages when viral replication and infectivity is high appears to be beneficial. Once that stage is crossed, i.e., from the second-week cytokine storm sets in which is responsible for ALI/ARDS, multiorgan dysfunction, and other adverse events like thrombosis.

The safety of melatonin as an adjunct to multimodal analgesia is well established. Melatonin has antinociceptive properties and has been shown efficacious in managing acute postoperative pain and chronic neuropathic pain as a component of multimodal analgesia. Due to its anti-inflammatory, antioxidative, and antinociceptive effects, anesthesiologists can consider starting oral melatonin to COVID-19 positive patients who are coming for emergency or urgent surgeries. When administered orally, the T_{max} of oral melatonin is about 50 minutes in healthy volunteers. Ramllall et al. reviewed data from 791 intubated patients with COVID-19. Authors concluded that patients who were treated with melatonin after intubation had a statistically significant positive outcome (demographics and comorbidities adjusted hazard ratio: 0.131, 95% confidence interval: 0.076 to 0.223). However, the authors did not mention the dose and duration of melatonin therapy in these patients. There are several ongoing studies which are currently ongoing which is investigating the dose, efficacy, safety, and duration of melatonin use in critically ill COVID-19 patients. A study has suggested a dose ranging from 5–8 mg/kg per day in COVID-19 patients for its anti-inflammatory and immunomodulatory effects.

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ologists could consider using melatonin as a part of multimodal analgesia when dealing with COVID-19 patients, suspected patients, or patients who have history of exposure as it could provide additional benefit. Further, ongoing studies could reveal the optimal time of starting, safest possible dose, and duration of melatonin therapy to provide anti-inflammatory and anti-oxidative benefits in COVID-19 patients.

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