



# ALL INDIA INSTITUTE OF MEDICAL SCIENCES

## RISHIKESH

Patient name:

UHID:

Admitted location:

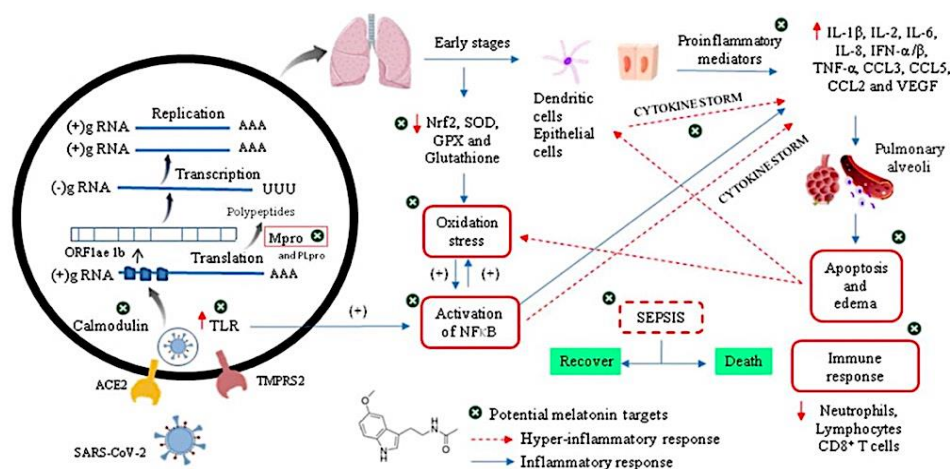
### Hospital Treatment Policy – “Melatonin Therapy” Information Sheet

**(16.05.21 onwards)**

**Melatonin** should not be considered as a man-made substance (although most of its commercial products contain synthetic melatonin), but rather as a naturally occurring molecule, since it is present in almost all organisms from the bacteria to the human. This hormone is secreted during the period of darkness and facilitates transition to sleep.

#### Role in SARS-CoV-2 infection:

- SARS-CoV-2 infection is associated with an enhanced immune response with surge of cytokines e.g., IL-1, IL-6, TNF-alpha along with reduction of CD4+ and CD8+ T cells.
- Virus-induced internalization of pulmonary ACE2 and loss of its function may be considered as an important cause in the pathology of SARS-CoV-2 associated acute respiratory distress syndrome.
- ACE2 internalization by SARS-CoV-2 may result in a dysfunction of RAS and amplification of pulmonary tissue destruction initially inflamed by SARS-CoV-2. Therefore, reduced expression of ACE2 and RAS dysfunction following SARS-CoV-2 infection may influence fluid/electrolyte balance and blood pressure.
- Diminution of ACE2 may exacerbate airway inflammation and vascular leakage, contributing to chronic loss of pulmonary function, and enhanced tissue fibrosis.
- These effects may be reversed by melatonin as, melatonin besides being a sleep promoting hormone, also has antioxidant, anti-inflammatory, anti-excitatory and immunoregulation properties.
- Melatonin is a regulator of autophagy due to its properties as a potent antioxidant and suppressor of endoplasmic reticulum stress suggests a potential beneficial role for this molecule in the management of some viral infections.
- Viruses, including Ebola, dengue, encephalomyocarditis, Venezuelan equine encephalitis, rabbit haemorrhagic disease, human papilloma, and inter alia, have demonstrated the success of melatonin in protecting against viral infections.
- There is no evidence that melatonin is viricidal but rather it reduces the severity of these infections.
- Melatonin's beneficial effects derive from its anti-inflammatory properties, free radical scavenging activity, and immunomodulatory functions, as already stated above (Fig 1).



**Fig 1: Possible mechanisms of action for the Melatonin in SARS-CoV-2 infection**

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### Indications in COVID-19:<sup>1-3</sup>

Mild to moderately severe SARS-CoV-2 infection

### Contraindications:

- Pregnancy
- Breastfeeding
- Liver disorders

### Dose schedule & Administration:

**3-9 mg/day 30 min before bedtime;** start with low dose 3mg/day for 2days, if tolerated and no benefit in sleep/anxiety problems, increase 3mg/day dose in two days intervals (upto 9mg/day)

### Safety profile:

Data indicate that large doses of melatonin, whether given chronically or for acute treatment will not cause intolerable or uncontrollable side effects and that the safety margin of melatonin for humans can be up to 3,750 mg/day for a 75kg individual.

### Warnings/precautions:

#### Pharmacokinetics:

Oral bioavailability of melatonin ranges between 9-33%.

Patients taking following medications should be **watched for the adverse effects** as CYP1A2 inhibitors such as **fluvoxamine, cimetidine, ciprofloxacin and enoxacin** as well as, to a lesser extent, competing substrates such as **flutamide, mirtazapine, olanzapine and tacrin** can, in principle, delay the catabolic decay of melatonin.

Melatonin also exhibits the anticoagulating activity. However, in case of bleeding tendency it may be discontinued and because of short  $t/2$ , the concomitant use of anticoagulants and melatonin is safe, at least, it will not cause prolonged bleeding problem after its withdraw.

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### Monitoring parameters:

- Chart sleep quality everyday in the provided sheet
- Determine blood glucose levels and administer, if necessary, insulin.
- PT/INR if patient is taking anticoagulants

### Melatonin monitoring sheet

**(This to be submitted in patient file during discharge/transfer to CCU)**

UHID:.....		Age:.....Years			Gender: M/F	Any adverse effect
Day and date	Dose of melatonin	Sleep time	Wake time	Naps, if any with duration in hours	Compared to previous night, how was your sleep last night?	
1 .....	.....mg	.....PM	.....AM	....hr	<input type="radio"/> Similar <input type="radio"/> Better <input type="radio"/> Worse	
2 .....	.....mg	.....PM	.....AM	....hr	<input type="radio"/> Similar <input type="radio"/> Better <input type="radio"/> Worse	
3 .....	.....mg	.....PM	.....AM	....hr	<input type="radio"/> Similar <input type="radio"/> Better <input type="radio"/> Worse	
4 .....	.....mg	.....PM	.....AM	....hr	<input type="radio"/> Similar <input type="radio"/> Better <input type="radio"/> Worse	
5 .....	.....mg	.....PM	.....AM	....hr	<input type="radio"/> Similar <input type="radio"/> Better <input type="radio"/> Worse	
6 .....	.....mg	.....PM	.....AM	....hr	<input type="radio"/> Similar <input type="radio"/> Better <input type="radio"/> Worse	
7 .....	.....mg	.....PM	.....AM	....hr	<input type="radio"/> Similar <input type="radio"/> Better <input type="radio"/> Worse	

### References:

1. Tan D-X, Hardeland R. Estimated doses of melatonin for treating deadly virus infections: focus on COVID-19. Melatonin Research. 2020;3(3):276-96.
2. Reiter RJ, Abreu-Gonzalez P, Marik PE, Dominguez-Rodriguez A. Therapeutic Algorithm for Use of Melatonin in Patients With COVID-19. Frontiers in Medicine. 2020;7.
3. Bahrapour Juybari K, Pourhanifeh MH, Hosseinzadeh A, Hemati K, Mehrzadi S. Melatonin potentials against viral infections including COVID-19: Current evidence and new findings. Virus Res. 2020;287:198108.

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