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Melatonin and its agonists in pain modulation and its clinical application.

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Abstract

Melatonin, the hormone of darkness has many physiological functions in the body and also exerts a number of pharmacological effects. Most of these actions of melatonin are mediated through melatonin membrane receptors like MT1/MT2 receptors or through nuclear orphan receptors like RZR/ROR receptors or through calcium binding proteins in the cytosol. The finding that pain perception is circadian in nature has prompted many to suggest that "pain modulation" is one of the most important physiological functions of melatonin. By using a number of animal models of pain perception, it has been found that melatonin exerts antinociceptive and antiallodynic effects. Number of studies has shown that melatonin modulates pain perception by acting through opioid receptors, NMDA receptors and G-protein, and they have been analyzed using specific antagonists like naloxone or NMDA-G protein receptor antagonists. Recently it has been shown that melatonin exerts its antinociceptive effects through MT1 and MT2 melatonergic receptors located in the dorsal region of the spinal cord as well as in various parts of the brain concerned with pain modulation. Evidences for this have been obtained by using common melatonergic receptor antagonist like luzindole or specific MT2 receptor antagonist like 4P-PDOT or K-185. In a few clinical studies undertaken during surgery, melatonin has been shown to have analgesic effects. Melatonin is emerging as a new analgesic drug with a novel mechanism of actions and has the potential to be used as a natural pain killer in inflammatory, neuropathic pain conditions and also during surgical procedures.

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