Melatonin and Anxiety: from animal models to clinical practice

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Abstract

Introduction: There has been a considerable amount of scientific literature focusing the role of circadian disturbances and sleep changes in depression, bipolar disorders and even in schizophrenia but few have explored the relationship between disruption of melatonin circadian release and anxiety symptoms. This association is frequent, for example, in shift work disorder with important implications on social and professional capacity and quality of life. Disruption in circadian rhythms has been related with low nighttime and 24h levels of melatonin, a neurohormone known to be involved in the regulation of anxiety. The underlying mechanism correlating disruption of circadian rhythms and melatonin levels to the emergence of anxiety is not well understood.

Objectives: This study aims to review the state of the art on the subject concerning pathophysiological mechanism, clinical findings and relevance as well as treatment options for anxiety.

Methods: A nonsystematic review of all English language PubMed articles published between 1991 and 2014 using the terms “anxiety”, “circadian”, “melatonin”, “treatment” and “sleep”.

Results: Chronic circadian disruption has been associated with higher levels of anxiety. Studies with animal models have been used to study the effects of internal and external melatonin on anxiety showing a correlation between melatonin levels and anxiety. In healthy subjects, anxiety levels were significantly and negatively correlated with melatonin production in summer and winter. This neurohormone is also known to have an anti-inflammatory activity in central nervous system, which is a general underlying mechanism in neuropsychiatric disorders. It has also been hypothesized that melatonin could be evolved in the immune-opioids network that mediate the return to baseline states after stressful events. The disruption in this system could be more specific in anxiety pathophysiology. Recently some melatonin receptor agonists like UCM765 and agomelatine have shown anti-anxiety effects on animal models. Effects on clinical samples are yet to be determined.

Discussion and Conclusion: Chronic circadian disruption through could make neural systems less able to cope with stress and lead to the development of anxiety disorders. The interaction between opioid system and melatonin mechanism could provide a possible explanation for the pathophysiological mechanism underlying this symptomatology.

Supplementary material: Complete presentation available at http://ijcnmh.arc-publishing.org