

## Melatonin: Miracles far beyond the pineal gland

Sir,

Melatonin has recently been recognized to have a role as an anti-oxidant in the human ovarian follicle, and its use may result in improved fertility.<sup>[1]</sup> Studies on animal models have also revealed the anti-obesity effects of melatonin and found this hormone to prevent hyperadiposity. Thus, melatonin may play a potential therapeutic role in metabolic syndrome.<sup>[2]</sup>

I read this fresh add-on in literature along with articles in the IJEM<sup>[3,4]</sup> with keen interest. This prompted a review of literature for current clinical indications of melatonin, as well as its potential, versatile role.

Melatonin, chemically named as N-acetyl-5-methoxytryptamine, is a naturally occurring lipophilic compound found in animals, plants and microbes.<sup>[5]</sup> Melatonin is synthesized not only by the pineal gland, but also in epithelial cells, bone marrow cells and lymphocytes.<sup>[6]</sup> Furthermore, melatonin receptors are dispersed throughout the body emphasizing its widespread role in regulating various physiological<sup>[6]</sup> and psychological processes.<sup>[7]</sup> Three types of melatonin receptor have been recognized and classified as MT1, MT2 and MT3.<sup>[5,8]</sup> In humans, MT1 and MT2 receptor subtypes have found to be expressed, mainly

in human brain and retina and also in different organs which include cardiovascular system, liver and gallbladder, intestine, kidney and skin.<sup>[8]</sup>

Melatonin is known to influence sleep and mood patterns; act as scavenger molecule and anti-oxidant; regulate immune mechanisms and carcinogenic processes; and also control reproductive functions.<sup>[6,9,10]</sup>

Keeping all the above mentioned functions of melatonin in mind, we can conclude that treatment with melatonin may show promising results in the treatment of circadian rhythm sleep disorders; depression and seasonal affective disorder (SAD); bacterial infections, viral infections, sepsis and cardiovascular diseases; immune disorders and cancers; and sexual problems and infertility.<sup>[6]</sup>

Nduhirabandi *et al.* have found melatonin beneficial in the treatment of metabolic syndrome along with the prevention and/or reversion of obesity-related detrimental effects associated with the syndrome. Furthermore, ischemic heart disease and hypertension have also been benefited with melatonin administration.<sup>[9]</sup> These preliminary results are promising but need further evaluation to establish and standardize this treatment.

Mortality with breast cancer is consistently increasing. In this regard, we can at least address breast cancer-related problems which include anxiety, depression, sleep disturbances and cognitive dysfunction<sup>[11]</sup> to provide a complication-free survival in patients with breast cancers. Owing to its effects on mood and sleep, melatonin may relieve these symptomatic problems.<sup>[11]</sup>

Due to actions of immunomodulation, anti-oxidation and inhibition of pro-inflammatory mediators, melatonin is also recommended for the treatment of severe respiratory distress syndrome in pre-mature infants and septic shock.<sup>[6]</sup> Other pediatric conditions which have been benefited with melatonin treatment include autism spectrum disorders, sleep disorders of various origins, epilepsy and febrile seizures.<sup>[12]</sup>

Melatonin is also a geroprotective agent which slows the aging process. As melatonin may delay aging process with its versatility of actions, it may also reduce and/or delay the occurrence of Alzheimer's disease.<sup>[13]</sup>

Abnormal pattern of plasma melatonin levels has been associated with chronic migraine and chronic tension-type headache.<sup>[14,15]</sup> Melatonin has a potential therapeutic role in treating several types of headache.<sup>[15]</sup>

Melatonin is naturally secreted by the entero-chromaffin

cells of gastro-intestinal tract and is thought to play a role in mucosal protection against injury.<sup>[16,17]</sup> Melatonin is also suggested for the treatment of GERD, functional dyspepsia and irritable bowel syndrome.<sup>[17]</sup>

In the light of the literature cited above, melatonin is now evolving as a versatile and multifunctional molecule, with promising role in different clinical conditions. It is yet all-important to determine the efficacy of melatonin in more clinical trials, to further confirm its efficacy as well as to investigate its possible side effects in longer durations of therapy.

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