INTENSIVE CARE, HEART FAILURE AND MELATONIN

Melatonin (5-methoxy-N-acetyltryptamine) is a neurohormone that is produced in the pineal gland mainly during the night by stimulation of beta-1- and alpha-1-adrenergic receptors, and it affects a variety of heart functions including cardiac rhythms, arterial blood pressure and heart rate. Some studies suggest that melatonin may have utility in the treatment of several cardiovascular conditions such as advanced heart failure. Melatonin has been shown to be highly effective in limiting abnormal cardiac physiology and the loss of critical heart tissue resulting from ischemia/reperfusion injury. It may also be useful in reducing cardiac hypertrophy in some situations and thereby limiting the frequency of heart failure. Taken together, the findings from this studies may support the consideration of melatonin as a cardioprotective agent at the intensive care patients with advanced heart failure.
Key words: Melatonin, kalp yetmezliği, intensive care

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Melatonin (5-methoxy-*N*-acetyltryptamine) is a neurohormone synthesized in the pineal gland, mainly during the night by stimulation of beta-1- and alpha-1-adrenergic receptors, and regulates several physiological functions, including cardiac rhythms, arterial blood pressure, heart rate, immune function and sleep (1). Light has an inhibitory effect on the pineal melatonin secretion. Melatonin is metabolized rapidly in the liver. Urinary excretion of its major metabolite -6-sulfatoxymelatonin- is a useful measure of the total amount of melatonin produced. Melatonin influences the catecholamine such as norepinephrine levels in perivascular nerves, influences pulmonary arteries and veins by endothelium dependent factors, induces relaxation of the rat aorta, directly affects calcium dependent cardiac sarcolemma adenosinetriphosphatase (2-6).

The studies suggest that melatonin may have utility in the treatment of several cardiovascular conditions such as coronary artery disaese, hypertension (7-12). Brugger et al (7) and Domínguez-Rodríguez et al (8) showed a decreased nocturnal plasma melatonin in coronary heart disease and acute myocardial infarction, respectively (7,8). The melatonin as an antioxidant agent could be beneficial to prevent the adverse effects of reactive oxygen radicals during myocardial ischemia-

reperfusion. Melatonin is probably involved in the control of the circadian rhythm of arterial blood pressure. Holmes et al (9) showed that pinealectomy leads to hypertension in the rat. Also, Jonas et al (10) demonstrated that nocturnal melatonin secretion is impaired in non-dipper hypertensive patients. Melatonin has also been shown to modulate vascular smooth muscle tone and to induce hemodynamic effects (11,12). Shibata et al (11) suggest that melatonin and nifedipine, a calcium channel blocker, inhibit the same calcium channels activated by KCl. Further, 5-hydroxytryptamine-activated calcium channels which are inhibited by melatonin may be different from nifedipine-sensitive calcium channels activated by 5-hydroxytryptamine.

Heart failure is a syndrome characterized by high mortality, develop the clinical symptoms such as shortness of breath, fatigue, confusion, nocturia and signs including edema and rales that may lead to hospitalizations at intensive care unit, reduced quality of life, and a complex therapeutic regimen (13). Therefore, the patients with refractory heart failure are required special interventions including hospitalizations at intensive care unit, intensive medical therapy, cardiac resynchronization therapy and cardiac transplantation (13). Melatonin may have good effects for the patients with heart failure in the intensive care unit. Girotti et al (14) assessed urinary 6-sulfatoxymelatonin excretion in patients admitted to the hospital because of congestive heart failure; and they found 6-sulfatoxymelatonin levels were significantly lower in patients with congestive heart failure than controls (median 2.6 vs 6.02 microg, $p< 0.0001$). Finally, they suggested that circulating melatonin levels are low in patients with congestive heart failure and this decrease may precede aggravation of heart failure.

Melatonin has been shown to be highly effective in limiting abnormal cardiac physiology and the loss of critical heart tissue resulting from ischemia/reperfusion injury which refers to myocardial, vascular, or electrophysiological dysfunction that is induced by the restoration of blood flow to previously ischemic tissue (15). By preventing lipid peroxidation, melatonin may be highly effective in protecting against adriamycin (is a potent, broad-spectrum chemotherapeutic agent whose clinical use is limited by its cardiotoxicity) induced cardiomyopathy (15). Taken together, the findings from this studies may support the consideration of melatonin as a cardioprotective agent at the intensive care patients with advanced heart failure (14,15).

In this brief review, it has been summarized the data describing the protective actions of the melatonin and its metabolites on myocardial damage at intensive care patients with advanced heart failure. In view of the large amount of positive data that has already accumulated, additional studies in this field should be of high priority.

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