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Aging and vascular dysfunction: beneficial melatonin effects

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The study of biological aging has seen spectacular progress in the last decade. Aging is characterized by a progressive deterioration of physiological functions and metabolic processes. Moreover, aging is accompanied with the development of age-related diseases, such as cardiovascular diseases, which are the major causes of morbidity and mortality in the developed nations.

Sirtuin1 (SIRT1) is a well investigated member of the sirtuin family of protein deacetylases which has attracted attention as a potent mediator of life span extension.

Recently, melatonin, a pleiotropic molecule which functions as a highly effective antioxidant and free radical scavenger, was shown to activate SIRT1 in primary neurons of young animals, as well as in aged neurons of a murine model of senescence. Melatonin is known to modulate oxidative stress-induced senescence and pro-survival pathways.

We treated ApoE-deficient mice with two melatonin formulations (kindly provided by Nathura s.r.l, Reggio Emilia, Italy), showing different pharmacokinetic: melatonin Fast, rapid-release formulation, and Retard, extended-release formulation.

Morphological changes in vessels were evaluated using histological procedures and immunohistochemical analyses of SIRT1, p53, eNOS and ET-1 markers. We demonstrate that SIRT1 and eNOS dropped dramatically in ApoE mice and that atherogenesis induced an elevated expression of p53 and ET-1. Melatonin not only improved the impairment of endothelial damage, but also reduced the loss of SIRT1 and eNOS decreasing p53 and ET-1 expression. Also, the extended-release melatonin preparation (Retard) caused a greater improvement of aorta cytoarchitecture.

In summary, our findings implicated the SIRT1-p53-eNOS axis as one of the important process involved in endothelial senescence. Moreover, the role of SIRT1 as a driver of cellular stress resistance and longevity is noteworthy in the context of its expression profile. Finally, we suggest that extended-release melatonin provides a more appropriate option for cellular longevity compared with rapid-release melatonin administration.

Keywords: Key words: Melatonin, Atherosclerosis, Sirtuin1, Senescence

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