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Vascular cell dysfunctions: a possible atheroprotective role of melatonin

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Atherosclerosis is a chronic disease of the arterial wall and a leading cause of death and loss of productive life years worldwide. It is considered a chronic inflammatory vascular disease characterized of monocyte extravasation into the arterial wall (Libby et al., 2011). Researches into the disease have led to many compelling hypotheses about the pathophysiology of atherosclerotic lesion formation and of complications such as myocardial infarction and stroke (Ross, 1999). The last several decades have witnessed aburgeoning growth of understanding of the molecular pathways involved in atherogenesis, atherosclerotic lesion progression and the pathogenetic mechanisms involved.

In this study was evaluated the role of cyclophilin A (CyPA) in early phase of atherosclerosis, the beneficial effects of melatonin in vascular remodelling due to its ability to modulate rolling of mononuclear cells and its acting on vascular smooth muscle cell proliferation and neointima formation.

In particular, in this study APOE null mice at 6 and 15 weeks of age were used; they were treated with melatonin at dose of 0.1mg/kg/day and 10mg/kg/day. We evaluated both CyPA expression and its signaling pathways in atherosclerosis development.

CyPA expression increased in mononuclear cells and, in turn, stimulated vascular cell adhesion and interleukin-6 increase in the endothelial cells and vascular smooth muscle cells in a time-dependent manner. Melatonin treatment at the dose of 10mg/kg/day completely improved vascular injury inhibiting the increase of CyPA.

In summary, these findings suggest that CyPA induces the early step of atherosclerosis and indicate that the antioxidant effects of melatonin are both on antioxidant enzymes and other proteins, such as CyPA. Moreover, CyPA will be considered the bridge between inflammation and atherosclerosis. Thus, melatonin use could be a safe strategy of improving the development and progression of atherosclerosis.

References

Libby et al. (2011) Progress and challenges in translating the biology of atherosclerosis. Nature 473: 317-325.

Ross (1999) Atherosclerosis is an inflammatory disease. Am Heart J 138: S419-S420.

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