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Letter to the Editor

Relationship Between Nighttime Blood Pressure, the Renin-angiotensin System, and Melatonin

Relación entre la presión arterial nocturna, el sistema renina-angiotensina y la melatonina

To the Editor,

We have read with great interest the article on nighttime blood pressure (BP) and neurohormonal activation in patients with idiopathic atrial fibrillation in the *Revista Española de Cardiología*.[1] According to the authors, nighttime BP values are directly associated with left atrial size and atrial and brain natriuretic peptides in patients with idiopathic atrial fibrillation. We think it may be of interest to discuss a number of issues related to nighttime BP and neurohormonal activation.

First, the authors do not mention the effect of another neurohormone, melatonin, on BP. Oscillations in physiological functions that occur over a 24-h period are known as circadian rhythms.[2] During sleep, there is a decrease in BP in the cardiovascular system. Melatonin is one of the main hormones serving as an endocrine signal in the circadian rhythm.[2] Its secretion is mainly controlled by light via the suprachiasmatic nucleus (biological clock), such that darkness stimulates its secretion and light inhibits it.[3] Recently, our group demonstrated an association between an abnormal pattern of melatonin secretion and alterations in BP in healthy subjects.[4]

Second, the authors discuss from a physiological point of view the important role of nighttime BP in remodeling and growth of the left atrium, possibly mediated by activation of the renin-angiotensin system (RAS).[1] Several articles have been published on the association between the RAS and melatonin.[5–7] Angiotensinogen is the precursor of the RAS and has been identified in pineal glial cells and the receptors type AT1b in pinealocytes.[5] Angiotensin II, as part of the RAS, acts on receptors type AT1b in pinealocytes to influence the synthesis and activity of tryptophan hydroxylase, an enzyme that limits melatonin production.[7] The demonstration of a functional pineal RAS interfering with melatonin synthesis indicates that this may affect the modulation of circadian rhythms. In fact, the majority of published studies suggest that the relationship between angiotensin and melatonin synthesis in cardiovascular disease is antagonistic.[7]

Finally, the administration of low pharmacologic doses of melatonin (1 mg) reduces BP as a consequence of various mechanisms, such as a direct hypothalamic effect, a lowering of catecholamine levels, the relaxation of the smooth muscle wall and, above all, as a result of its antioxidant properties. There is evidence suggesting that melatonin may have a hypotensive effect,[8] especially in non-dipper hypertensive patients.[9] Thus, the interaction between the RAS and melatonin in relation to BP should be taken into account. From a clinical standpoint, more research is needed on the interaction between angiotensin and melatonin to further our understanding of the pathophysiology of cardiovascular disease, with a possible impact on chronotherapeutic strategies.

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