

The mitral valve and endothelin-1 in cardiovascular homeostasis

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The mitral valve, once considered an inert structure with a mechanical response to the demands of intracardiac flow, has been the aim of research that may reveal different functions from those we are used to assign. The action of substances with autocrine or paracrine effect may be co-responsible for constant adjustments in their morphology and function. The use of techniques of biology and molecular pharmacology to elucidate these issues offers a fertile field for research.

The observation of receptors in valve tissue reveals that this tissue may be subject to change. It is noteworthy that, in addition to being a site capable of morphogenetic changes, the mitral valve appears as a source of substances with cardiovascular effects. In this scenario, endothelin-1 (predominant isoform in the endothelium) seems to be a good example: its complexity is shown by pharmacological diversity of actions in the cardiovascular system [1,2]. After its identification in 1988, huge interest in its functions led scientists to write more than 20 000 scientific papers about the subject [3,4]. However, many questions still remain enigmatic. Among them, we highlight the mitral valve involvement in certain diseases, sometimes suffering morphofunctional adaptations, sometimes enhancing and perpetuating these pathological conditions.

Through its receptor, endothelin-1 has one of the most potent vasoconstrictors effect known by Science. It affects the inotropism and chronotropism, and is an adjunct in diseases such as pulmonary hypertension [5], systemic hypertension [6] and atherosclerosis [7]. It is a mediator of hypertrophy and cardiac remodeling in congestive heart failure [2]. But what is the real participation of the mitral valve in the pathophysiology of these diseases as a possible source of endothelin-1 in

adjacent cardiomyocytes and to its own structure? And what is the action of these diseases over the mitral valve morphogenesis, taking into consideration that this valve is site for endothelin receptor-1?

Such pathophysiological dilemmas hide potential therapeutic responses to highly prevalent diseases that victimize millions of people. The use of receptor antagonists (A and B) of endothelin-1 is already a reality in medical practice [8]. Logically, the affinity of the antagonist for the receptor type resonates with its pharmacological action. Mapping these receptors in different tissue sites, typifying its action, establishing the selectivity and the effects of its chemical block, we will be able to act more accurately in the treatment of these diseases.

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However, there is still much doubt about the approach to this issue, taking into account the difficulty in obtaining normal and viable tissue valve for comparative quantitative study. This research would allow us to determine whether there is more or less density of endothelin-1 and its receptors in normal mitral valves. This is due to two main reasons: the rapid degeneration of messenger RNA by RNases, only allowing its extraction *in vivo* (as the chosen technique) and the importance of the valve structure in healthy individuals, preventing the removal of endothelin-1 genes quantification sample and its receptors in valves free from pathological changes. One option would be derived tissue of organ donation, however, the acquisition of samples from this source lacks specific legislation [9].

Therefore, the mitral valve is no longer the same, nor should be the approach of their duties. Its ultrastructure certainly still hides many unknown molecules. The answer to their interference in pathological situations

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may lie in these molecules, and possible modulatory effects on homeostasis. Such responses will mark the left atrioventricular valve in an indelible way.

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