Chapter 22

iECA: physiology behind veterinary pharmacology

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ABSTRACT
The increase in dogs' life expectancy has been related to the identification of cardiac affections that present dyspnoea, cyanosis, dry cough, and syncope. A fundamental strategy for the treatment of heart disease is pressure control by blockade of the renin-angiotensin-aldosterone (RAS) system with inhibitors of angiotensin-converting enzyme (ACE). Those agents that are specific antagonists of angiotensin II have allowed veterinary medicine to increase since 1970 and 1980. ACE inhibitors are generally well tolerated and they improve hemodynamics and clinical sign by controlling vasoconstriction, caused by alpha-adrenergic receptors stimuli. These vasodilator drugs act to prevent the impairment of myocardial function, helping in the chronic condition of heart failure (HF) which, as a result of the reduction in cardiac output, could compromise pre- and after-load due to the increase in blood volume. Their usefulness in the treatment of dogs with chronic heart failure, especially in those with chronic valvular disease.

Keywords: heart failure, ACE, mitral valve endocarditis

1 INTRODUCTION

ACE inhibitors are proposed for the treatment of Heart Failure (HF) using prevention of ventricular remodeling, reduction of pre- and after-load, and possible regression of the left ventricular hypertrophy condition. Its mechanism of action involves the systemic and focal suppression of the activation of the Renin-Angiotensin-Aldosterone System (RAAS).

The prescription of this vasodilator increases the life expectancy of two patients affected by HF, mainly due to dilated cardiomyopathy, and also presents better clinical manifestations of its manifestations, some of which are: fatigue, tachycardia, respiratory distress, and exercise intolerance. Even, in a clinical evaluation, during auscultation, the gallop rhythm, arrhythmia, and wheezing can be observed.

In various cases, these can remain asymptomatic for a long period due to compensatory mechanisms. These increase the blood volume and the size of the heart, such as dilation of the ventricle and atrium, eccentric myocardial hypertrophy, or even using the mechanism of the sympathetic autonomic nervous system, associated with the renin-angiotensin-aldosterone system. Through them, there will be cardiac remodeling through the activation of the sympathetic autonomic nervous system, the renin-angiotensin-aldosterone system (RAAS), and the release of antidiuretic hormone (ADH).

At first, this physiological compensation will help circulation, since when the blood is regurgitated back into the atrium, there is a general blood flow drop. Thus, it is feared that blood volume increases by

sodium and water retention, thanks to aldosterone function, and also promotes vasoconstriction, activated by angiotensin, helping tissue perfusion. Yes, the SNA Sympathetic work does not increase heart rate and also does not increase positive inotropy, aiming to restore physiological normalization of blood volume and cardiac output that is decreased by blood regurgitation generated by valve prolapse.

This mechanism saves many lives, but the chronicity of its activation will accelerate the process of declining cardiac function, causing systemic alterations, one of which is excessive volume retention caused by aldosterone and ADH action, leading to a lack of sodium accumulation, or which directly influences the possibility of pulmonary and limb edema, ascites, effusion, and congestion. Yes, chronic vasoconstriction following angiotensin activation increases after load, reduces cardiac output, and still provides greater valve reflux.

Yes, the activation of the sympathetic autonomic nervous system in a chronic way will have consequences on cardiac function directly. Due to the post-load, it requires greater cardiac effort, promoting a greater requirement of oxygen by the myocardium, to the point of contributing to the occurrence of cell damage, and at the same time myocardial fibrosis, and evolving into cardiac arrhythmia.

The baroreceptors are the ones that provide the necessary feedback for the normalization of these mechanisms, but due to heart failure due to valve prolapse, they will have greater responsiveness, and will further stimulate the activation of two compensatory systems and, consequently, are feared. a decrease in the vagal inhibitory response.

In addition, the compensatory hormonal mechanism of the RAAS aims to increase the vascular volume through alterations such as water retention, sodium and chloride reabsorption, and potassium and hydrogen secretion. And aldosterone also plays a compromising role in influencing two processes of inflammation and fibrosis or contributing, chronically, to the process of pathological remodeling and myocardial fibrosis. The antidiuretic hormone will promote fluid retention and vasoconstriction. Renin, which is produced in the kidneys, and acts to facilitate the conversion of angiotensinogen into angiotensin I, in its inactive form, undergoes the action of the angiotensin-converting enzyme, to transform it into angiotensin II, which is a potent vasoconstrictor stimulant of the release of ADH. Yes, Angiotensin II, also produced in the heart, influences the structures and functioning of the own organ, increasing the action of sympathetic effects, or which also has consequences such as alterations in the cardiac tissue, such as remodeling, hypertrophy, inflammation, and fibrosis.

2 ACTION MECHANISM

The inhibition of the angiotensin-converting enzyme by its action does not block the enzyme that is responsible for the transformation of Angiotensin I to II, or that allows arteriolar and venous vasodilation, in addition to reducing sodium reabsorption, which promotes increased pre-load, myocardial fibrosis, cardiac remodeling, and myocyte apoptosis, stabilizing hemodynamic parameters. In sum, the deleterious effects of the chronic activation of the RAAS will be inhibited, directly reflecting the pre- and post-loading

and the survival of the animal.

3 DRUGS

The ACEI group is made up of drugs such as enalapril, benazepril, ramipril, and or lisinopril that are prescribed in the area of Veterinary Medicine. From these, the first three need their biotransformation using hydrolysis of hepatic esterases to become prodrugs, and they will be excreted via the kidneys.

Therefore, the proper selection of the prescribed active principle will be based on pharmacokinetic characteristics, especially related to its bioavailability, route of elimination, and daily dose, and also considering whether or not hepatic activation is required.

4 CONCLUSION

The initial prescription of ACE inhibitors for animals that have clinical manifestations related to mitral valve regurgitation are two main steps for it to occur: increasing life expectancy and preventing secondary diseases such as dilated cardiomyopathy and congestive heart failure that, in turn, would lead to, to edema of cardiogenic origin.

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