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Benefits of Intravenous Vagal Stimulation in an Experimental Model of Myocardial Ischemia and Reperfusion

Arimura T, Saku K, Kakino T, Nishikawa T, Tohyama T, Sakamoto T, et al. Intravenous electrical vagal nerve stimulation prior to coronary reperfusion in a canine ischemia-reperfusion model markedly reduces infarct size and prevents subsequent heart failure. **Int J Cardiol. 2017 Jan 15; 227: 704-10.http://doi.org/f9hbkr**

Although advances in early reperfusion techniques in acute myocardial infarction (AMI) have achieved a very marked reduction in short-term mortality, a significant percentage of patients who have suffered an infarction progress to heart failure. Thus, heart failure due to ischemic heart disease remains one of the main causes of mortality worldwide. A key determinant in the evolution and prognosis of a patient with ischemic heart disease is infarct size. Another important aspect, strongly related to the previous one is dysautonomia, characterized by an increase of sympathetic nervous tone and a reduction of parasympathetic nervous tone. This dysautonomia is observed in numerous comorbidities (hypertension, diabetes, dyslipidemia, sedentary lifestyle, and stress) which represent risk factors for the development of coronary heart disease and accompany the torpid evolution of the ischemic heart in chronicity.

Great efforts have been made during the last decades to reestablish the balance between the two components of autonomic cardiovascular regulation, thus improving patients' prognosis. This was partly achieved with the use of adrenergic blockers to counteract sympathetic hyperactivity. However, significant benefits have not yet been attained by increasing the parasympathetic tone. Preclinical studies in recent years have shown that electrical stimulation of the vagus nerve has beneficial effects on AMI and subsequent ventricular remodeling because it increases the parasympathetic activity at the heart level. However, the technical difficulties involved in placing a stimulator in the vagus nerve at the cervical level, limit its implementation as a technique to treat AMI.

In this work, Arimura et al. studied the effects of electrical vagal stimulation (VS) through apuncture-implanted intravenous electrode in the superior vena cava. The experiments were performed in dogs undergoing 3-hour myocardial ischemia by anterior descending coronary artery occlusion, followed by reperfusion. Vagal stimulation was intermittently applied during ischemia and the first hour of reperfusion. Then, the animals were recuperated and evaluated during 4 weeks. The authors observed that intermittent transvascular VS reduces infarct size and improves subsequent infarct evolution, as evidenced by enhanced left ventricular function with higher ejection fraction, reduced end-diastolic pressure and greater contractility. Interestingly, these VS effects depended on reduced heart rate, since in an additional experimental group in which VS was applied with constant heart rate through an inserted pacemaker, no reduction in infarct size or hemodynamic improvements were observed. This last result is surprising since previous studies have shown favorable outcomes of VS irrespective of heart rate, such as anti-inflammatory effects, reduction of apoptosis and arrhythmias, improvement in the distribution of collagen, etc.

This study adds to the encouraging results, which have appeared regularly in numerous publications for little more than a decade on the benefits of experimental VS on AMI and ventricular remodeling. This interesting work provides an additional technical detail: it achieves intravenous VS, which would reduce the obvious technical difficulties of direct stimulation of the vagus nerve in patients. Although the experimental studies are conclusive in terms of benefits, the first clinical trials of VS in patients with heart failure are not entirely encouraging. It is possible that the same comorbidities leading to dysautonomia become an obstacle to achieving benefits with VS, as the cholinergic pathways may be damaged in diseases such as diabetes. Further studies will allow us to know the parameters and the appropriate moments to achieve these benefits of VS in clinical practice.