Adenosine in Ventricular Arrhythmias: Moving Towards New Pathophysiologic Frontiers

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Adenosine-sensitive ventricular tachycardias are a subgroup of tachycardias seen in patients without structural heart disease. They generally appear after episodes of sympathetic hypertony induced by emotional stress or physical excercise.[1] The complete mechanism of these arrhythmias is unknown, though there are several arguments to suggest that they originate through triggered activity induced by abnormal depolarizations of the cell membrane (delayed after depolarizations), all within a context of excess intracellular calcium induced by catecholamines.[1] Not all areas of the heart appear to develop such a pro-arrhythmic background. Intracavity electrogram maps obtained in the electrophysiology laboratory during episodes of tachycardia, plus information derived from radiofrequency ablations of pro-arrhythmic foci, indicate that ventricular tachycardias sensitive to adenosine preferentially originate in the right ventricular outflow tract.[2] They may also originate, though less frequently, in the left ventricular outflow tract.[3] The typical electrocardiographic pattern of tachycardia originating in the right ventricle shows left bundle branch block and a downward deviation of the electrical axis. When the origin is in the left ventricle, a left bundle branch block with an upwards or indeterminate deviation of the axis is seen.

Adenosine can help characterize the mechanism of idiopathic ventricular tachycardia. However, although its administration is usually innocuous in patients without heart problems, serious pro-arrhythmic effects have been recorded in patients with structural heart disease.[4,5]

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In the clinical context of ischemic heart disease and ventricular tachycardia with reentry, no cases of adenosine-sensitive ventricular tachycardia have been documented.[1] This issue of REVISTA ESPAÑOLA DE CARDIOLOGÍA contains a report by researchers at the *Instituto Nacional de Cardiología de México* who tried to determine (in dogs) whether adenosine has an anti-arrhythmic effect on tachycardia originated by repetitive activity maintained by a reentry mechanism.[6] A large number of experiments were undertaken in which aconitine crystals were applied to the myocardium to induce ventricular tachycardia through repetitive activity. The myocardium of these animals had been damaged by the intramyocardial administration of phenol, which produces a lesion thought to facilitate a reentry circuit that perpetuates arrhythmia. In this model, the acute administration of 6 mg or 12 mg of adenosine during tachycardia (produced by aconitine in the presence of these myocardial lesions) restored sinus rhythm in 45% and 67% of cases respectively. The authors report that this anti-arrhythmic effect is greatest just after the administration of adenosine, and that another, less intense effect is seen between 30 min and 60 min later.

Although the sensitivity of the ventricular tachycardia generated in this model was very sensitive to adenosine, extrapolating the results to the clinic would be unwise for two reasons. First, the authors do not show that the tachycardia induced is actually produced by repetitive activity, nor do they demonstrate that this arrhythmia is maintained by a reentry mechanism. Second, the pathological characteristics and pro-arrhythmic milleu produced by the intramyocardial injection of phenol are unknown. Micheli et al[6] clearly record the possibility that adenosine exerts a late anti-arrhythmic effect, but the mechanism needs to be clarified.

In the context of atrial fibrillation, the abnormal release of sarcoplasmic calcium that can generate repetitive activity has recently been described in human myocardiocytes[7]; this might favor the recurrence of an arrhythmia. Under these circumstances, drugs such as

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adenosine that attenuate arrhythmias induced by repetitive activity may be of potential use although their bring into play still warrants further investigation.

In summary, adenosine has anti-arrhythmic activity in idiopathic ventricular tachycardias induced by repetitive activity, but its routine therapeutic administration is not justified if structural heart disease is suspected. Further studies are required to assess the potential of adenosine in other arrhythmias whose mechanism is the generation of repetitive activity.

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