MATHEWS Open Access Journals

Short Communication | Mathews Journal of Cardiology

Abolition of Ventricular Tachycardia by Revascularization: When Blood Flow is All You Need to Terminate a Recurrent Ischemic Ventricular Arrhythmia

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Received Date: 26 Aug 2016

Accepted Date: 29 Aug 2016

Published Date: 13 Sep 2016

Citation: Centurión OA. (2016). Abolition of ventricular tachycardia by revascularization: When blood flow is all you need to terminate a recurrent ischemic ventricular arrhythmia. M J Cardiol. 1(2): 006.

ABSTRACT

Active vascular events such as spasm, plaque rupture or thrombosis in the setting of acute coronary syndromes precipitate fatal arrhythmias due to acute ischemia. Lethal ventricular tachycardia (VT) in the setting of ischemic heart disease (IHD) results either from acute ischemia or from chronic scar. Ischemia produces several intra, and extra-cellular changes in ionic concentration and acid-base balance. In this context, the surviving Purkinje fibers exhibit several electrophysiological changes, namely, abbreviated action potentials of reduced amplitude, and depolarized membrane potentials, and reduced conduction velocity. These biochemical and electrophysiological disturbances act in accordance with a number of probable genetic predispositions. The resultant ischemia-induced VT may be suppressed by revascularization of the occluded vessel ameliorating the ischemic tissue. Sustained VT in the peri-infarction period may develop due to transient arrhythmogenic phenomena in ischemic and infarcting tissue such as the following: abnormal automaticity, triggered activity, and re-entrant circuits created by heterogeneous conduction and repolarization. Combining different diagnostic techniques, a relation between myocardial ischemia and induction of ventricular arrhythmias can be demonstrated in patients with IHD. Coronary revascularization must be the main goal and may constitute definitive therapy in certain patients with ischemic ventricular arrhythmias. This pure anti-ischemic therapeutic strategy seems to be justified in certain cases of patients with preserved left ventricular function, demonstrable reversible ischemia and non-inducible VT pre and post revascularization. In all other instances an additional treatment with antiarrhythmic drugs and an implantable cardioverter defibrillator is paramount.

INTRODUCTION

"When ischemia forms a crucial part of an arrhythmogenic histological substrate, the best antiarrhythmic is adequate blood flow" ***Osmar Centurión Alcaráz*****.**

Ischemic heart disease (IHD) is the most common cause of sudden cardiac death (SCD) resulting from fatal ventricular arrhythmias, and some of these events occur in persons without any history of cardiac disease [1, 2]. Sustained ventricular tachycardia (VT) and, in particular, ventricular fibrillation (VF), are the immediate causes of cardiac arrest in the majority of the estimated 350,000 cases of SCD that occur annually in the USA [3-8]. A major cause of SCD is acute myocardial infarction (AMI). Cardiac arrest secondary to AMI induced-VF occurs commonly without warning. Because spontaneous conversion of VF to non-lethal rhythms is rare, out-of hospital VF progresses to death within minutes in more than 95% of the victims. AMI induced-VF leads to SCD as the first manifestation of a preexisting coronary artery disease in about 80,000 people per year [3-5]. Polymorphic VT in patients with a normal QT interval during sinus rhythm is most frequently seen in the context of acute ischemia. In addition, it may be also seen with other cardiac diseases such as cardiomyopathy, heart failure, and even in the absence of overt cardiac disease, namely, idiopathic polymorphic VT, catecholaminergic VT [9-15].

Since the electrophysiological changes and ventricular arrhythmias induced by ischemia could be transient and temporary if the ischemic episode subsides, the suppression of ventricular arrhythmias and the ischemia-induced electrophysiological changes by coronary revascularization is the focus of this manuscript.

Ischemia-induced ventricular arrhythmias

Lethal VT in the setting of IHD results either from acute ischemia or from chronic scar. Active vascular events such as spasm, plaque rupture or thrombosis in the setting of acute

coronary syndromes precipitate fatal arrhythmias due to acute ischemia [9]. Moreover, transient coronary ischemia resulting from coronary vasospasm, anomalous coronary arteries or myocardial bridges can lead to polymorphic VT and sudden death [13-15]. Ventricular fibrillation is the most common terminal rhythm in this context, preceded at times by polymorphic VT [9]. Myocardial scars from a previous infarction may provide the anatomic substrate for reentrant ventricular arrhythmias usually manifested as monomorphic VT in patients with impaired left ventricular function. The incidence of ischemic ST changes before fatal arrhythmia has been observed in 13 to 52% of patients [10, 11]. It was also shown an increased ventricular ectopic activity during periods of ischemia [12]. The investigation of the mode of onset of VT in using various recording techniques gives insight into the mechanism of the ventricular arrhythmia. The use of 24 hs ambulatory Holter electrocardiogram recordings, as well as, the analysis of stored intracardiac electrograms from implantable cardioverter defibrillators gives important data on the initiation patterns of ventricular arrhythmias, providing the opportunity to assess mechanisms of VT onset and potential future therapeutic implications.

Hassine M et al [16], in this issue of this Journal, are reporting a 64 year old male with an old history of anterior myocardial infarction and apical aneurysm who was admitted with recurrent apical left VT that was definitively controlled only after coronary stenting of a right coronary artery stenosis which apparently supplied collaterals to the left anterior descending coronary artery. No recurrence of ventricular tachycardia was observed up to seven years after coronary stenting. This report emphasizes the important role of an appropriate myocardial revascularization in the electrical stability of the ventricle after myocardial infarction. Ischemic changes generate electrophysiological alterations that may produce lethal ventricular arrhythmias. There is a rise in intracellular calcium level and extracellular potassium level within seconds of acute ischemia as demonstrated in experimental animal investigations [15]. If the ischemia persists, continued influx of Ca2+ may produce afterdepolarizations as triggering response for Ca2+ dependent arrhythmias. Raised extracellular K+ results in shortening of repolarization leading to slow conduction and ultimately to inexcitability. This response is better seen in the subepicardial zone as compared to the subendocardial layers leading to prominent dispersion of repolarization across the myocardium during transmural ischemia. This non-homogeneous alteration produces an increased dispersion of repolarization resulting in prolongation of the QT interval dispersion in patients with IHD [17]. Dispersion of conduction and refractoriness favors re-entrant ventricular arrhythmias to develop [18]. Other abnormalities that may contribute to the occurrence of ventricular arrhythmias during the process of acute ischemia include alteration of distribution of connexin 43, the production of free fatty acids and oxygen free radicals, acidosis, and an increased catecholamine level [19, 20]. Experimental data obtained from animal and human studies have shown that ischemia induces heterogeneities in excitability, refractoriness and/or conduction. It also creates the substrate for ectopic excitation by a variety of mechanisms which may provide the clinical premature contractions that trigger lethal ventricular arrhythmias [21-26]. Ventricular arrhythmias may develop as a consequence of focal as well as non-focal mechanisms. The focal ones develop due to automatic and non-automatic ectopic excitation, while the non-focal ones develop due to re-entry resulting from disordered conduction of the cardiac impulse.

Ischemia-induced cellular changes

Ischemia produces several intra, and extra-cellular changes in ionic concentration and acid-base balance. Ischemia-induced intracellular acidification activates the Na+/H+ exchanger resulting in H+ extrusion in exchange for Na+ entry leading to elevated intracellular Na+. This in turn results in cell swelling and Ca2+ overload. This process of calcium overload is secondary to activation of the Na+/Ca++ exchanger operating in the reverse mode, namely, Na+ is extruded in exchange for Ca++. These metabolic changes produce electrophysiological alterations, like membrane depolarization which is mainly due to accumulation of K+ in the extracellular space [21-24]. This extracellular potassium accumulation causes Na+ channel inactivation and reduced fast Na+ current, leading to slowed conduction and altered refractoriness. In addition, an increase in the late sodium current (late INa) has been recently suggested to contribute to elevating intracellular Na+ and thus to be responsible for the initial prolongation of the action potential duration.

The decrease in action potential duration observed during ischemia is the consequence of both decreased inward currents including inward calcium current (ICa) which is inhibited by the acidosis, and enhanced outward currents including IK-ATP (ATP-sensitive potassium current) which is activated by the reduction in intracellular ATP following hypoxia [27-29]. During the late phase of an ischemic episode there is a nearly complete cessation of anaerobic glycolysis. This is characterized by low glycogen and high lactic acid intracellular content, reduction of ATP levels, Na+ and Ca++ overload, and further extracellular K+ accumulation. In this context, the surviving Purkinje fibers exhibit abbreviated action potentials of reduced amplitude, and depolarized membrane potentials and reduced conduction velocity. These altered Purkinje fibers may be the main arrhythmogenic foci during this late ischemic period [30]. These biochemical and electrophysiological disturbances mentioned above act in accordance with a number of probable genetic predispositions [29]. The resultant ventricular arrhythmias may be suppressed by revascularization of the occluded vessel ameliorating the ischemic tissue. Sustained VT in the peri-infarction period occurs in approximately 3% of patients with an ST elevation AMI, and may develop due to transient arrhythmogenic phenomena in ischemic and infarcting tissue such as the following: abnormal automaticity, triggered activity, and re-entrant circuits created by heterogeneous conduction and repolarization [31-40].

Sustained VT is a life threatening ventricular arrhythmia that usually occurs after AMI. Conventional anti-arrhythmic man-

agement is often an insufficient medical therapy, and most of the cases require additional measures such as coronary revascularization, radiofrequency catheter ablation, and implantable cardioverter defibrillators [41-45]. Several cases of intractable ventricular arrhythmia successfully treated by emergent percutaneous coronary intervention or surgical coronary revascularization have been reported [46-50]. Although, a revascularization procedure may be sufficient to terminate VT in these reported cases, it may not be enough in the vast majority of the clinical VT patients. Most of them would require a device implantation and substrate VT ablation to appropriately treat their clinical VT [51-54]. A close and detailed follow-up would also determine the efficacy of concomitant anti-arrhythmic therapy, which has been proved to be efficient in some patients. The proper way of treating these difficult VT patients is to begin an individualized therapeutic management for each patient considering the entire context and the patho-physiological mechanism of the VT. The absence of VT recurrence after revascularization in some reported cases confirms the important pathogenic role of ischemia acting on a susceptible anatomic substrate. Therefore, the main objective in ischemic driven ventricular arrhythmias is to restore adequate coronary perfusion if possible. Indeed, "When ischemia forms a crucial part of an arrhythmogenic histological substrate, the best antiarrhythmic is adequate blood flow."

Conclusion

Combining different diagnostic techniques, a relation between myocardial ischemia and induction of ventricular arrhythmias can be demonstrated in patients with IHD. Myocardial ischemia can have an important role in monomorphic or polymorphic VT of an incessant nature in patients with an infarction scar, even in the absence of angina or ischemic changes in the conventional electrocardiogram. Reentrant circuits, as well as, disturbances in automaticity and triggered activity secondary to myocardial ischemia could be involved in the mechanism of these arrhythmias. The use of Holter electrocardiogram recordings and analysis of stored intracardiac electrograms from implantable cardioverter defibrillators enabled us to study the initiation patterns of ventricular arrhythmias, providing the opportunity to assess mechanisms of VT onset and potential future therapeutic implications. Coronary revascularization must be the main goal and may constitute definitive therapy in certain patients with ischemic ventricular arrhythmias. A revascularization procedure in some patients with ischemic induced VT represents an adequate and sufficient therapeutic option. This pure anti-ischemic therapeutic strategy seems to be justified in certain cases of patients with preserved left ventricular function, demonstrable reversible ischemia and non-inducible VT pre and post revascularization. In all other instances an additional treatment with antiarrhythmic drugs and an implantable cardioverter defibrillator is paramount.

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