Can We Prevent Ventricular Fibrillation in Brugada Syndrome?

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Introduction

In 1992, Brugada et al described a syndrome of idiopathic ventricular fibrillation (VF) in patients with a characteristic ECG pattern of ST segment elevation in leads V_1 to V_3. Class I antiarrhythmic agents may unmask the presence of such ECG pattern in patients with latent or intermittent forms of this syndrome. The genetic basis of this syndrome is being studied, and mutations affecting the structure and function of sodium channel SCN5A have been identified. In general, antiarrhythmic drugs are not advocated, and implantable cardioverter-defibrillator (ICD) is the standard treatment of choice.

Discussion

In Asia, sudden unexpected death syndrome (SUDS) is prevalent among healthy young men. It is characterized by sudden death at night during sleep. This is known as 'Lai Tai' in Thailand, meaning death in sleep, 'Bangungut' in Philippines, meaning sudden death with moaning during sleep, and 'Pokkuri' meaning unexpected nocturnal death in Japan. Although the underlying cause is uncertain, it is believed that the Brugada syndrome accounts for a significant proportion of these cases. The circadian pattern of the development of VF in patients with Brugada syndrome has been reported in Japan. The data from the episode counters of ICDs showed that VF occurred most frequently between midnight and 6 am during sleep. The result suggested that increased nocturnal vagal activity, withdrawal of sympathetic activity, and nocturnal decrease in heart rate might play important roles in the arrhythmogenesis of the Brugada syndrome.

Subsequently, our group also reported a patient with Brugada syndrome who underwent dual chamber ICD implantation after an episode of VF, and that pacing was shown to be effective in preventing the recurrence of VF. That patient had typical Brugada syndrome and was resuscitated from VF during sleep. A dual chamber ICD was implanted. He experienced multiple ICD shocks for recurrent VF, all occurring in early morning hours during sleep. Analysis of the stored electrograms in the ICD showed that all episodes occurred during a period of sinus bradycardia, with the preceding R to R interval varying from 1200 msec to 1450 msec. When the pacing rate of the ICD was increased to DDD 90 bpm, he had no more ventricular arrhythmia or ICD shock over

the next four months. When the device was programmed back to VVI 40 bpm, he received two appropriate shocks due to VF within one week. Stored electrograms of the device revealed that the onset of VF was preceded by long RR intervals of 1300-1450 msec. After this, the device was programmed to AAI 90 bpm so as to prevent bradycardia and minimize battery drainage. Two months later, he reported receiving one shock during sleep. Interrogation of the device showed that VF occurred during AAI pacing with Wenkebach phenomenon, resulting in a RR pause of 1290 msec and a long-short sequence. After reprogramming of the device to DDD 90 bpm, the patient remained asymptomatic with no further tachyarrhythmic episodes requiring device therapy for eight months.

The electrocardiographic changes in Brugada syndrome are known to be variable and dynamic. The ECG may look entirely normal at times and become abnormal at some other times. Factors that may influence the ECG appearance include autonomic changes, changes in heart rate including that induced by atrial pacing, and pharmacological agents like isoproterenol and class I antiarrhythmic drugs.

The underlying cellular mechanism of the downsloping ST elevation in Brugada syndrome is thought to be related to premature repolarization of some right ventricular epicardial sites resulting in a transmural repolarization gradient. This may cause local reexcitation or phase 2 reentry which in turn may trigger VF. The unique electrocardiographic appearance is caused by failure of the dome of the action potential to develop. It occurs when the outward currents (mainly I_{to}) overwhelm the inward currents (mainly I_{Ca}) at the end of phase I of the action potential.

Increase in heart rate during exercise and atrial pacing is known to be associated with decrease ST segment elevation on electrocardiogram. It has also been demonstrated that isoproterenol suppressed the inducibility of VF in Brugada patients during electrophysiology study. Since I_{to} becomes less prominent at a faster rate, this observation is consistent with the theory that loss of the dome of the action potential at epicardial level is the cause for ST elevation in Brugada syndrome. Previously, the effect of pacing on arrhythmia suppression has not been described in Brugada syndrome. In our patient, it was demonstrated that DDD pacing at 90 bpm was effective in suppressing the occurrence of VF, confirming the protective effect of accelerated

heart rate. In Asia, sudden death or ventricular arrhythmia in Brugada syndrome commonly occurs during sleep. A bradycardia dependent mechanism may play an important role. Similar to the situation in congenital long QT syndrome, pacing may reverse the arrhythmogenic ionic changes and prevent ventricular fibrillation.

Conclusions

The unique electrocardiographic appearance of Brugada syndrome is caused by failure of the dome of the action potential to develop. It occurs when the outward currents (mainly I_{to}) overwhelm the inward currents (mainly I_{ca}) at the end of phase I of the action potential. Since I_{to} becomes less prominent at a faster rate, increase in heart rate is associated with decrease ST segment elevation on electrocardiogram and potentially decreased arrhythmogenecity. Bradycardia may be one of the underlying mechanisms of arrhythmogenesis in Brugada Syndrome, especially in the Asian population. The potential role of pacing in non-pharmacological prevention of VF in patients with Brugada syndrome warrants further investigation.

References

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