CLINICAL STUDIES

Autonomic and Antiarrhythmic Drug Modulation of ST Segment Elevation in Patients With Brugada Syndrome

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Objectives. We examined the modulatory effects of autonomic nervous system and antiarrhythmic drugs on the ST segment in patients with Brugada syndrome to gain an insight into the mechanism of ST segment elevation.

Background. Right bundle branch block, ST segment elevation and ventricular tachyarrhythmias define a distinct clinical and electrocardiographic (ECG) syndrome (Brugada syndrome). However, the mechanism of ST segment elevation and the causes of this syndrome are unknown.

Methods. The study included four patients in whom structural heart or coronary artery disease was excluded by noninvasive and invasive tests. High take-off ST segment elevation of either the coved or saddle-back type in precordial leads V1, V2 and V3 was seen in all patients. Three patients experienced recurrent episodes of syncope or aborted sudden cardiac death, and the remaining patient had palpitation. Autonomic receptor stimulation and blockade and intravenous administration of antiarrhythmic drugs were performed during sinus rhythm while the 12-lead ECG was recorded. Metaiodobenzylguanidine (MIBG) scanning and Holter monitoring were also performed.

Results. Beta-adrenoceptor stimulation by intravenous isoproterenol consistently reduced (≥0.1 mV) ST segment elevation at or 80 ms after the J point in all four patients. Selective alpha-adrenoceptor stimulation by intravenous norepinephrine in the presence of propranolol or by intravenous methoxamine consistently augmented, whereas alpha-adrenoceptor blockade reduced, ST segment elevation in three patients. Intracoronary acetylcholine or intravenous edrophonium or neostigmine augmented ST segment elevation without inducing coronary spasm in three of four patients. Class IA antiarrhythmic drugs also consistently augmented (three patients), whereas class IB drugs had no effect on (two patients) ST segment elevation. No abnormality was found on MIBG imaging or heart rate variability in three patients, suggesting that autonomic dysfunction is not a primary disease process. Class IA drugs had no effect on ST segment in three control patients, suggesting that the ST segment elevation seen in patients with Brugada syndrome in response to the drugs is not a nonspecific response.

Conclusions. ST segment elevation in patients with Brugada syndrome was augmented by selective stimulation of alpha-adrenoceptors or muscarinic receptors or by class IA drugs but was mitigated by beta-adrenoceptor stimulation or alpha-adrenoceptor blockade. These responses might be explained by postulating the presence of an area of early repolarization or a local "depolarized" area in the ventricle causing ST segment elevation in this syndrome. Because only a small number of patients were studied, these possibilities need further evaluation.

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In 1992, Brugada and Brugada (1) reported data on eight patients with right bundle branch block, persistent ST segment elevation with a normal QT interval and sudden cardiac death and proposed that these abnormalities constituted a distinct clinical and electrocardiographic (ECG) syndrome, different from "idiopathic" ventricular fibrillation without such ECG abnormalities (2,3). Structural heart disease or coronary artery disease was excluded in most patients by noninvasive and invasive tests, but the causes of this syndrome are still unknown.

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Methods

Patients. The study included four male patients, 29 to 47 years old, with Brugada syndrome under observation for 21 months. Each patient was treated according to the ethical guidelines of our institutions, and written informed consent was obtained before the following tests. Table 1 summarizes the clinical and ECG characteristics of the patients. During sinus rhythm, high take-off ST segment elevation of either the coved or saddle-back type was recognized in precordial leads V1 to V3 in all patients (Fig. 1 to 4). During the hospital period, day to day variability in degree of precordial ST segment elevation was seen in all patients, especially in Patients 3 and 4. Right bundle branch block was diagnosed definitively in Patient 1. The QT and corrected QT intervals were within normal limits in all patients. Patients 1 and 3 had recurrent episodes of syncope after palpitation, and Patient 4 experienced multiple episodes of aborted sudden cardiac death from ventricular fibrillation. ST segment elevation was augmented in Patient 4 immediately before and shortly after spontaneous episodes of ventricular fibrillation that occurred during the hospital period. Ventricular fibrillation was terminated by application of direct current shock (200 J) or spontaneously. Sustained monomorphic ventricular tachycardia of left bundle branch configuration (240 beats/min) causing hypotension was documented in Patient 1. Patient 2 had a history of hypertension and complained of palpitation. During Holter monitoring, frequent premature ventricular complexes (4,582 beats/day) were recorded. Although Patient 2 had neither syncope nor documented ventricular tachycardia or fibrillation, we included him in the present series because of ECG findings characteristic of Brugada syndrome and a bout of palpitation that appeared attributable to ventricular tachyarrhythmias.

Table 1. Clinical and Electrocardiographic Characteristics of Four Male Study Patients

<table>
<thead>
<tr>
<th>Pt No./Age (yr)</th>
<th>Arrhythmias</th>
<th>ST Segment Elevation</th>
<th>QTc Interval (ms)</th>
<th>CAG (Ach test)</th>
<th>LVG (RVG)</th>
<th>Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/29</td>
<td>+ SVT</td>
<td>V2-V4</td>
<td>410</td>
<td>Normal (negative)</td>
<td>Normal (62%)</td>
<td>NP</td>
</tr>
<tr>
<td>2/47</td>
<td>- PVCs</td>
<td>V4-V6</td>
<td>390</td>
<td>Normal (negative)</td>
<td>Normal (60%)</td>
<td>NP</td>
</tr>
<tr>
<td>3/41</td>
<td>+ -</td>
<td>V4-V6</td>
<td>390</td>
<td>Normal (negative)</td>
<td>Normal (74%)</td>
<td>NA</td>
</tr>
<tr>
<td>4/38</td>
<td>+ VF</td>
<td>V1-V2</td>
<td>404</td>
<td>Normal (negative)</td>
<td>Normal (59%)</td>
<td>NP</td>
</tr>
</tbody>
</table>

Ach test = acetylcholine provocation test for induction of coronary spasm (*ergonovine was used instead of acetylcholine); biopsy = histologic examination of endomyocardial biopsy specimens taken from interventricular septum; CAG = coronary angiogram; EF = ejection fraction; LVG = left ventriculogram; NA = not available; NP = no particular findings; Pt = patient; PVCs = premature ventricular complexes; QTc interval = corrected QT interval; RVG = right ventriculogram; SVT = sustained monomorphic ventricular tachycardia; VF = ventricular fibrillation.
During electrophysiologic testing, ventricular fibrillation was induced in Patients 1, 2 and 3 with single (Patient 1) or double extrastimuli (Patients 2 and 3) applied to the right ventricular outflow tract. Ventricular fibrillation was induced during baseline conditions in Patients 1 and 3 and during alpha-adrenoceptor and muscarinic stimulation in Patient 2 (see autonomic tests). In Patient 1, sustained monomorph ic ventricular tachycardia of the same configuration as the clinical one was also induced by single extrastimulus applied to the right ventricular apex during beta-adrenoceptor stimulation, and neither ventricular fibrillation nor sustained ventricular tachycardia was inducible after beta-adrenoceptor blockade with intravenous propranolol (see autonomic tests). In Patient 4,
ventricular fibrillation was noninducible, with up to three extrastimuli applied to the right ventricular apex and outflow tract at baseline and during isoproterenol infusion. The AH and HV intervals on the His bundle electrogram were normal, except in Patient 1 (HV interval 100 ms). Sinus node recovery time and sinoatrial conduction time were normal in all patients. Delayed potential during sinus rhythm was not recorded from the right ventricle in any patient during electrophysiologic testing. Late potential on the signal-averaged ECG was positive in Patient 1 (RMS40 8.71 μV, LAS 51.0 ms) and negative in Patients 2 and 4.

All patients had normal findings on physical and neurologic examination. Serum electrolyte levels and renal, hepatic and thyroid test results were within normal limits in all patients. Chest roentgenographic and echocardiographic findings were normal in all patients, and all patients underwent cardiac catheterization. Pressure study, cardiac output and right and left ventriculographic results were normal in all patients. Coronary angiography revealed no stenotic lesions in any patient. No inducible coronary spasm was demonstrated by intracoronary injection of acetylcholine (up to 50 μg in the right coronary artery, up to 100 μg in the left coronary artery) in Patients 1, 2 and 4 and by ergonovine in Patient 3. Endomyocardial biopsy specimens taken from the interventricular septum revealed no abnormalities on histologic examinations in Patients 1, 2 and 4. Thus, structural heart disease or coronary artery disease was excluded in all four patients.

**Autonomic tests.** Autonomic tests were performed during electrophysiologic testing (Patients 1 and 2) or at bedside (Patients 3 and 4) to determine the effects of autonomic receptor stimulation and blockade on the ST segment. Twelve-lead ECGs were recorded. During sinus rhythm, isoproterenol was infused intravenously at a dose of 1 to 2 μg/min for beta-adrenoceptor stimulation of the ventricles. Propranolol was injected intravenously at a dose of 8 mg (0.14 mg/kg as body weight-corrected mean dose) for beta-adrenoceptor blockade. Intravenous norepinephrine at a dose of 5 to 12.5 μg/min after beta-adrenoceptor blockade or intravenous methoxamine (6 mg) was used for selective stimulation of alpha-adrenoceptors. Intravenous phenolamine (5 or 10 mg) or oral prazosin (4 mg) was used for alpha-adrenoceptor blockade. For muscarinic stimulation, edrophonium (10 mg) or neostigmine (0.5 mg) was injected intravenously. The acetylcholine provocation test during cardiac catheterization was also used for muscarinic stimulation of the ventricles.

**Administration of antiarrhythmic drugs.** Antiarrhythmic drugs were injected intravenously to examine their effects on the ST segment. Disopyramide (50 mg) or procainamide (450 mg) was used as a class 1A antiarrhythmic drug, and mexiletine (125 mg) or lidocaine (100 mg) was used as a class 1B drug. Verapamil (5 or 10 mg) was used as a calcium channel blocking agent.

Twelve-lead ECGs were recorded every 1 min after the injection of the drugs or neurotransmitters. Maximal ST segment changes (see Results) were observed usually between 1 and 5 min. When prazosin was administered orally, ECGs were recorded every 1 h.

**Autonomic function.** Metadobenzylquaniidine (MIBG) scanning was performed to assess the sympathetic innervation of the ventricles. To examine the integrated function of the autonomic nervous system, heart rate variability was analyzed by Holter monitoring.

**Control group.** The effects of intravenous disopyramide (50 mg) or procainamide (200 mg) on the ST segment were examined in two patients with classic right bundle branch block and without underlying cardiac disease and in one patient with hypertrophic cardiomyopathy and ST segment elevation.

**Results**

**Effects of autonomic tests on ST segment.** Beta-adrenoceptor stimulation by intravenous isoproterenol consistently reduced ST segment elevation by ≥0.1 mV at or 80 ms after the J point in all four patients (Fig. 5 and 6 [see also Fig. 9, later]). In contrast, selective alpha-adrenoceptor stimulation increased ST segment elevation in all three patients studied (Patients 1, 2 and 3) (Fig. 5 and 6), whereas alpha-adrenoceptor blockade reduced ST segment elevation in all patients examined (Patients 2, 3 and 4) (see Fig. 9, later). Intracoronary acetylcholine increased ST segment elevation in all three patients examined (Patients 1, 2 and 4) (Fig. 5) without inducing coronary spasm. Intravenous edrophonium also augmented ST segment elevation in two of three patients examined (Patients 1 and 2) (Fig. 5 and 6). Intravenous atrial stimulation as assessed by HV interval on the His bundle electrogram remained unaffected during the autonomic tests in Patients 1 and 2.

**Effects of antiarrhythmic drugs on ST segment.** Procainamide or disopyramide augmented ST segment elevation in all three patients examined (Patients 1, 3 and 4) (Fig. 7 to 9) and increased premature ventricular complexes in Patients 1 and 4 (0 to 42 premature ventricular complexes/min; 0 to 2 premature ventricular complexes/min, respectively). In Patient 4, intravenous nico(nadil (8 mg), a potassium channel opener (7), reduced ST segment elevation only modestly (0.05 mV) but mitigated disopyramide-induced ST segment elevation (Fig. 9).

In contrast, neither mexiletine nor lidocaine had any effect on the ST segment. Verapamil had no effect on the ST segment in Patients 1 and 4 (Fig. 9), and reduced ST segment elevation in Patient 3. The effects of autonomic testing and antiarrhythmic drugs on the ST segment are summarized in Table 2. Disopyramide or procainamide did not affect the ST segment in three control patients (Fig. 10), suggesting that ST segment elevation in response to these drugs in patients with Brugada syndrome is not a nonspecific response.

**Autonomic function.** No abnormality was found on MIBG imaging or in heart rate variability in all three patients studied (Patients 1, 2 and 4), suggesting that autonomic dysfunction is not a primary disease process.

**Clinical course.** Patient 1 has received propranolol for 8 months without recurrence of syncope and is scheduled to
receive an implantable cardioverter-defibrillator. Patient 2 has been asymptomatic for 8 months after receiving doxazosin mesilate for alpha-adrenoceptor blockade, prescribed for treatment of hypertension. Patient 3 is scheduled to receive an implantable cardioverter-defibrillator. Patient 4 received an implantable cardioverter-defibrillator (Ventak PRX II, CPI) 17 months ago. Ventricular fibrillation recurred three times within 1 month after implantation, two of which were terminated by shock delivery by the device, and the remaining episode terminated spontaneously before delivery of shock. Since then he has been taking oral mexiletine and remained asymptomatic without syncope or ventricular fibrillation for 16 months.

**Discussion**

*Electrocardiographic features of Brugada syndrome.* Reports of patients with ECG and clinical findings compatible with Brugada syndrome, published before or after the multicenter report by Brugada and Brugada (1), can be found (5,6,8–10). The most prominent and common ECG feature among these patients seems to be a high take-off ST segment elevation of either the coved or saddle-back type (4). Such ST segment elevation was documented in all our patients. The day to day variability in degree of ST segment elevation seen in our patients was observed in some previous reports (5,6). Augmentation of ST segment elevation before and after a spontaneous episode of ventricular fibrillation has also been previously documented (5), as in our Patient 4. In the present study, we showed that autonomic nervous system and class IA antiarrhythmic drugs could modulate ST segment elevation profoundly.

In contrast, right bundle branch block was not always diagnosed definitively in previous reports. Bjerregaard et al. (6) did not interpret ECG patterns of their patients as right bundle branch block; rather, they believed that a wide QRS complex represented a prominent J wave, most often seen in patients with hypothermia.

*Possible mechanisms of ST segment elevation in Brugada syndrome as estimated by autonomic tests and antiarrhythmic drugs.* There are several possible explanations for ST segment elevation in Brugada syndrome, including intraventricular conduction disturbance, early ventricular repolarization, local ventricular "depolarization" and sympathetic imbalance (11). Right bundle branch block or intraventricular conduction disturbance could be an explanation for ST segment elevation. However, the ST segment abnormalities seen in Brugada syndrome are clearly different from those observed in uncom-
A Sinus rhythm (HR 68/min)

RA Pacing (HR 100/min)

RA Pacing (HR 120/min)

1 sec

B ECG V2 Lead

Baseline

Isoproterenol 1.5 μg/min iv

Propranolol 8 mg iv

Norepinephrine 5 μg/min iv

Edrophonium 10 mg iv

1 sec

Figure 6. Effect of heart rate (HR) (A) and autonomic receptor stimulation and blockade (B) on ST segment elevation in lead V2 in Patient 2. ST segment elevation remained unchanged by right atrial (RA) pacing at 100 and 120 beats/min at baseline (A). In contrast, ST segment elevation was reduced by isoproterenol, unaffected by propranolol and augmented by selective alpha-adrenoceptor stimulation with norepinephrine in the presence of propranolol, or by muscarinic stimulation with edrophonium (B). Other abbreviations as in Figure 5.

does not appear to be a pivotal mechanism of ST segment elevation.

Early ventricular repolarization or a combination of early and delayed ventricular repolarization could cause ST segment elevation in this syndrome, and there might be an argument for this hypothesis. If the presence of early repolarization causes ST segment elevation, class IA antiarrhythmic drugs are expected to mitigate the ST segment elevation by prolonging the action potential duration of the early repolarized (diseased) site, thereby reducing the difference between the diseased and normal sites because the drugs are thought to affect the “diseased” site selectively (12,13). Conversely, beta-adrenoceptor stimulation is expected to augment ST segment elevation by increasing the difference. In contrast, class IA antiarrhythmic drugs and selective stimulation of alpha-adrenoceptors or muscarinic receptors, the interventions that would reduce potassium conductance and slow repolarization of the ventricle (14–19), in fact augmented ST segment elevation, whereas beta-adrenoceptor stimulation, which would increase the potassium conductance (20), reduced it. To reconcile the early repolarization hypothesis and these responses, it is necessary to postulate that the interventions affected the normal or delayed repolarization site selectively. However, the QT intervals were not prolonged long enough by the interventions that augmented the ST segment elevation to validate this postulation (Fig. 5 to 9).

There is another point of view in support of the early repolarization hypothesis. Antzelevitch et al. (21) showed that a transient outward current-mediated spike and dome (notch) configuration in the action potential is more prominent in ventricular epicardium than in endocardium and suggested that this difference could be a cause of ST segment changes on ECG. Furthermore, they demonstrated that the dome portion of the epicardial action potential is lost by acetylcholine (10⁻⁵ mol/liter) (22) and high concentration of extracellular calcium (23), probably by an outward shift in the balance of currents active at the end of phase 1 of the action potential, principally transient outward and inward calcium currents, whereas the endocardial action potential response is minimal. Therefore, muscarinic stimulation, which suppresses the inward calcium current, and alpha-adrenoceptor stimulation, which increases intracellular calcium concentration, thus causing a net increase in outward current, would suppress the dome of the epicardial action potential and give rise to ST segment elevation or the early repolarization syndrome on the ECG. In contrast, beta-adrenoceptor stimulation might mitigate ST segment elevation by increasing inward calcium currents. Also, sodium channel blocking agents could produce a marked abbreviation of the action potential in the canine ventricular epicardium but not in endocardium, thus causing ST segment elevation (24). The ST segment responses to autonomic tests and class IA drugs in the present study are consistent with these findings in vitro. Finally, the finding that loss of the action potential dome with the interventions previously described is usually observed in right, but not left, ventricular epicardium (21) is also consistent with the appearance of ST segment elevation only in the right precordial leads in patients with Brugada syndrome.
Morace et al. (25) reported that isoproterenol reduced, whereas propranolol augmented, RST segment elevation, in patients with the early repolarization syndrome, a normal variant condition. They postulated that isoproterenol exerted its effect on a site with slower repolarization, most probably the posterobasal region of the heart. Whatever mechanism of ST segment elevation operates, the common response to isoproterenol suggests that Brugada syndrome and the early repolarization syndrome might share at least in part a common mechanism that causes ST segment elevation. This possibility needs further evaluation.

If we postulate that there is a local “depolarized” area in the ventricle where potassium conductance is reduced for some reason, that the rest membrane potential and action potential amplitude are reduced and that the interventions have affected such areas preferentially, then the ST segment responses observed in the present study might be reasonably explained. It is known that alpha-adrenoceptor stimulation by

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**Figure 7.** Effect of procainamide on ST segment elevation in Patient 1. ST segment elevation in leads V₁ to V₃ seen at baseline was augmented by intravenous (iv) procainamide in a dose-related manner, and premature ventricular complexes developed.

**Figure 8.** Effect of intravenous (iv) disopyramide on ST segment elevation in Patient 3 who was taking oral disopyramide (300 mg/day). In this patient, day to day variability in degree of ST segment elevation was observed before and after the start of oral disopyramide. ST segment elevation in leads V₁ to V₆ was augmented by intravenous administration of disopyramide, and coved-type ST segment elevation characteristic of Brugada syndrome developed. However, reinduction of ventricular fibrillation was prevented by oral plus intravenous disopyramide.
nepinephrine, methoxamine or phenylephrine inhibits transient outward calcium current in rabbit myocytes (17). This effect may slow action potential repolarization and augment the depolarization of the rest membrane potentials in the depolarized area by decreasing potassium conductance further, thereby augmenting ST segment elevation. Vagal stimulation might exert a similar effect because it slows ventricular repolarization (18,19). The class IA antiarrhythmic drugs used in the present study might also exert a similar effect by inhibiting delayed rectifying outward potassium and transient outward currents (14,15). This local depolarization hypothesis might also explain the high take-off ST segment elevation characteristic of Brugada syndrome.

Abnormal autonomic innervation or sympathetic imbalance (11) may cause ST segment elevation. Morace et al. (25) hypothesized that ST segment elevation in patients with the early repolarization syndrome was related to an enhanced activity of the right cardiac sympathetic nerves. In Brugada

Table 2. Effects of Autonomic Tests and Antiarrhythmic Drugs on Precordial ST Segment Elevation

<table>
<thead>
<tr>
<th>Pt No.</th>
<th>Beta Stimulation</th>
<th>Beta Blockade</th>
<th>Alpha Stimulation</th>
<th>Alpha Blockade</th>
<th>Muscarinic Stimulation</th>
<th>Class IA</th>
<th>Class IB</th>
<th>Ca&lt;sup&gt;2+&lt;/sup&gt; Channel Blocker</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>NA</td>
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<td>↑</td>
<td>↑</td>
<td>→</td>
</tr>
<tr>
<td>2</td>
<td>↓</td>
<td>→</td>
<td>↑</td>
<td>↓</td>
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<td>↑</td>
<td>↑</td>
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<td>→</td>
</tr>
</tbody>
</table>

↓ (↑) = reduced (augmented) ST segment elevation by ≥0.1 mV at or 80 ms after the J point; → = no effect on ST segment (<0.1 mV). Abbreviations as in Table 1.
syndrome, a role played by the sympathetic nervous system has also been suggested because 50% of the patients reported by Brugada and Brugada (1) were controlled with drugs with beta-blocking properties. Abnormal circadian rhythm of the parasympathetic nervous activity has been also reported (6). However, no abnormality was found on MIBG imaging or in heart rate variability in our patients, suggesting that abnormal innervation of the heart or autonomic dysfunction is not a primary disease process. Rather, the autonomic nervous system seems to act as an important modulator in this syndrome.

Thus, the plausible mechanism of ST segment elevation in Brugada syndrome appears to be that of the early repolarization hypothesis or the local depolarization hypothesis, or both. However, in the clinical setting it is difficult to validate these possibilities directly. Monophasic action potentials can be recorded with an electrode catheter during electrophysiologic testing. However, it is difficult to record ventricular epicardial monophasic action potentials. Also, a local depolarized area may not be identified with this method because the absolute value of the rest membrane potential cannot be measured.

Because only a small number of patients were examined in the present study, it is obvious that more patients need to be studied to elucidate the pathophysiologic mechanisms of this new syndrome. Nevertheless, it is likely that distinct electrophysiologic mechanisms are involved in the unique ECG findings in patients with Brugada syndrome. On the basis of this notion, we think it appropriate to distinguish Brugada syndrome from "idiopathic" ventricular fibrillation without ECG abnormalities. Therefore, we refer to the clinical entity first proposed by Brugada and Brugada (1) in a multicenter report as Brugada syndrome in the present report.

**ST segment elevation and arrhythmias.** Marked ST segment elevation might cause arrhythmias based on a variety of mechanisms. If a local depolarized area exists, arrhythmias due to injury current (26) or abnormal automaticity (27) might occur. Also, reentrant arrhythmias might occur because conduction over such area would be slowed. If an area of early repolarization exists, it may set the stage for reentry due to dispersion of repolarization.

In fact, there was a correlation between the augmentation of ST segment elevation and occurrence of premature ventricular complexes or ventricular fibrillation during the hospital period in our Patients 1 and 4. A similar correlation has been previously reported (5). Furthermore, class IA antiarrhythmic drugs and selective stimulation of alpha-adrenoceptors or muscarinic receptors augmented ST segment elevation and increased premature ventricular complexes in our Patients 1 and 4. These observations suggest a proarrhythmic potential of class IA drugs and a potential benefit of alpha-adrenoceptor blockade in patients with Brugada syndrome. It appears worth examining the effect of alpha-adrenoceptor blockade on the recurrence of lethal ventricular tachyarrhythmias in patients with Brugada syndrome who have received an implantable cardioverter-defibrillator.

However, the relation between augmentation of ST segment elevation and arrhythmias needs further evaluation for several reasons. In a report by Bjørgregard et al. (6), there was no definite correlation between the extent of ST segment elevation and occurrence of polymorphic ventricular tachycardia and syncope. In our Patient 3, intravenous disopyramide also caused inducible ventricular fibrillation to nonsustained ventricular tachycardia despite the fact that it augmented ST segment elevation. Mexiletine, which had no effect on ST segment, appeared to be effective in preventing the recurrence of ventricular fibrillation in our Patient 4. Finally, Belhassen et al. (28) reported that class IA antiarrhythmic drugs are highly effective in preventing reinduction of ventricular tachyarrhythmias in patients with idiopathic ventricular fibrillation without ECG abnormalities, although such patients may belong to a category different from those with Brugada syndrome.

**References**


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