Effect of baroreflex stimulation using phenylephrine injection on ST segment elevation and ventricular arrhythmia-inducibility in Brugada syndrome patients

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Aims
Patients affected by Brugada syndrome (BrS) are at risk of sudden cardiac death specifically at rest, when vagal tone is high. The aim of our study was to assess whether a phenylephrine injection, which provokes a baroreflex stimulation, could induce modification of the ST segment elevation and ventricular arrhythmias.

Methods and results
Baroreflex test was performed with the administration of phenylephrine (2 mg/kg) to four highly symptomatic patients in a setting fully equipped for cardiac resuscitation. Phenylephrine injection induced a deep vagal stimulation with a decrease in the mean heart rate from 75 ± 7 to 50 ± 8 bpm and an increase in the mean systolic blood pressure from 141 ± 14 to 204 ± 46 mmHg. ST segment elevation was not modified and no ventricular arrhythmias were induced during the test.

Conclusion
Although phenylephrine injection induced a major α-adrenergic vasoconstriction followed by an arterial baroreflex, this test failed to provoke ventricular arrhythmias or modification of the ST segment elevation in BrS patients.

Introduction
Brugada syndrome (BrS) is an arrhythmogenic disease characterized by an electrocardiogram (ECG) pattern of ST segment elevation in the right precordial leads and an increased risk of sudden cardiac death. In this disease, syncope and sudden cardiac death occur essentially at rest when the vagal tone is high. Additional evidence suggests that increased vagal tone may be proarrhythmic in BrS. ST segment elevation increases with intracoronary acetyl-choline or intravenous edrophonium, and a large meal or spontaneous vagal response after an exercise test also induce an increase in ST segment elevation. To date, there has been no description of the effect of a baroreflex test in BrS patients.

The aim of our study was to assess whether a phenylephrine injection, which induced an α-adrenergic vasoconstriction and provoked arterial baroreflex and vagal stimulation, could modify ST segment elevation amplitude and induce ventricular arrhythmias in BrS patients.

Methods
Informed written consent was obtained from the four patients who participated in the study according to a protocol authorized by our Local Ethics Committee. Electrocardiogram and blood pressure (BP) were permanently recorded. The amplitude of the ST segment elevation was

Figure 1

Standard V1 and V2 leads of subjects studied. Diagnostic electrocardiograms are shown at the far left. Baseline (‘pre-test’) and representative morphologies obtained during the test are also shown.
A first 2 μg per kg intravenous phenylephrine injection was performed to obtain an increase of 15 mmHg in the systolic BP. Where the increase was insufficient, a further bolus of 0.5–3.5 μg per kg was injected to obtain an increase of at least 15 mmHg.

Four symptomatic male BrS patients were included in the study.

**Results**

The age of the patients at the time of the test was 50 ± 5 years. Time since the last arrhythmic event was 29 ± 33 months. The number of documented ventricular fibrillation (VF) episodes was 4.7 ± 1. The ECG at the time of the first arrhythmic event was spontaneous type 1 in three patients and a type 2 ECG converted to type 1 in one.

**Patients' clinical history**

In Patient 1, BrS was diagnosed after the occurrence of three episodes of VF at rest. The patient remained asymptomatic for 11 years with a normal ECG. Eleven years later, he received six defibrillation shocks while he was asleep.

In Patient 2, BrS was diagnosed after the occurrence of several episodes of VF at rest.

In Patient 3, BrS was diagnosed after the occurrence of one episode of VF during a fever episode.

In Patient 4, BrS was diagnosed after the occurrence of several episodes of syncope while sleeping. The day before ICD implantation, the patient presented an episode of VF while sleeping at the hospital. Ventricular fibrillation resolved spontaneously within 3 min.

**Phenylephrine challenge**

The ECG performed before phenylephrine injection revealed a type 1 pattern in one patient whereas a normal repolarization was present in three patients (Figure 1).

**Haemodynamic effect of phenylephrine injection**

Phenylephrine injection induced a major increase in the systolic (141 ± 14 to 204 ± 46 mmHg) and diastolic (70 ± 14 to 94 ± 17 mmHg) BP and a concomitant dramatic decrease in heart rate (75 ± 7 to 50 ± 8 bpm; Table 1).

**Electrocardiographic effect of phenylephrine injection**

There was no change in the conduction parameters during the test, and the amplitude of the ST segment elevation was unchanged at the systolic BP peak (Figure 1 and Table 2). Two patients complained of headache during the test, and for this reason the test was stopped prematurely in Patient 4.

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**Table 1** Haemodynamic changes during the phenylephrine challenge

<table>
<thead>
<tr>
<th>Heart rate (bpm)</th>
<th>Systolic blood pressure (mmHg)</th>
<th>Diastolic blood pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>Systolic BP</td>
<td>Diastolic BP</td>
</tr>
<tr>
<td>Pre-test</td>
<td>Test</td>
<td>Pre-test</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td>Patient 1</td>
<td>83</td>
<td>50</td>
</tr>
<tr>
<td>Patient 2</td>
<td>80</td>
<td>53</td>
</tr>
<tr>
<td>Patient 3</td>
<td>70</td>
<td>40</td>
</tr>
<tr>
<td>Patient 4</td>
<td>69</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>75 ± 7</td>
<td>50 ± 8</td>
</tr>
</tbody>
</table>

**Table 2** Electrocardiogram changes during the phenylephrine challenge

<table>
<thead>
<tr>
<th>PR (ms)</th>
<th>QRS (ms)</th>
<th>ST segment elevation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-test</td>
<td>Test</td>
<td>Pre-test</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Patient 1</td>
<td>160</td>
<td>160</td>
</tr>
<tr>
<td>Patient 2</td>
<td>156</td>
<td>140</td>
</tr>
<tr>
<td>Patient 3</td>
<td>198</td>
<td>190</td>
</tr>
<tr>
<td>Patient 4</td>
<td>140</td>
<td>140</td>
</tr>
<tr>
<td>163 ± 24</td>
<td>157 ± 23</td>
<td>117 ± 43</td>
</tr>
</tbody>
</table>

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measured in V1 or V2. A first 2 μg per kg intravenous phenylephrine injection was performed to obtain an increase of 15 mmHg in the systolic BP. Where the increase was insufficient, a further bolus of 0.5–3.5 μg per kg was injected to obtain an increase of at least 15 mmHg.
In these four highly symptomatic patients neither ventricular arrhythmia nor any ventricular premature beat occurred during the test.

**Discussion**

The aim of our study was to evaluate the effect of phenylephrine injection in BrS patients. Phenylephrine injection normally induces an α-adrenergic stimulation leading to an increase in BP, a baroreflex stimulation, and then a deep vagal stimulation with a major decrease in the heart rate. However, in these four highly symptomatic patients, phenylephrine injection induced no modification of the ST segment elevation and no ventricular arrhythmia occurred. The reasons why no ECG modification was induced remain unclear. It is possible that the vagal stimulation induced by the phenylephrine injection is not physiological and does not reflect the condition in which arrhythmia and modification of the ST segment elevation occurs. It is also possible that the induction of a vagal stimulation is a necessary but not sufficient condition to induce arrhythmia.

**Conclusion**

Although phenylephrine injection induced a major α-adrenergic vasoconstriction followed by an arterial baroreflex, this test failed to provoke modification of the ST segment elevation or ventricular arrhythmias in BrS patients.

**Conflict of interest:** none declared.

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**References**