Carotid sinus syncope treated by pacing

Analysis of persistent symptoms and role of atrioventricular sequential pacing

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SUMMARY Seventy patients have been paced for carotid sinus syndrome over four years. Twelve patients had persistent symptoms despite adequate ventricular pacing. Patients with persistent symptoms were found to have a significant vasodepressor response, a significant hypotensive response to ventricular pacing (pacemaker effect), and a severe hypotensive response to carotid sinus massage with introduction of ventricular pacing, which reproduced symptoms in all patients.

A group of 14 asymptomatic paced carotid sinus patients was found to have a significantly lower vasodepressor response, pacemaker effect, and combined vasodepressor response plus pacemaker effect than the group with persistent symptoms.

Atrioventricular sequential pacing was shown to eliminate the hypotensive effect of ventricular pacing and is considered to be the treatment of choice for patients with carotid sinus syndrome who have both cardioinhibitory and significant vasodepressor responses.

There has been controversy concerning the need to treat patients with a hypersensitive carotid sinus reflex since this was first recognised as a cause of syncope in man.¹ There is, however, evidence that syncopal patients with a hypersensitive carotid sinus reflex will continue to suffer disabling symptoms unless treated.²

Pacing is now accepted as the treatment of first choice for syncopal patients with a pure or predominant cardioinhibitory response to carotid sinus massage.²⁻⁴ Indeed, a total of 159 patients paced for carotid sinus syndrome were reported from four cardiac centres at a recent minisymposium on carotid sinus syndrome,⁵⁻⁹ with very satisfactory results.

A predominant cardioinhibitory response to carotid sinus massage is found in up to 80% of patients with carotid sinus syndrome.¹⁰ A pure vasodepressor response is rare, occurring in 5 to 10% of cases,¹¹⁻¹² but a mixed vasodepressor and cardioinhibitory response may not be uncommon.¹⁰ Patients with such a mixed type of response pose a therapeutic problem as ventricular pacing does not correct their vasodepressor response and symptoms may persist. Recurrence of symptoms after ventricular demand pacing for carotid sinus syndrome has been previously reported¹³⁻¹⁴ and has been attributed to the vasodepressor response.¹³⁻¹⁵ Hypotension occurring with the onset of ventricular pacing (pacemaker effect) has not been previously reported as a cause of persistent symptoms, either alone, or in combination with the vasodepressor response in paced carotid sinus syndrome patients. This paper presents a sufficiently large series of patients paced for carotid sinus syndrome to allow analysis of persistent symptoms.

Patients and methods

Seventy patients with a primary diagnosis of carotid sinus syndrome were paced over a four year period. Fifty patients were men and 20 were women, and their mean age was 68 years. Sixty-one patients presented with syncope, with a mean of eight syncopal episodes per patient. The remaining nine patients had severe recurrent dizziness. The mean duration of symptoms before pacing was 20 months. One or more episodes of significant injury caused by syncope were experienced by 24% of the patients.

Carotid sinus massage was performed by standard technique¹⁶ for six seconds, using pressure insufficient to occlude the ipsilateral temporal arterial pulse. A hypersensitive response was defined as asystole (62 patients) or complete atrioventricular block

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(eight patients) exceeding three seconds. Carotid sinus massage was positive on the right side in 52% of cases, on the left side in 15%, and on both sides in 33% of patients.

All patients with significant spontaneous symptoms and a hypersensitive carotid sinus reflex were investigated with an electrophysiological study to record the His bundle electrocardiogram, measure the sinus node recovery time, observe the presence or absence of retrograde atrioventricular conduction, and demonstrate the benefit of temporary pacing during carotid sinus massage. The electrophysiological study and resting electrocardiographic findings are summarised in Table 1.

The criteria for pacing patients with a hypersensitive carotid sinus reflex were reproduction of symptomatic asystole exceeding three seconds and abolition of symptoms by temporary ventricular pacing during repeated carotid sinus massage. The effectiveness of carotid sinus massage was ensured in most patients by observing atrial asystole during temporary ventricular pacing (Fig. 1).

**ANALYSIS OF PERSISTENT SYMPTOMS**

Patients have been followed up for a mean duration of 18 months since first pacemaker implant. Three groups of patients have been studied using intraarterial pressure monitoring.

**Group 1**: 12 patients with carotid sinus syndrome who had persistent symptoms despite ventricular pacing giving adequate bradycardia control.

**Group 2**: 14 patients with carotid sinus syndrome who were asymptomatic after pacing.

**Group 3**: 11 patients who did not suffer from the carotid sinus syndrome. These patients had been investigated for syncope or dizziness, but had no evidence of carotid sinus syndrome.

Measurements of either brachial or radial intraarterial pressure were taken using 40° head up tilt to control the effect of posture on arterial pressure. Phasic arterial pressure and the electrocardiogram were recorded simultaneously using a Statham P23ID transducer and Hewlett Packard recorder. The midaxilla was used as the zero reference point. The following variables were investigated to determine the role of hypotension in causing persistent symptoms in patients paced for carotid sinus syndrome.

**VASODEPRESSOR RESPONSE**

Vasodepressor response was measured as the greatest fall in systolic arterial pressure after carotid sinus massage during atrioventricular sequential (DVI) pacing (Fig. 2). Nine patients had permanent DVI pacing. Patients without DVI units were investigated either with temporary DVI pacing (21 patients) or after atropine to eliminate the cardioinhibitory response to carotid sinus massage (seven patients) so that they remained in sinus rhythm during carotid sinus massage, with minimal bradycardia.

**PACEMAKER EFFECT**

The pacemaker effect was measured as the maximum fall in systolic arterial pressure after the introduction of ventricular demand pacing from sinus rhythm (Fig. 3). This was achieved by externally programming the pacemaker from a rate less than sinus rate to a rate just sufficient to override sinus rhythm. Patients with DVI units were reprogrammed to ventricular pacing mode. The effect of the introduction of DVI pacing on arterial pressure (Fig. 2) was similarly measured in the 30 patients studied with either permanent or temporary DVI pacing.

**COMBINED PACEMAKER EFFECT AND VASODEPRESSOR RESPONSE**

Pacemaker effect plus vasodepressor response was measured as the maximum fall in systolic arterial pressure after simultaneous carotid sinus massage and introduction of ventricular pacing (Fig. 2). This was achieved by programming to a demand rate just below sinus rate before carotid sinus massage. The carotid sinus cardioinhibitory reflex results in bradycardia and onset of ventricular pacing.

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**Table 1** Resting electrocardiogram and electrophysiological study results

<table>
<thead>
<tr>
<th>Electrocardiogram (70 patients)</th>
<th>Electrophysiological study (67 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Ischaemia</td>
<td>Sinus node recovery time prolonged</td>
</tr>
<tr>
<td>Left anterior hemiblock</td>
<td>Paroxysmal atrial fibrillation</td>
</tr>
<tr>
<td>Left bundle-branch block</td>
<td>HV&gt; 60 ms</td>
</tr>
<tr>
<td>First degree heart block</td>
<td>AH&gt; 110 ms</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>His bundle electrocardiogram</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Retrograde atioventricular conduction present</td>
</tr>
<tr>
<td>Other minor electrocardiographic abnormalities</td>
<td><em>(mean stimulus to retrograde “p” wave interval = 179 ms)</em></td>
</tr>
</tbody>
</table>

*In this three-letter code the first letter indicates the chamber paced; the second, the chamber sensed; and the third, the mode of response (I=inhibited; T=triggered; A=atrium; V=ventricle; D=both chambers; O=neither chamber) (Purman S, Furman S, Smyth NPD. Report of the Interociety Commission for Heart Disease Resources: implantable cardiac pacemakers—status report and resource guideline. *Am J Cardiol* 1974; 34: 487–500).
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Fig. 1 Criteria for diagnosing carotid sinus syndrome at electrophysiological study. Simultaneous recording of scalar electrocardiogram lead I with endocardial recording from high right atrium. RCSM, right carotid sinus massage.

Fig. 2 Arterial pressure recordings during sinus rhythm, ventricular pacing, atrioventricular sequential pacing, and carotid sinus massage. Scalar electrocardiogram lead I (upper panel) recorded simultaneously with intra-arterial pressure (brachial or radial) in the lower panel. Paper speed 1 mm per second. DVI, atrioventricular sequential pacing; VVI, ventricular pacing; ECG, electrocardiogram; BP, arterial pressure; LCSM, left carotid sinus massage.

INCIDENCE OF CAROTID SINUS SYNDROME
An estimate of the incidence of carotid sinus syndrome was calculated from the figures for referral from a single district general hospital (Worthing Hospital, West Sussex). All patients presenting to Worthing Hospital with syncope of possible cardiac origin are referred to Westminster Hospital for consideration of pacing. The calculation was made in a similar way to that in which Johansson first estimated the incidence of complete heart block in the population. The catchment population of Worthing Hospital was 235,000 people in 1979. Thirty-three patients have
been referred over four years (1977 to 1981) with a primary diagnosis of carotid sinus syndrome and 77 patients with either atrioventricular block or sick sinus syndrome. From these figures the estimated incidence of carotid sinus syndrome for the Worthing area was 35 new patients per million population per year and for atrioventricular block plus sick sinus syndrome 82 new patients per million population per year. This compares with the United Kingdom figure (1978) for average new pacemaker implants of 75 new patients per million per year.\(^{18}\)

**Results**

The initial and final pacing modes and the incidence of persistent symptoms in the 70 patients with carotid sinus syndrome are shown in Table 2.

Complete relief of symptoms before unit change was achieved in 77% of patients (85% of patients with VVI pacing, all patients with DVI/DDD pacing, and none of the eight patients with atrial pacing). After conversion of pacing symptoms (see Table 2), complete relief of symptoms was achieved in 89% of patients. There have been only four deaths: three in the asymptomatic group (two deaths from carcinoma and one from cerebrovascular accident) and one death in the group with persistent symptoms which was sudden and unexplained.

**PERSISTENT SYMPTOMS**

Initially 16 patients had persistent symptoms. Eight of these patients had atrial (AAI) pacemakers, and eight had ventricular (VVI) pacemakers. All eight atrially paced patients had symptomatic atrioventricular block during carotid sinus massage (Fig. 4). Their symptoms were therefore attributed to lack of adequate control of bradycardia, and these patients were electively converted to either a ventricular or dual-chamber pacing system (VVI or DVI/DDD).

Four of these patients are now asymptomatic with DVI or DDD pacemakers, but four had persistent symptoms despite conversion to VVI (two patients), DVI (one patient), and DDD (one patient). Thus 12 patients were left with persistent symptoms despite adequate control of bradycardia (10 VVI, one DVI, one DDD).

The results of the arterial pressure studies in these 12 patients, the asymptomatic carotid sinus syndrome group, and the group without carotid sinus syndrome are shown in Table 3 and Fig. 5. The vasodepressor response was significantly greater in the patients with carotid sinus syndrome (groups 1 and 2) than in the controls (group 3), with \(p<0.05\). The vasodepressor response was also significantly greater (\(p<0.001\)) in the group with persistent symptoms (group 1) than in the asymptomatic group with carotid sinus syndrome (group 2). The combined hypotensive effect of vasodepressor action of the carotid sinus syndrome.
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Carotid sinuses massage could be abolished by temporary pacing (Fig. 1). There was a high incidence (55%) of electrophysiological evidence of sinoatrial disease (either prolonged sinus node recovery time or paroxysmal atrial fibrillation precipitated by atrial pacing). This association has been noted by others. 19 None of the patients had overt sick sinus syndrome on resting or 24 hour electrocardiogram. All patients were therefore considered to have a primary diagnosis of carotid sinus syndrome.

Eight patients early in this series were selected for atrial pacing on the grounds of haemodynamic benefit of atrial pacing shown at catheterisation (cardiac output and mean aortic pressure recordings) and control of bradycardia without atrioventricular block at electrophysiological study. Atrial pacing, however, is clearly contraindicated in view of the appearance of recurrent symptoms in all atrially paced patients with carotid sinus syndrome and the demonstration of symptomatic atrioventricular block with carotid sinus massage at follow up.

Four of the atrially paced patients continued to have symptoms after pacemaker conversion, two to VVI, one to DVI and one to DDD pacing. Of these four patients, the two with VVI pacing were shown to have a combination of vasodepressor response plus pacemaker effect sufficient to explain their symptoms and the DVI and DDD patients both had severe vasodepressor responses.

Ventricular demand (VVI) pacing was successful in 85% of patients who were initially selected for VVI pacing. These results are superior to results of irradiation 10 20 or carotid sinus denervation. 21 23 The 12 patients with persistent symptoms were all shown to have a significant vasodepressor response and consider-
Table 3  Arterial line results

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>Symptoms</th>
<th>↓ SBP mmHg</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Vasodepressor response (VDR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSS symptomatic</td>
<td>12</td>
<td>4</td>
<td>51.8±15</td>
<td>≤0.001</td>
</tr>
<tr>
<td>CSS non-symptomatic</td>
<td>14</td>
<td>Nil</td>
<td>28.9±14</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Non CSS</td>
<td>11</td>
<td>Nil</td>
<td>14±19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(2) Pacemaker effect (PME) SR—VVI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSS symptomatic</td>
<td>11†</td>
<td>Nil</td>
<td>52.2±10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CSS non-symptomatic</td>
<td>14</td>
<td>Nil</td>
<td>42±12</td>
<td>NS</td>
</tr>
<tr>
<td>Non CSS</td>
<td>11</td>
<td>Nil</td>
<td>35.4±14</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>(3) VDR+PME</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSS symptomatic</td>
<td>11†</td>
<td>11</td>
<td>76±19</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CSS non-symptomatic</td>
<td>14</td>
<td>4</td>
<td>50±16</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>(4) PME SR—DVI</td>
<td>All groups</td>
<td>30</td>
<td>6±9</td>
<td></td>
</tr>
</tbody>
</table>

*Student's t test for unpaired data.
†One symptomatic CSS patient was in chronic atrial fibrillation and therefore PME and VDR+PME could not be measured.

Table 4  Comparison of groups 1, 2, and 3 of arterial pressure study

<table>
<thead>
<tr>
<th></th>
<th>Group 1 CSS symptomatic</th>
<th>Group 2 CSS non-symptomatic</th>
<th>Group 3 Non CSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>12</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Male</td>
<td>7</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>69</td>
<td>67</td>
<td>65</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>3</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>6</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Intermittent atrioventricular block</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

was in chronic atrial fibrillation) but in all patients by vasodepressor response plus pacemaker effect. No patient was symptomatic with onset of ventricular pacing alone, even when retrograde ventriculoatrial conduction was observed, and therefore the pacemaker effect is unlikely to be the only cause of their symptoms.

The pacemaker effect was found to be greatest in the group with persistent symptoms of carotid sinus syndrome, but not significantly different between the asymptomatic group with carotid sinus syndrome and the group without carotid sinus syndrome. The three groups were comparable for age and incidence of hypertension and ischaemic heart disease. It is therefore unlikely that the difference in pacemaker effect was caused by a significant difference in cardiac function. Alicandri et al.24 have proposed that the hypotension that occurs during ventricular pacing is not solely the result of the haemodynamic consequences of the increased cardiac output.
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ences of atrioventricular dissociation but that there may be an atrial stretch reflex in man (as shown in cats) which is activated by the high atrial pressures. These occur when the atria contract against closed atrioventricular valves. The response to this reflex might be expected to be greater in patients with a vasodepressor response to carotid sinus massage as presumably they have a hypersensitive vasomotor centre.

Atrioventricular pacing has been shown to abolish the pacemaker effect and is therefore likely to be helpful in the persistent symptoms group. Four of the patients with ventricular pacemakers have been converted to DVI pacing with improvement, but follow up is too short to make further comment. The remaining six symptomatic VVI paced patients have been considered for conversion to DVI pacing. One patient is excluded because of chronic atrial fibrillation, one patient has refused conversion, and four patients have only mild or infrequent symptoms and are being followed up closely.

Four patients (two VVI, one DVI, one DDD) were shown to have a vasodepressor response sufficient to cause symptoms without additional pacemaker effect and at present there is no satisfactory treatment for these patients, but DVI pacing may, however, reduce the severity of their symptoms by eliminating the carotid sinus cardioinhibitory response and pacemaker effect. Arterial pressure study before pacing in patients with carotid sinus syndrome is helpful in selecting the most appropriate mode of pacing. Patients with a vasodepressor response or combinations of vasodepressor response plus pacemaker effect sufficient to reproduce symptoms, in addition to cardioinhibitory response, should be selected for DVI pacing.

In this series 89% of patients have been rendered asymptomatic with appropriate choice of pacing system. Forty-eight patients (68%) are asymptomatic with VVI pacing, and 14 with DVI/DDD pacing. A further four patients symptomatic with VVI pacing would almost certainly benefit from conversion to DVI pacing which is therefore considered the most appropriate mode of pacing in 18 patients (26%). Only four patients (6%) are likely to remain symptomatic, regardless of pacing mode, in view of severe vasodepressor response.

The hypersensitive carotid sinus syndrome is thus more common than previously recognised and cardiac pacing is a highly effective treatment provided the correct mode is selected.

References


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