Clinical usefulness of head-up tilt test in patients with syncope and intraventricular conduction defect


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Head-up tilt test was performed in 99 patients with syncope of unknown origin and intraventricular conduction defect. Twenty-five per cent had a positive response to tilt with reproduction of spontaneous clinical symptoms. Holter recording revealed paroxysmal atrioventricular (AV) block in three patients. Carotid sinus massage was positive in four patients. An electrophysiological study was performed in 76 patients with abnormal findings in 17 (22%). Thus, vasovagal syncope was the discharge diagnosis in 25 patients (25%). Therefore, tilt test should be considered in patients with intraventricular conduction defect presenting with syncope of unknown origin, especially if clinical findings suggest the possibility of a vasovagal mechanism, or if the results of the electrophysiological study are inconclusive.

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Key Words: Syncope, tilt test, intraventricular conduction defects.

Introduction

The head-up tilt test is being increasingly used to diagnose vasovagal syncope[1–13]. This diagnosis is clinically suspected in patients (especially young individuals) without organic heart disease and with a normal ECG, whose syncopal episodes are triggered by identifiable stimuli or preceded by prodromal symptoms[14]. In patients with intraventricular conduction defects, syncope may be related to paroxysmal atrioventricular block, with the subsequent consideration of permanent pacing. However, this assumption is not always correct, as in some patients syncope may be due to other causes, such as tachyarrhythmia[15,16] or vasovagal responses. Syncope recurs in a large proportion of patients with intraventricular conduction defects after the implantation of a permanent pacemaker[16–20]. In the present paper we report our experience on the usefulness and diagnostic yield of the head-up tilt test in patients with syncope and intraventricular conduction defects.

Patients and Methods

The present study is a retrospective evaluation of all patients with syncope of unknown origin and intraventricular conduction defects seen by physicians from the Syncope Unit in our institution, either as outpatients or inpatients, who underwent a head-up tilt test between July 1990 and August 1994. In the Syncope Unit, patients with syncope, in whom a specific diagnosis is not made on the basis of clinical history, physical examination, ECG and chest X-ray film, are considered as having syncope of unknown origin. The routine practice in the Syncope Unit is to submit these patients to a head-up tilt test, carotid sinus massage and Holter monitoring. Echocardiography, an exercise stress test and neurological evaluation are performed for specific indications. An electrophysiological study is performed in patients with organic heart disease, intraventricular conduction defects or suspected tachyarrhythmia. The head-up tilt test protocol used in the patient population of this study has been previously described[12,21]. Patients were placed in a supine position and an intravenous line was inserted; blood pressure was assessed by repeated measurements with an automatic sphygmomanometer (BP 103 N, Nippon Colin) every 2–5 min or more frequently if symptoms developed; the ECG was continuously monitored.

Ten minutes after the insertion of the intravenous line, blood pressure and heart rate were measured, and after 5 min of stable heart rate and blood pressure in the supine position, patients were tilted to 75° for 30 min. If no positive response was elicited; an isoproterenol infusion was administered at a dose of 3 µg. min⁻¹ over 10 min and increased to 5 µg. min⁻¹ for an additional 10 min. Patients were not returned to
the supine position before the dosing increased. The rate of infusion was adjusted so that the heart rate did not exceed 140 beats min\(^{-1}\). The head-up tilt test was considered to be positive if syncope or pre-syncope developed in association with severe hypotension (systolic blood pressure \(\leq 70\) mmHg); in such instances the test was stopped and the patient was placed in the Trendelenburg position until complete recovery. The protocol used for the electrophysiological study was as follows: patients were non-sedated, but post-absorptive; multipolar electrode catheters were inserted percutaneously through femoral veins after local anaesthesia and were positioned under fluoroscopic guidance at the high right atrium, at the right ventricular apex and in the region of the His bundle. Three surface electrocardiographic leads (1, 2 and V\(_1\)), intracardiac electrograms and time lines were simultaneously displayed on a multichannel oscilloscope. Hard copies were produced on paper at a speed of 25 to 100 mm s\(^{-1}\). Programmed stimulation was performed with a digital stimulator (Biotronik UHS 20, Berlin, Germany). Electrophysiology was directed at testing sinus node function, atrioventricular conduction and at trying to induce supraventricular or ventricular tachyarrhythmias with programmed stimulation. Whenever an intraventricular conduction defect was detected on the surface ECG, ajmaline at a dose of 1 mg kg\(^{-1}\) over 3 min was administered to unmask infrahisian conduction delays. The following data were considered abnormal: corrected sinus node recovery time \(>550\) ms, AV node effective refractory period \(>400\) ms, HV interval \(>60\) ms in the basal state or \(>100\) ms in the infrahisian block after ajmaline administration, pacing-induced infranodal block, induction of supraventricular tachycardia by AV nodal re-entry or by accessory pathways and induction of sustained monomorphic ventricular tachycardia.

For the purposes of this study, vasovagal syncope was diagnosed when head-up tilt test provoked a positive response with reproduction of symptoms of spontaneous syncopal episodes in patients with no abnormal findings in the other examinations. Paroxysmal AV block was suspected as a cause of syncope when the HV interval was longer than 60 ms or when atrial pacing elicited an infranodal block, and no other apparent causes of syncope could be demonstrated. Carotid sinus hypersensitivity was diagnosed when carotid sinus massage provoked asystole for longer than 3 s or significant hypotension with reproduction of clinical symptoms.

Proportions were statistically compared using Fisher’s exact test.

**Results**

From July 1990 to August 1994, the head-up tilt test was performed in 600 patients with syncope of unknown origin. Ninety-nine out of these 600 patients had a definite intraventricular conduction defect. The study population comprised these 99 patients (67 males and 32 females, aged 16 to 88 years, mean age 66 years). Table 1 shows the clinical and demographic characteristics of the 99 patients with intraventricular conduction defects as compared with 501 patients who did not have intraventricular conduction defects. As can be seen, the group of patients with intraventricular conduction defects was older and there was a significantly higher proportion of males, hypertension, and diabetes than

<table>
<thead>
<tr>
<th>Table 1 Population: clinical features</th>
<th>Patients with IVCD n=99</th>
<th>Patients without IVCD n=501</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66 ± 15</td>
<td>50 ± 19</td>
<td>0·001</td>
</tr>
<tr>
<td>Males</td>
<td>67 (67)</td>
<td>279 (56)</td>
<td>0·03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>33 (33)</td>
<td>114 (28)</td>
<td>0·02</td>
</tr>
<tr>
<td>Diabetes</td>
<td>14 (14)</td>
<td>37 (7)</td>
<td>0·03</td>
</tr>
<tr>
<td>Organic heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>76 (77)</td>
<td>408 (82)</td>
<td></td>
</tr>
<tr>
<td>CAD</td>
<td>15 (15)</td>
<td>62 (12)</td>
<td>ns</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>8 (8)</td>
<td>31 (6)</td>
<td></td>
</tr>
<tr>
<td>Clinical type of syncope</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sudden</td>
<td>45 (46)</td>
<td>204 (41)</td>
<td>0·001</td>
</tr>
<tr>
<td>Autonomic symptoms</td>
<td>25 (25)</td>
<td>282 (56)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>28 (28)</td>
<td>10 (3)</td>
<td></td>
</tr>
<tr>
<td>Post-exercise</td>
<td>1 (1)</td>
<td>5 (10)</td>
<td></td>
</tr>
<tr>
<td>Syncopal attacks (mean, SD)</td>
<td>4·8 7·6</td>
<td>6·2 10</td>
<td>ns</td>
</tr>
<tr>
<td>Duration of symptoms (years, mean, SD)</td>
<td>3·5 7·1</td>
<td>6·2 10</td>
<td>0·006</td>
</tr>
</tbody>
</table>

IVCD=intraventricular conduction defects. Age and duration of symptoms are expressed in years. Males, hypertension, diabetes, organic heart disease and clinical type of syncope are expressed in number of patients and in brackets as a percentage. Syncopal attacks are expressed in number.
in patients without intraventricular conduction defects. The clinical differences between the groups were revealed in the syncopal episodes; there were significantly more patients without intraventricular conduction defects but with autonomic symptoms preceding syncope.

Of the 99 patients with an intraventricular conduction defect, 23 had left bundle branch block, 29 right bundle branch block, 28 left anterior hemiblock, and 19 had right bundle branch block plus left anterior hemiblock. No patients had left posterior hemiblock. In 10 patients, a permanent pacemaker had been implanted previously because of syncope, intraventricular conduction defect, and recurrent syncopal episodes. Carotid sinus massage provoked a positive response in four patients. Holter monitoring revealed advanced AV block in three patients. A head-up tilt test was performed in all 99 patients. An electrophysiological study was performed in 76 patients, with abnormal findings in 13 (25%) of 52 patients, with abnormal findings in 10 (33%) of 30 patients, and in one out of seven patients with bifascicular block (prolonged HV interval). An electrophysiological study was performed in 19 of 23 patients with a left bundle branch block, with abnormal findings in eight (42%); prolonged HV interval and infranodal block provoked by atrial pacing in five and three patients, respectively; in 21 of 29 patients with right bundle branch block, with abnormal findings in one (5%) (induction of sustained monomorphic ventricular tachycardia); in 21 of 28 patients with left anterior hemiblock, with abnormal findings in three (15%) (prolonged HV interval); and in 15 of 19 patients with bifascicular block, with abnormal findings in five (33%) (prolonged HV interval and infranodal block under atrial pacing in three and two patients, respectively). The remaining 23 patients did not undergo electrophysiology because diagnostic evidence was considered sufficient by the physician in four patients (bundle branch block and prolonged PR), syncope was considered to be vasovagal after a head-up tilt test in five patients (positive response with reproduction of symptoms), there was difficulty in advancing catheters through the vein in one patient, four patients did not consent, and in nine patients the reasons were unclear.

Table 3 illustrates the number and results of electrophysiological studies, according to the results of the head-up tilt test. In 24 patients with positive response to the test, electrophysiology was also performed with positive findings in four (12%): three out of eight patients with left bundle branch block (prolonged HV interval in two patients and infranodal block under atrial pacing in one patient), and in one out of seven patients with bifascicular block (prolonged HV interval). Among the 66 patients with a negative response to the head-up tilt test, electrophysiology was performed in 52 patients, with abnormal findings in 13 (25%); prolonged HV interval in eight, infranodal block under atrial pacing in four, and sustained ventricular tachycardia in one. The rate of abnormal electrophysiological responses was higher among patients with a negative response to the head-up tilt test than in those with a positive response, but the difference was not statistically significant.

Table 4 gives the diagnosis for each type of intraventricular conduction defect at hospital discharge. In 50 (50%) patients, no specific diagnosis could be made because no abnormal findings were revealed by the study protocol.

Patients with vasovagal syncope were given advice on how to avoid possible precipitating factors.
Table 4  Diagnoses at hospital discharge

<table>
<thead>
<tr>
<th></th>
<th>Vasovagal</th>
<th>A-V block</th>
<th>CSH</th>
<th>VT</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBBB (23)</td>
<td>6 (26%)</td>
<td>8 (34%)</td>
<td>1 (4%)</td>
<td>0</td>
<td>8 (34%)</td>
</tr>
<tr>
<td>RBBB (29)</td>
<td>6 (21%)</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
<td>20 (68%)</td>
</tr>
<tr>
<td>LAH (28)</td>
<td>7 (25%)</td>
<td>4 (14%)</td>
<td>1 (3%)</td>
<td>0</td>
<td>16 (51%)</td>
</tr>
<tr>
<td>LAH+RBBB (19)</td>
<td>6 (31%)</td>
<td>6 (31%)</td>
<td>1 (5%)</td>
<td>0</td>
<td>6 (31%)</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>19</td>
<td>4</td>
<td>1</td>
<td>50=99</td>
</tr>
</tbody>
</table>

A-V=atrioventricular; CSH=carotid sinus hypersensitivity; VT=ventricular tachycardia; LBBB=left bundle branch block; RBBB=right bundle branch block; LAH=left anterior hemiblock.

Table 5  Relapses of syncope diagnosis at hospital discharge

<table>
<thead>
<tr>
<th></th>
<th>Vasovagal</th>
<th>A-V block</th>
<th>CSH</th>
<th>VT</th>
<th>Unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBBB</td>
<td>2 (1)/6</td>
<td>2 (2)/8</td>
<td>0/1</td>
<td>—</td>
<td>3 (1)/8</td>
<td>7/23 (30%)</td>
</tr>
<tr>
<td>RBBB</td>
<td>3 (1)/6</td>
<td>0/1</td>
<td>0/1</td>
<td>0/1</td>
<td>7 (2)/20</td>
<td>10/29 (34%)</td>
</tr>
<tr>
<td>LAH</td>
<td>1 (0)/7</td>
<td>0/4</td>
<td>0/1</td>
<td>—</td>
<td>3 (3)/16</td>
<td>4/28 (14%)</td>
</tr>
<tr>
<td>LAH+RBBB</td>
<td>3 (0)/6</td>
<td>0/6</td>
<td>0/1</td>
<td>—</td>
<td>2 (1)/6</td>
<td>5/19 (26%)</td>
</tr>
</tbody>
</table>

Numbers in brackets indicate patients with a pacemaker implanted. Abbreviations explained in Table 4.

and urged to adopt postural measures if premonitory symptoms began, but no pharmacological treatment was initially administered.

In this series, a pacemaker was only indicated if data suggested that the aetiology of syncope was bradyarrhythmic, that there was a possible presence of prolonged HV interval or infranodal block during E-P study, paroxysmal A-V block during Holter monitoring or a clinically significant abnormal response to carotid sinus massage. At the end of the study 32 patients had a permanent pacemaker implanted, 10 had had a pacemaker previously implanted and in 22 a new indication was established.

The patient with ventricular tachycardia received treatment with sotalol.

Follow-up

Follow-up time was 22 ± 11 months (4–50 months). The rates of syncope relapse are shown in Table 5. Six patients died (three from malignancy, one from heart failure, one from diabetic complications, and one from acute gastric haemorrhage). None of these patients died suddenly. New diagnoses were made in two patients with left bundle branch block (neurological seizures, and atrioventricular block).

Discussion

Vasovagal syncope in patients with intraventricular conduction defects

The major finding of this study is that the response to the head-up tilt test was positive in 33% of a group of patients with intraventricular conduction defects and syncope of unknown origin. If only the positive responses reproducing the symptoms of spontaneous syncopal episodes are considered, then 25% of patients had such a response. This proportion is higher than that of patients in which electrophysiology disclosed abnormal findings (22%). Accordingly, the most prevalent diagnosis at hospital discharge was vasovagal syncope (in 25% of patients), while the presumptive diagnosis of paroxysmal AV block (on the basis of Holter findings or a prolonged HV interval) or ventricular tachycardia were made in only 19% and 1%, respectively. The type of clinical syncope had a clear relationship with the final diagnosis, as vasovagal syncope was diagnosed in 10 (40%) of the 25 patients whose syncopal episodes were preceded by prodromal autonomic symptoms, and only in seven (15%) of the 45 patients whose syncopal episodes were sudden. It is outstanding that in 50% of patients no presumptive diagnosis could be established, in spite of the performance of a head-up tilt test in all the patients, and that most underwent an electrophysiological study. This emphasizes once more the difficulty of reaching a diagnosis in patients with syncope of unknown origin.

Selection bias in the present series

A selection bias may be present in our patient population. The common practice of the attending physicians of the Syncope Unit from which our series originated, is to perform a head-up tilt test and electrophysiology in all patients with syncope of unknown origin. However, patients with syncope and intraventricular conduction defects seen in other hospital areas during the period in
which our series was recruited may not have undergone a head-up tilt test because the mechanism of syncope was considered, either correctly or not, to be established on the basis of other findings. Thus, our patients with a positive head-up tilt test may not be fully representative of the whole population with syncope and intraventricular conduction defects. In spite of this shortcoming, our findings are very likely to be meaningful for the population of patients with intraventricular conduction defects who present with syncope and no direct evidence of its mechanism.

Accuracy of the diagnosis of the mechanism of syncope

The possibility that some patients with a positive response to the head-up tilt test and a diagnosis of vasovagal syncope could have had syncopal episodes due to paroxysmal AV block cannot be absolutely ruled out. Although the specificity of the head-up tilt test has been reported to be relatively high, some data suggest that in patients with intraventricular conduction defects, the specificity is lower than in the general population\[22\]. However, our series shows the good overall accuracy of our diagnosis of vasovagal syncope: (1) for this diagnosis we only considered those patients with a positive response and in whom there was a close reproduction of spontaneous clinical symptoms; (2) in 24 out of the 33 patients with a positive response to the head-up tilt test, electrophysiology was performed and abnormal findings were obtained in only four patients; (3) in the follow-up, no patients died suddenly and in only one patient (with left bundle branch block) was a new diagnosis of atrioventricular block made. Furthermore, a normal electrophysiological study does not exclude the possibility of paroxysmal AV block\[23,24\]. On the other hand, the converse error (a false-positive diagnosis of syncope due to paroxysmal AV block) cannot be excluded, as ascribing syncope to abnormalities of HV measurements is often difficult\[15,25\], moreover, it is not easy to determine whether a response of AV block during Holter monitoring is due to an intrinsic mechanism or to a neurally-mediated one; some of these patients could really have had vasovagal syncope. Although an incorrect diagnosis could have been made in a minority of patients, the diagnosis was probably accurate in most of them.

Clinical implications

The findings of the present study are relevant for clinical practice. Usually, when a patient attends hospital because of syncopal attacks and an intraventricular conduction defect is found on the ECG, AV block is usually considered with the implication of permanent pacing. However, this assumption can be incorrect. In the series of Dhingra et al.\[15\], which includes 186 patients with chronic bifascicular block, syncope occurred in 30 patients: probable and possible causes of syncope included intermittent heart block in five patients, sinus exit block in one, orthostatic hypotension in two, seizure disorders in three, ventricular arrhythmia in nine, and acute blood loss in one. In the series of McAnulty et al.\[16\] reporting 554 patients with ‘high-risk’ bundle branch block, 47 patients had syncopal episodes; syncope was caused by sinoatrial disturbances in 10 patients, AV block in nine and tachyarrhythmias in five, while the cause of syncope was uncertain in 23. The results of our series show that the possibility of vasovagal syncope should always be considered. In fact, different authors\[16–20\] have pointed out that in up to 12–28% of patients with intraventricular conduction defects, syncopal episodes relapse after the implantation of a permanent pacemaker. In our series, syncope recurred in 11 out of 32 (34%) patients with a pacemaker (Table 5), a recurrence rate that is similar to that reported by other authors in patients with vasovagal syncope and no other abnormalities\[26\].

The head-up tilt test has helped explain the mechanism of syncopal episodes in patients with an apparent cause of syncope, such as supraventricular tachycardia\[27\], paroxysmal atrial fibrillation\[28\] or carotid sinus hypersensitivity syndrome\[29\], since an important proportion of these patients have positive responses to head-up tilt test, suggesting that a vasovagal reaction plays a role in the mechanism of syncope. In the present work we emphasize the usefulness and the diagnostic yield of the head-up tilt test in a group of patients with syncope and intraventricular conduction defects, showing that as much as 25% of these patients may, in fact, have vasovagal syncope. Therefore, the performance of the head-up tilt test is worthwhile before implantation of a permanent pacemaker if clinical data suggest the possibility of vasovagal syncope or when the data provided by electrophysiology are not strongly conclusive.

Limitations of the study

Although this series includes a group of patients with syncope prospectively studied following a specific protocol, the collection of data was retrospective. As previously mentioned, selection bias is likely as patients presenting to other hospital areas with syncope and intraventricular conduction defects, perhaps with a different likelihood of syncope due to AV block, may not have been tilted. These patients are not included in the present study. However, we think that our patients illustrate well the diagnostic dilemmas posed by patients with syncope and intraventricular conduction defects. Moreover, we feel that our data enrich the knowledge of this puzzling syndrome by showing that the mechanism of syncope cannot often be easily assumed from indirect evidence, such as the finding of intraventricular conduction defects, and that a complete work-up study should be performed in most of these patients.
References