Comparison of provocative tests for unexplained syncope: isoprenaline and glyceryl trinitrate for diagnosing vasovagal syncope

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Aims To compare the sensitivity, specificity and adverse event profile of glyceryl trinitrate head-up tilt with isoprenaline head-up tilt in the diagnosis of vasovagal syncope in patients with unexplained syncope and healthy controls

Methods and Results Forty-eight patients with unexplained syncope and negative passive head-up tilt at 70 degrees for 40 min, and 14 healthy controls underwent glyceryl trinitrate head-up tilt and isoprenaline head-up tilt (maximum dose 5 μg·min⁻¹) one week apart in random order. Outcome measures were production of symptoms (syncope, pre-syncope) with development of hypotension. In those with negative passive head-up tilt, the sensitivity of glyceryl trinitrate for diagnosing vasovagal syncope was 48% and the specificity was 71%. Glyceryl trinitrate was well tolerated. Isoprenaline sensitivity was 21% with specificity 64%. Side-effects prevented completion of the test in 68%. Commonest adverse events were the development of hypertension or tachycardia and intolerable flushing or nausea.

Conclusions Glyceryl trinitrate head-up tilt is as effective as isoprenaline head-up tilt as a provocative agent for vasovagal syncope and has a lower incidence of adverse events

Key Words: Syncope, vasovagal syndrome, head-up tilt testing.

Introduction

Vasovagal syndrome, loss of consciousness due to neurally mediated hypotension, sometimes accompanied by bradycardia, is a common cause of syncope. The precise underlying mechanisms are still incompletely understood but, in susceptible individuals in response to certain triggers, activation of complex neural and humoral reflexes result in withdrawal of sympathetic tone and augmented vagal activity causing inappropriate vasodilatation and hypotension[1]. Stimulation of cardiopulmonary mechanoreceptors and high levels of circulating catecholamines play major roles in the pathophysiological mechanism[2].

In the majority of patients with vasovagal syncope a good history can clearly elicit the diagnosis and further testing is unnecessary. In patients with atypical symptoms or complex comorbidity, attributing a diagnosis is more difficult and tests which provoke symptom reproduction are needed. In these individuals it is necessary to determine the separate contribution that heart rate slowing and hypotension make to symptom reproduction in order to choose appropriate therapies.

Head-up tilt table testing is an established method of provoking vasovagal responses in clinical practice[3-5]. Increased venous pooling in response to orthostatic stimulus results in relative intracardiac hypovolaemia. Left ventricular mechanoreceptors consequently respond to vigorous ventricular contraction and decreased filling volume to trigger hypotension and syncope[2]. In patients with unexplained syncope, reproduction of symptoms accompanied by such a haemodynamic response to tilt, constitutes a diagnosis of vasovagal syncope.

Numerous studies over the past decade have used differing angles and duration of head-up tilt[3-5]. No ‘gold standard’ exists and sensitivity is very variable[6]. Studies in normal volunteers have also produced a wide range of specificity of results[3-6].
Isoprenaline infusion has been added to many protocols to increase study sensitivity [7–9]. Isoprenaline creates a catecholamine surge similar to endogenous elevations prior to syncope, and increases ventricular inotropy to stimulate intracardiac mechanoreceptors [10]. Again the reported sensitivity and specificity varies widely. Interpretation of results is confounded by variable false positive rates in healthy subjects [11], effect of cannulation [12], age-related variation in responses [13] and side-effects, which preclude isoprenaline use in patients with ischaemic heart disease and hypertension [14].

Glyceryl trinitrate, which acts to increase venous pooling [15], has been used with some success as a provocative agent for vasovagal syncope, both intravenously [16] and sublingually [17,18]. The potential advantages are a shorter, non-invasive test with a less severe side-effect profile. We hypothesized that glyceryl trinitrate is as specific and as sensitive as isoprenaline and has a lower adverse event profile. Our objective was to compare sensitivity, specificity and adverse effects of glyceryl trinitrate and isoprenaline as provocative agents in vasovagal syncope.

**Methods**

**Screening procedure**

A consecutive series of patients referred to a Regional Syncope Facility and who had more than two episodes of syncope in the previous year were studied. All patients had detailed history and examination, and investigations including 12-lead electrocardiograph, supine and upright carotid sinus massage, 24-h Holter electrocardiograph monitoring, and 24-h ambulatory blood pressure (Spacelabs) revealed no attributable cause for symptoms. Electro-encephalogram, echocardiogram, computed tomography brain scan and exercise testing were carried out in selected cases if indicated. Medication was continued during the test protocol and was unchanged from the time of syncopal symptoms.

**Contraindications to isoprenaline infusion**

Patients with a history of uncontrolled hypertension (190/100), tachyarrhythmia, recent myocardial infarction or angina requiring more than occasional use of nitrate, or cerebrovascular events were excluded from further study.

**Healthy volunteers**

Healthy volunteers were recruited by poster advertising. Recruits had no history of cardiovascular comorbidity or syncope or presyncope in the past 5 years, were not on medication and had a normal 12-lead electrocardiograph. Local ethical approval was obtained and all subjects gave written consent.

**Study protocols**

Studies were daycase procedures between 2 and 4 pm. Subjects were fasting (to avoid postprandial hypotension). Nicotine, caffeine and alcohol were omitted for 24 h prior to testing. Continuous non-invasive monitoring of blood pressure using the finger plethysmography method (OhMeda Finapres) and surface electrocardiograph monitoring were applied during all tilt studies.

**Passive head-up tilt**

After lying supine for 10 min, patients were tilted to 70 degrees for a maximum of 40 min, or to time of symptom occurrence [3]. Subjects who had a positive response to unprovoked head-up tilt, defined as development of typical presyncopal symptoms accompanied by hypotension, did not undergo further testing.

**Randomization**

Patients who had negative head-up tilt underwent two further provocative tests 1 week apart. Randomization was carried out by block randomization (opaque sealed envelope technique).

**Isoprenaline head-up tilt**

Isoprenaline head-up tilt was carried out according to standard protocol after intravenous cannulation [8]. Incremental doses of 0, 1, 3 and 5 µg.min⁻¹ were infused during 5 min supine and 5 min in 70-degree head-up tilt position with a 2-min supine rest period between each incremental increase. The procedure was terminated if symptoms or predetermined adverse effects developed (tachycardia >150 beats.min⁻¹, hypertension >190/95 mmHg, vomiting, chest pain) or at the patient’s request if symptoms became intolerable.

**Glyceryl trinitrate head-up tilt**

Patients rested supine for 10 min, after which two metered dose puffs (800 µg) of glyceryl trinitrate were applied sublingually. Subjects were then tilted head up to 70 degrees for 25 min [19]. The test was terminated prematurely if symptoms developed.

**Outcome measures**

The primary end-point was the reproduction of symptoms. Syncope was defined as loss of consciousness...
accompanied by hypotension (fall in systolic blood pressure greater than or equal to 50 mmHg from baseline, or to less than 70 mmHg) accompanied by bradycardia (heart rate less than 60 beats min⁻¹). Presyncope was defined as a sensation of impending syncope and other symptoms (nausea, sweating, blurred vision) which were similar to the patient’s usual symptoms and accompanied by hypotension with or without bradycardia.

A positive test referred to syncope or presyncope accompanied by the patient’s usual prodromal symptoms. In those patients who had no prodrome, who had presented with unexplained syncope only, syncope accompanied by hypotension was the end-point. A negative test was one in which the patient’s usual symptoms were not reproduced, or the test protocol was terminated before completion due to adverse events.

Statistical analysis
Data was analysed using SPSS v7.5 for Windows statistical package. McNemar’s test was used to compare sensitivity and specificity of each test. Sensitivity and specificity are presented with 95% confidence intervals. Student’s t test of independent samples was used to compare mean age between positive and negative tests.

Results
Screening process
Two hundred and fifty-two patients with unexplained syncope were screened between October 1996 and September 1997. One hundred and sixty-four patients were not suitable for study inclusion. One hundred and eighteen (72%) had contraindications to isoprenaline infusion. Of these, 25% (n=29) had hypertension, 45% (n=52) ischaemic heart disease, 12% (n=14) cerebrovascular disease and 13% (n=15) had a history of documented serious arrhythmia (supraventricular or ventricular tachycardia). Forty-six patients had other reasons for exclusion. Thirty per cent (n=14) of this group had an attributable diagnosis identified after the detailed screening assessment (e.g. epilepsy), 14% (n=6) were unable to tolerate tilt table testing (e.g. due to severe arthritis), 30% (n=14) had other reasons, e.g. cognitive impairment. Twenty six per cent (n=12) declined to enter the study (Fig. 1).

Medications
Five of 57 patients undergoing provocative tilt testing were taking cardioactive medications. Three patients in this group were taking occasional prophylactic GTN spray. Medications did not affect test outcome.

Unprovoked head-up tilt
Eighty-eight patients underwent tilt table testing (mean age 50 years, range 16–87 years), 30 were male and the median syncopal frequency was one episode per week. Thirty-one of these patients, (mean age 48 ± 22) had symptom reproduction during head-up tilt without provocation and 57 were subsequently randomized to provocative tests.

Healthy controls
Twenty-six healthy volunteers (mean age 44 ± 20), 12 of whom were male were recruited as controls. Two controls had a positive baseline head-up tilt, and so were excluded from further study (Fig. 2).

Provocative tilt table testing
Forty-eight patients, (mean age 52 ± 18, 18 male) underwent both provocative tilt tests. Nine additional patients completed only one limb of the study because of unwillingness to complete the second test if the first reproduced symptoms. Twenty-four control subjects entered the provocative testing stage of the protocol, but ten did not complete both tilts. Six did not attend for follow up, three declined a second test after experiencing syncope or presyncope in the first limb of the study and one was
excluded due to the development of symptomatic ischaemic heart disease during the course of the study. Thus, 48 patients and 14 controls completed the full protocol.

### Sensitivity and specificity

#### Analysis of results including positive passive head-up tilt

The sensitivity and specificity of isoprenaline and glyceryl trinitrate head-up tilt tests for patients in this study who had a positive response to the drug-free test are given in Table 1. If patients with a positive unprovoked head-up tilt are included in the analysis, as is the case in many previous publications,[8, 11, 17, 18] 41 of 79 patients and 7 of 16 controls had a positive isoprenaline study, giving a sensitivity of 52% and specificity of 56%. For glyceryl trinitrate head-up tilt, 54 of 79 patients (sensitivity 68%) and six of 16 controls (specificity 63%) were positive.

#### Results of provocative tilts in head-up tilt negative group

The sensitivity and specificity of isoprenaline and glyceryl trinitrate head-up tilt tests for patients who did not have a positive response to drug-free testing are given in Table 2. In patients who had negative baseline tilt, 10 out of 48 had positive isoprenaline head-up tilt (sensitivity 21%) and five out of 14 controls (specificity 64%) were positive. For glyceryl trinitrate head-up tilt, 23 out of 48 patients (sensitivity 48%) and four out of 14 controls (specificity 71%) were positive.

### Side-effects

Isoprenaline head-up tilt was poorly tolerated in patients and controls. Eighty per cent (n=50) experienced adverse effects; 68% (n=43) requested termination of the test before completion of the protocol (Table 3). Thirty of 62 requested termination of the test due to either intolerable palpitation, or intolerable flushing or tremor or a combination of these adverse effects. In 10 cases the test was terminated due to development of predetermined adverse events. One patient and one control had significant asymptomatic hypotension (46/20 mmHg and 53/29 mmHg respectively) which resulted in test termination. One control had nausea resulting in termination of glyceryl trinitrate tilt. No patients had adverse events resulting in termination of glyceryl trinitrate head-up tilt. Headache was reported by 17 patients and two controls, but was not severe enough to preclude completion of the test protocol. Adverse events reported in

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### Table 1 Sensitivity and specificity of isoprenaline and glyceryl trinitrate head-up tilt tests in patients with unexplained syncope and asymptomatic controls, including those who had a positive response to drug-free head-up tilt

<table>
<thead>
<tr>
<th></th>
<th>Isoprenaline</th>
<th>Glyceryl trinitrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients positive</td>
<td>41/79</td>
<td>54/79</td>
</tr>
<tr>
<td>Sensitivity* (95% confidence intervals)</td>
<td>52% (40–63%)</td>
<td>68% (57–78%)</td>
</tr>
<tr>
<td>Total number of controls positive</td>
<td>7/16</td>
<td>6/16</td>
</tr>
<tr>
<td>Specificity† (95% confidence intervals)</td>
<td>56% (30–80%)</td>
<td>63% (35–85%)</td>
</tr>
</tbody>
</table>

*McNemar’s test, P=0.006; †McNemar’s test, P=0.7.

### Table 2 Sensitivity and specificity of isoprenaline and glyceryl trinitrate head-up tilt in patients and asymptomatic controls who did not have a positive response to drug-free head-up tilt

<table>
<thead>
<tr>
<th></th>
<th>Isoprenaline</th>
<th>Glyceryl trinitrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients positive</td>
<td>10/48</td>
<td>23/48</td>
</tr>
<tr>
<td>Sensitivity* (95% confidence interval)</td>
<td>21% (10–35%)</td>
<td>48% (33–63%)</td>
</tr>
<tr>
<td>Total number of controls positive</td>
<td>5/14</td>
<td>4/14</td>
</tr>
<tr>
<td>Specificity† (95% confidence intervals)</td>
<td>64% (35–87%)</td>
<td>71% (42–92%)</td>
</tr>
</tbody>
</table>

*McNemar’s test, P=0.006; †McNemar’s test, P=0.7.

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Figure 2 Randomization of control subjects. HUT = passive head-up tilt; provocative tilts = glyceryl trinitrate HUT and isoprenaline HUT 1 week apart in random order.
respectively. The subjects studied were considerably isoprenaline and specific sensitivities of 55% for glyceryl trinitrate and 58% for isoprenaline (Table 4).

Between glyceryl trinitrate and isoprenaline head-up tilt was longer in those who had a positive provocative test (52 ± 18), or those in whom syncope remained unexplained (52 ± 19).

Table 3 Adverse events during isoprenaline head-up tilt necessitating test termination

<table>
<thead>
<tr>
<th>Reason for test termination</th>
<th>Patients (n=35)</th>
<th>Controls (n=8)</th>
<th>Median dose of isoprenaline (µg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia &gt;150 beats . min⁻¹</td>
<td>4</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Palpitations &lt;150 beats . min⁻¹</td>
<td>20</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Hypertension &gt;190/95 mmHg</td>
<td>12</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Intolerable flush/tremor</td>
<td>17</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Chest pain</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Asymptomatic hypotension</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total in whom test terminated</td>
<td>75%</td>
<td>58%</td>
<td>—</td>
</tr>
</tbody>
</table>

Table 3 refer to those events severe enough to result in test termination.

Haemodynamic parameters

The time to positive test for isoprenaline was longer in both patients and controls. The time taken for blood pressure and heart rate to recover to baseline levels and the mean fall in blood pressure did not differ between glyceryl trinitrate and isoprenaline head-up tilt (Table 4).

Effect of age on results

There was no age difference in those who had a positive unprovoked head-up tilt (47 years ± 22), a negative unprovoked tilt (52 ± 18) and a positive provocative test (52 ± 18), or those in whom syncope remained unexplained (52 ± 19).

Discussion

Glyceryl trinitrate head-up tilt was more sensitive and as specific as isoprenaline-provoked head-up tilt, and had a lower adverse event profile. Moreover, as expected, glyceryl trinitrate head-up tilt was of shorter duration and did not require cannulation. Few studies have compared sublingual glyceryl trinitrate with isoprenaline infusion. A recent paper by Oraii et al. reported sensitivities of 55% for glyceryl trinitrate and 58% for isoprenaline and specificities of 94-7% and 89.5%, respectively. The subjects studied were considerably younger than those in this series, the mean age of patients being 34 years.

In the current series isoprenaline was poorly tolerated. This is at variance with other reports and most likely reflects the older average age of patients in this series compared with other studies (Fig. 3). Forty-seven percent of those screened were ineligible for the isoprenaline limb of the study. The principal contraindication was cardiovascular comorbidity. This is the very group of patients in whom the clinical history alone does not always reveal a clear diagnosis for syncope. Glyceryl trinitrate head-up tilt is not necessarily contraindicated in these patients. Of those who did not have contraindications to isoprenaline, 75% of patients and 58% of controls did not complete the test protocol. At the time of study design, use of incremental dosage increases as per study protocol was common practice. Recent consensus guidelines suggest infusions up to 5 µg . min⁻¹ are acceptable, although some centres now use only low-dose regimen. In this study the 5 µg . min⁻¹ dose was effective in producing a positive response in only two patients and two controls. In 83% of those for whom isoprenaline head-up tilt was aborted, (44 out of 62 undergoing the test), the studies were discontinued at doses of 3 µg . min⁻¹ or less, suggesting that adverse events were not all related to the higher dose. Most previous studies do not record side-effect profiles during isoprenaline head-up tilt. In two series 16-18% of the patients studied tolerated the test poorly. Subjects were noted to have been extremely uncomfortable, especially at higher doses. A recent report of myocardial ischaemia induced by isoprenaline head-up tilt is evidence that caution is needed in those with pre-existing ischaemic heart disease and in the elderly. These limitations are reflected in the strict criteria we used for recruitment into the study and withdrawal from isoprenaline head-up tilt, in view of the older average age of the patients studied, and this may be reflected in the results.

Isoprenaline head-up tilt has been used for over a decade as the test of choice for those patients in whom passive head-up tilt does not reproduce symptoms. Although the exact mechanism of action is unclear, isoprenaline exaggerates sympathetic neuro-humoral activity to produce vigorous ventricular contractions, which in combination with the catecholamine surge provokes intracardiac mechanoreceptor stimulation. Despite many studies, as described in a previous published review, protocols and results vary widely. Isoprenaline sensitivity of up to 87% and specificity in the range 55-100% have been reported, depending on the dosage regimen and angle of tilt used. The high proportion of patients who were ineligible for isoprenaline and the high adverse event rate are most likely explained by the older age of the majority of patients in this study (Fig. 3). This population is significantly older than other groups studied elsewhere. The mean age of 50 years may reflect referral patterns to the Regional Syncope Referral Centre in Newcastle, which specializes in the management of unexplained syncope and falls in an older population. Increased comorbidity and medication use, in particular for cardiovascular disease in this age group may play a role in the results of this study. The differences in presentation of vasovagal syncope and response to tilt table testing in the elderly are the subject of an ongoing study. Patients were permitted to terminate the study if adverse features became intolerable and this high rate of early study termination has not
Table 4  Haemodynamic data during isoprenaline and glyceryl trinitrate head-up tilt testing in patients and controls who had symptomatic hypotension

<table>
<thead>
<tr>
<th></th>
<th>Isoprenaline positive patients (n=10)</th>
<th>Isoprenaline positive controls (n=5)</th>
<th>Glyceryl trinitrate positive patients (n=23)</th>
<th>Glyceryl trinitrate positive controls (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median dose isoprenaline</td>
<td>3 µg . min⁻¹ (range 9–42 min)</td>
<td>3 µg . min⁻¹ (range 7–43 min)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mean time to symptoms</td>
<td>27 min (range 11–99)</td>
<td>59 (range 28–100 mmHg)</td>
<td>—</td>
<td>8 min (range 8–107 beats . min⁻¹)</td>
</tr>
<tr>
<td>BP* nadir (mmHg)</td>
<td>58</td>
<td>59</td>
<td>62</td>
<td>42</td>
</tr>
<tr>
<td>BP recovery time</td>
<td>2 min (range 20 s–8 min)</td>
<td>41 s (range 26 s–1 min)</td>
<td>38 s</td>
<td>8 min (range 20 s)</td>
</tr>
<tr>
<td>HR† recovery time‡</td>
<td>58 s (range 8 s–2 min)</td>
<td>15 s (range 10–20 s)</td>
<td>38 s</td>
<td>5 min (range 8–1 min)</td>
</tr>
<tr>
<td>HR nadir</td>
<td>92 beats . min⁻¹ (range 34–147 beats . min⁻¹)</td>
<td>75 beats . min⁻¹ (range 35–113 beats . min⁻¹)</td>
<td>79 beats . min⁻¹ (range 32–132 beats . min⁻¹)</td>
<td>60 beats . min⁻¹ (range 0–107 beats . min⁻¹)</td>
</tr>
<tr>
<td>Mean BP drop from baseline</td>
<td>62 mmHg (range 46–95 mmHg)</td>
<td>70 mmHg (range 27–84 mmHg)</td>
<td>55 mmHg</td>
<td>88 mmHg</td>
</tr>
</tbody>
</table>

*BP=systolic blood pressure; †HR=heart rate; ‡recovery time=time to return to baseline values.

been previously reported. Again, a lower threshold for termination than applied in other studies may reflect the older age group of patients studied.

Glyceryl trinitrate acts to exaggerate venous pooling due to peripheral vasodilation, leading to decreased intraventricular volume, which triggers left ventricular mechanoreceptors in susceptible individuals. Glyceryl trinitrate was first used as a provocative agent for vasovagal syncope in 1994 when it was administered as an intravenous infusion[16]. This study and a further three, using sublingual glyceryl trinitrate, used glyceryl trinitrate head-up tilt following a period of passive head-up tilt. Sensitivities range from 51% to 81% and specificities from 85% to 94%[16–19]. In the current study, glyceryl trinitrate was given on a separate occasion and whether this is as sensitive and specific as the previous studies requires further investigation. In this series we used two puffs of Nitrolingual spray (800 µg) in accordance with our clinical practice to ensure adequate plasma concentration of glyceryl trinitrate, as rates of sublingual absorption are variable[25]. Previous reports have examined the sensitivity and specificity of lower doses of glyceryl trinitrate and further study may be needed to define the optimum dose required for the diagnosis of vasovagal syncope.

Although culprit medication may induce vasovagal syncope, drug therapy was continued throughout both studies to reflect clinical practice. Medications known to cause vasovagal syncope and orthostatic hypotension are not necessarily the cause of symptoms in all such patients. In this series, other common causes of syncope were excluded prior to provocative tilt testing.

There is still no gold standard test for the diagnosis of vasovagal syncope. Nonetheless, head-up tilt is a safe, simple widely applied test. Sensitivities vary from 32% to 85%[14,6,26], specificities from 50% to 90%[26], and reflect differences in tilt angle, test duration and subject selection. Reproducibility of test results varies from 35% to 87%[27,28] and the sporadic nature of vasovagal symptoms contributes to the diversity of responses. Tilt testing in this study was carried out in a randomized fashion with provocative tilt tests 1 week apart to overcome the poor repeatability of responses to tilt. A recent consensus document standardizing tilt table methodology[22] will be helpful in rectifying some of these conflicts. Recent studies of adenosine infusion suggest that this may provide better predictive diagnosis of those who will respond to cardiac pacing as therapy for vasovagal syncope[29].

Our results for glyceryl trinitrate head-up tilt show a sensitivity of 68% in the group overall and 48% in those in whom baseline head-up tilt is negative, compared

![Figure 3](image-url)  Age distribution of patients undergoing provocative head-up tilts. Number of patients=62-00; mean=50-4 years; standard deviation=20-93 years.
with 52% and 21% for isoprenaline head-up tilt alone. The specificity of glyceryl trinitrate head-up tilt alone was 71% and of isoprenaline head-up tilt was 64%.

Glyceryl trinitrate head-up tilt has the advantage of being a shorter test compared with isoprenaline, which has implications for patient throughput, staffing and resources. Glyceryl trinitrate drug costs are less than 1% of isoprenaline. The added advantage of the lack of need for venepuncture using glyceryl trinitrate is useful in practical terms and also with regard to maintaining test specificity, particularly in the elderly.

In our series, a diagnosis was not achieved in 61% of patients during passive head-up tilt, necessitating further study. Use of sublingual glyceryl trinitrate can be recommended in these patients, rather than isoprenaline.

Conclusions

Head-up tilt testing using sublingual glyceryl trinitrate is more sensitive than, and as specific as, head-up tilt with intravenous isoprenaline. In this series, isoprenaline head-up tilt was poorly tolerated. Glyceryl trinitrate is useful in the diagnosis of vasovagal syncope in those in whom passive head-up tilt is negative.

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References