UPRIGHT TILT TABLE TESTING IN THE EVALUATION OF SYNCOPE

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ABSTRACT

Objectives: To review our experience with the upright tilt table test for the diagnosis of vasovagal syncope in a group of unselected patients with a history of syncope or presyncope.

Methods: 179 patients with a history of syncope or presyncope were subjected to upright tilt test. After carotid sinus massage to exclude carotid sinus hypersensitivity, the patients were tilted on a motorised tilt table with footplate support to an angle of sixty to seventy degrees for thirty minutes. If syncope was not induced, isoprenaline was then infused for a further fifteen minutes. A positive response was defined as fulfilling at least two out of three criteria: (i) syncope or presyncope similar to the spontaneous episodes of syncope, (ii) relative slowing of the heart rate at the onset of symptoms, (iii) drop of systolic pressure to less than 90 mmHg or by more than 50 mmHg.

Statistical methods: Continuous variables are expressed as mean values ±one standard deviation and analysed for statistical significance by the unpaired Student's t-test. Chi-squared test with continuity correction was used for dichotomous variables.

Results: Ninety-four patients (53%) were positive for vasovagal syncope. Fourteen patients (8%) were positive at baseline tilt. An additional 80 patients (45%) were positive with the use of isoprenaline. Ten percent of the positive responses were purely cardioinhibitory, 10% purely vasodepressor and 80% mixed. The commonest cardiac rhythm during a positive response was junctional rhythm (46%) followed by sinus rhythm (44%). Sinus arrest with ventricular standstill occurred in only 5%. Accelerated idioventricular rhythm, 2:1 atrioventricular block and ventricular bigeminy accounted for the remaining 5%.

Conclusion: The upright tilt table test is useful for the diagnosis of vasovagal syncope.

Keywords: Bezold-Jarisch reflex, isoprenaline, recurrent syncope, upright tilt table test, vasovagal.

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INTRODUCTION

Syncope is a common and important problem seen in many patients in clinical practice. Its causes encompass a wide spectrum, ranging from malignant ones such as sudden cardiac death due to malignant ventricular arrhythmias, long QT syndrome or subarachnoid haemorrhage to relatively benign causes such as vasovagal syncope or hysteria.

Recurrent syncope is a distressing symptom in which the cause may remain undetermined in 25% to 47%[1-3] of patients. Up to 60% of such undiagnosed patients continue to have syncope despite extensive investigations including computerised scanning of the brain, electroencephalography and invasive cardiac electrophysiological testing[2]. In the past, vasovagal syncope was a diagnosis made on the basis of history and exclusion of other recognisable causes. The use of the upright tilt table test to verify and reproduce the symptoms of vasovagal syncope has revolutionised this approach. Objective documentation of the occurrence of vasovagal syncope not only avoids the unnecessary trauma and expense of further tests but may also be used to assess the impact of pharmacological and pacing therapy on its recurrence. We report our experience with upright tilt table testing in 179 unselected patients with syncope or presyncope.

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METHODS

Patients

The upright tilt table test was first performed in Singapore in March 1991. Between March 1991 to July 1993, 179 patients with a history of syncope or presyncope underwent upright tilt table testing to exclude vasovagal syncope.

The equipment used comprised the following:

(i) Tri-W G Incorporated motorised tilt table with footplate support and safety restraints.
(ii) Hewlett Packard Pagewriter XLi 12 lead electrocardiogram recorder with continuous three-channel screen display.
(iii) Non invasive automatic sphygnomanometer cuff blood pressure monitor.
(iv) Marquette Electronics Incorporated Holter electrocardiogram recorder.
(v) Infusion syringe pump
(vi) Resuscitation trolley with the standard supply of resuscitation equipment and drugs.
(vii) External defibrillator.

Tilt test protocol

The patients were fasted overnight and not sedated. An intravenous indwelling cannula was inserted into one of the hand veins before the procedure. They were strapped to the tilt table and baseline recordings of the electrocardiogram and blood pressure were made in the supine position. After auscultation to make sure there were no carotid bruits, carotid sinus massage was carried out, first on the right and then on the left, for 15 seconds each and the electrocardiogram and blood pressure measured continuously. When carotid sinus hypersensitivity had been excluded, recordings were made with the patients supine

and then with the table tilted to an angle of 60° to 70° to the horizontal and recordings were made every five minutes for thirty minutes, or sooner if the patients became symptomatic. If the test was not positive at the end of 30 minutes, isoprenaline was infused intravenously while the patients remained tilted, starting at one microgram per minute and increasing by at least one microgram per minute every five minutes for fifteen minutes up to a maximum of three or five micrograms per minute. The usual recordings of the electrocardiogram and blood pressure were made at every five minutes or when the patients became symptomatic during isoprenaline infusion. The table was not returned to the horizontal position between each dose increase of isoprenaline. If the test became positive at any time, it was terminated and the table was tilted down to supine or Trendelenberg position and the patients monitored till symptoms subsided and the blood pressure and cardiac rhythm stabilised. The cycle length for each stage of the test was measured from the recorded electrocardiogram and charted together with the blood pressure and the presence of any symptoms.

Definition of a positive test

The test was considered positive if it met at least two of the following criteria:

1. The patient experienced syncope or presyncopal symptoms similar to the spontaneous episode of syncope or presyncope.
2. There was relative slowing of the heart rate at the onset of symptoms.
3. There was a drop of systolic pressure to less than or equal to 90 mmHg or by more than 50 mmHg, associated with symptoms.

Types of positive responses

1. Predominantly cardioinhibitory – drop in heart rate without any drop in blood pressure.
2. Predominantly vasodepressor – drop in blood pressure without a drop in heart rate.
3. Mixed response – presence of both cardioinhibitory and vasodepressor components.

RESULTS

The patient characteristics and test results are summarised in Table I. Results are expressed as mean ± one standard deviation. Statistical significance was determined by using the unpaired student's t-test for continuous variables and chi squared test with continuity correction for dichotomous variables. There were 179 patients (106 male and 73 female). The mean age of the patients was 32 ± 14 years (range 6 to 73 years). None of the patients had carotid sinus hypersensitivity. Ninety-four patients (53%) were positive for vasovagal syncope. Fourteen (8%) were positive during the baseline tilt and 80 (45%) were positive only with the use of isoprenaline and tilt. The majority of positive responses were mixed (80%), 10% were purely vasodepressor and 10% were purely cardioinhibitory. The mean time to positivity was 36 ± 10 minutes. There was a mean drop of 50 mmHg in systolic blood pressure and 31 mmHg in diastolic blood pressure in the positive group ($p = 0.0001$ for both). All the positive patients had resolution of symptoms and return of blood pressure and heart rate to normal after being placed in the supine position and isoprenaline stopped if it was used. Table II shows the characteristics in tilt positive versus tilt negative patients. There was no significant difference in the frequency of positive responses between the sexes (55% of females versus 51% of males) ($p = 0.72$). The mean ages of the positive (31 ± 13 years) and negative (34 ± 14 years) groups were not significantly different ($p = 0.13$). In the negative group, one patient developed orthostatic hypotension immediately after being tilted upright, in contrast to tilt positive patients in whom symptoms developed after a latent period from the onset of tilt. In this patient, orthostatic hypotension and not vasovagal syncope was responsible for his symptoms.

Table I – Patients' characteristics and test results

Number of patients	179
Male: Female	106:73
Mean age ± standard deviation (years)	32 ± 14
Carotid sinus hypersensitivity	0
Positive (total)	94 (53%)
Positive (baseline)	14 (8%)
Positive (isoprenaline)	80 (45%)
Predominantly cardioinhibitory	9 (10%)
Predominantly vasodepressor	9 (10%)
Mixed	76 (80%)
Mean time to positivity (minutes)	32 ± 10
Mean systolic blood pressure (mmHg) * (p=0.0001)	
baseline	122 ± 21
positive	71 ± 29
Mean diastolic blood pressure (mmHg) ** (p=0.0001)	
baseline	74 ± 13
positive	43 ± 18

Table II – Characteristics in tilt-positive versus tilt-negative patients

	Tilt positive	Tilt negative
Mean age ± standard deviation (years)*	31 ± 13	34 ± 14
Males (%)	51 **	49
Females (%)	55 **	45

* $p = 0.31$ (Student's t test)
** $p = 0.72$ (chi squared = 0.126 with continuity correction)

Table III – Types of cardiac rhythms during positive tilt tests (n = 94)

Cardiac rhythm	Number (%)
Junctional rhythm	41 (44%)
Sinus rhythm	43 (46%)
Sinus arrest with ventricular standstill	5 (5%)
Accelerated idioventricular rhythm	3 (3%)
2 : 1 AV block	1 (1%)
Ventricular bigeminy	1 (1%)

The types of cardiac rhythm observed during a positive response are summarised in Table III. The commonest rhythm was sinus arrest with junctional rhythm in 43 patients (46%) as illustrated in Fig 1a,b,c, followed by sinus rhythm in 41 patients (44%). Asystole lasting 6 to 15 seconds was seen in only 5 (5%) patients as illustrated in Fig 2a,b,c and miscellaneous rhythms such as accelerated idioventricular rhythm (3 patients), ventricular bigeminy (1 patient) and 2:1 atrioventricular block

(1 patient) in another 5% of patients. The commonest side effects experienced during isoprenaline infusion in the negative patients were palpitations, nausea and giddiness. Only three patients in the negative group developed arrhythmias during isoprenaline infusion. One had accelerated junctional rhythm without symptoms, one patient with congenital long QT syndrome had torsade de pointes and one had non-sustained ventricular tachycardia during isoprenaline. The last patient subsequently underwent electrophysiological stimulation and was found to have catecholamine-sensitive ventricular tachycardia, probably automatic, which was responsible for her symptoms. Therapy with sotalol (a Class III antiarrhythmic drug) subsequently prevented recurrence of her symptoms.

DISCUSSION

Syncope may be broadly classified as being of cardiovascular or non-cardiovascular origin. Cardiovascular causes which constitute the majority may be further subdivided into those due to neurally mediated reflex disturbances of blood pressure, orthostatic and dysautonomic vascular control, primary cardiac arrhythmias and structural cardiovascular disease[4]. Neurally mediated syncopal syndromes are probably the most common and the most frequently encountered of these is vasovagal syncope[5,6]. In recent years, tilt table testing has been found to be a useful tool in the assessment of patients thought to have vasovagal syncope.

Mechanism of vasovagal syncope

Current understanding of the physiologic basis of the common or vasovagal faint is that afferent signals arising from receptors sensitive to stretch, pain or chemical stimuli trigger off neurally mediated reflexes which cause bradycardia and hypotension. Examples of such receptors are stretch-sensitive mechanoreceptors found in atrial and ventricular myocardium and chemical-sensitive (nicotine, veratridine) receptors in ventricular myocardium. In the tilt test, prolonged maintenance of the upright posture causes venous pooling in the extremities and reduced venous return to the heart, reduced stroke volume and systemic arterial pressure. This activates carotid and central baroreceptors which send impulses to the medullary centres to cause a reflex tachycardia and an increased inotropic state via a relative increase of sympathetic over parasympathetic neural traffic. In susceptible individuals, the vigorous contractions of a relatively small left ventricle activates mechanoreceptors which feed back to the medulla to cause an increase in parasympathetic activity (bradycardia) and withdrawal of sympathetic activity (systemic hypotension) (Bezold-Jarisch reflex)[7]. The use of isoprenaline increases the yield of the test by causing both peripheral vasodilatation and increased cardiac inotropicity and possibly by sensitisation of the mechanoreceptors as well[8-10].

Tilt test protocols

Although the usefulness of tilt table testing is generally accepted, there has been no standardised tilt test protocol. The various reports of tilt table testing have used different protocols with different sensitivities and specificities[1,8-12]. However a few general points are agreed upon. The use of a foot plate support produces fewer false positive results than a saddle support[12]. Tilting at an angle less than 60° lowers the sensitivity of the test[12]. Hence generally accepted protocols have used a tilt angle of 60°– 80°. The duration of tilt has varied from 10-60 minutes[1-3,8,9,12-15] and is a crucial determinant of the outcome of the test. Worldwide experience has leaned towards a duration of between 20-45 minutes[16]. The use of isoprenaline to enhance the sensitivity of the test and shorten the duration needed for baseline tilt is also controversial. There has been definite improvement in its sensitivity as shown by Almquist[8] and Grubb[17] and furthermore in children or young adults, the use of baseline tilt alone has been shown to have low yields[12,18]. However there has also been concern that isoprenaline may reduce the specificity of the test[12,13]. We chose a protocol that involved 30 minutes of baseline tilt and 15 minutes of tilt with isoprenaline infusion starting at one microgram per minute and increasing every 5 minutes if negative until a maximum of 3 or 5 micrograms per minute was reached. Three micrograms per minute was the usual maximum dose used unless the heart rate failed to increase to at least 120 beats per minute, in which case the dose was increased to five micrograms per minute. Using the above protocol, the test was positive in 94 of 179 patients (53%). This is well within the range of reported "sensitivities" which varies from 30% to 82%[1,2,8-10,12-15]. As there is no "gold standard" test for vasovagal syncope, the "sensitivity" of any protocol depends in part on the type of patients selected to undergo the test. Hence, inclusion of patients whose symptomatology were not suggestive of a vasovagal aetiology would decrease the "sensitivity" of the test. In addition, studies have shown that there may be day to day variability in the ability of the tilt test to reproduce vasovagal reactions in the same individual. Fitzpatrick et al[12] showed that 20% of tilt-positive patients did not have an abnormal response on repeat testing. Our patient population was relatively unselected in the sense that any patient with a history of syncope or presyncope seen by any cardiologist in the department and thought to be possibly vasovagal in origin could be sent for a tilt test. There was no attempt to preselect the patients by prior investigations such as electroencephalography, brain scan, echocardiogram, Holter monitoring, electrophysiological testing or psychiatric evaluation. This approximates the true clinical situation in which such patients with a normal preliminary clinical examination and electrocardiogram may proceed directly to tilt table testing for confirmation of the diagnosis of vasovagal syncope without further extensive investigations. We found no difference in mean age between the tilt positive and negative patients suggesting the test may be useful both in youthful and elderly subjects. Although more males were referred for the test than females, (106 versus 73) there was no significant difference in the percentage that was positive (51% males versus 55% females). We found no case of carotid sinus hypersensitivity (CSH) in this population, suggesting it must be very rare as a cause of syncope. CSH is in fact extremely rare in the first three decades of life but the incidence increases steadily thereafter[19]. Even if present, only 5% -20% will have carotid sinus syncope[20].

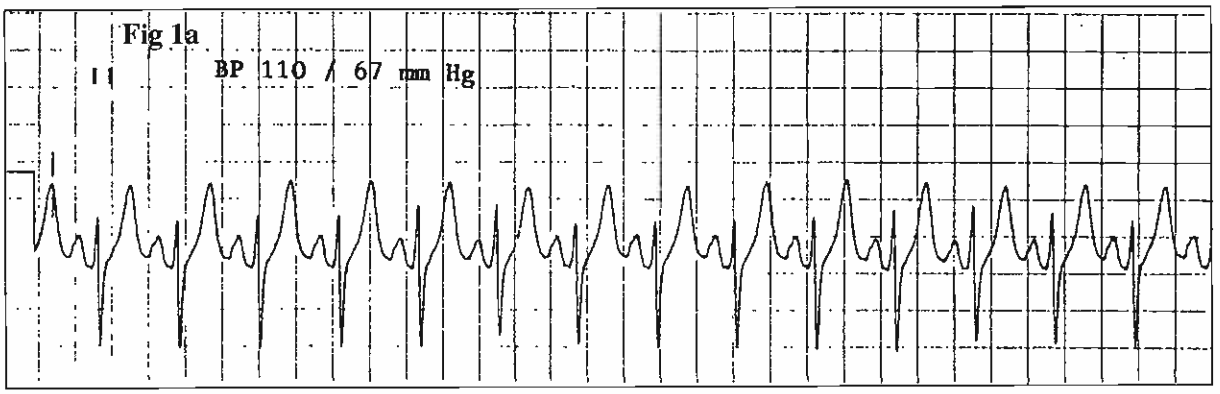
The majority of positive responses were mixed (80%); pure cardioinhibitory and pure vasodepressor responses accounted for 10% and 10% respectively by our definition. This pattern of response is similar to that reported by others[9,12]. The mean time to syncope in our patients was 36 ± 10 minutes. Fitzpatrick et al found a mean time to syncope of 24 ± 10 minutes using a protocol of 60° tilt for 60 minutes[12]. We also documented the cardiac rhythm at the time the tilt test became positive. Forty-six percent had sinus arrest with junctional escape rhythm. Forty-four percent had maintenance of sinus rhythm. Five patients (5%) had periods of sinus arrest and ventricular standstill lasting at least six seconds. Three patients had accelerated idioventricular rhythm and one developed 2:1 atrioventricular block and one had ventricular bigeminy. None of the previous reports have documented the types of arrhythmias associated with a positive response. One study using intracardiac electrodes during upright tilt testing with isoprenaline noted prolongation of AH intervals (atrio-His conduction time) in positive responders compared to shortening of AH intervals in negative responders, but there was

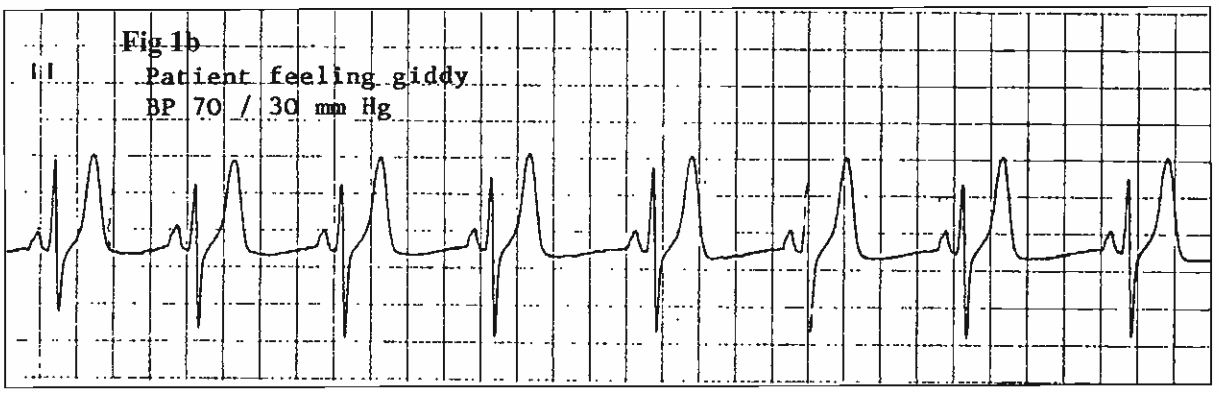
no observation with respect to sinus node activity[21]. The main limitation of this study is that we have not looked at the specificity of our tilt test protocol. However, we have recently begun using this protocol on normal controls who have had no previous history of syncope, and only one out of the 11 (9%) subjects studied has had a positive result. Most other studies have reported false positive rates of between 0 to 13% among various normal control groups[1,8,12,14,22,23].

Therapeutic implications

The tilt test may sometimes be used to test the therapeutic efficacy of drugs or pacing in preventing recurrence of symptoms. Drugs which have been tested in this fashion include atropine, propranolol, esmolol, disopyramide and etilephrine (an alpha sympathomimetic agent). In one study[1], atropine prevented tilt-induced syncope in 3 of 8 patients (37.5%), propranolol in 2 of 8 patients (25%), and etilephrine in 7 of 7 patients (100%). In another study[24], intravenous esmolol (an ultra short-acting beta blocker) was used to predict the efficacy of metoprolol treatment in preventing recurrence of syncope. All patients who were tilt negative after injection of esmolol were found to be tilt negative after starting metoprolol treatment whereas 90% of those who were tilt positive after esmolol were tilt positive after metoprolol treatment. In certain patients with the more "malignant" form of vasovagal syncope, characterised by prolonged ventricular standstill, pacemaker therapy may be necessary. Fitzpatrick et

Fig 1a, b and c - A patient with a positive response during upright tilt table testing and isoprenaline infusion. Fig 1a shows the patient's heart rate at 141 beats per minute and the blood pressure 110/67 mmHg with isoprenaline infusion at one microgram per minute after one minute. In Fig 1b, after four minutes of isoprenaline infusion at one microgram per minute, the patient complained of giddiness, the blood pressure dropped to 70/30 mmHg and there was relative sinus bradycardia of 70 beats per minute. In Fig 1c, at five minutes, the patient had junctional rhythm, with a heart rate of 62 beats per minute and blood pressure of 48/36 mmHg, and was presyncopal. These changes resolved after returning the table to the Trendelenberg position and stopping the isoprenaline infusion. (scale: 25 mm/second, 10 mm/mV)





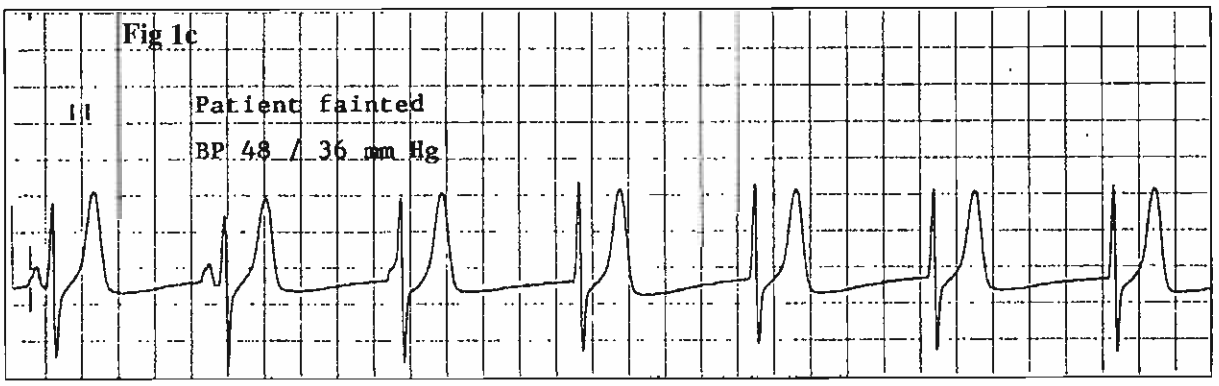
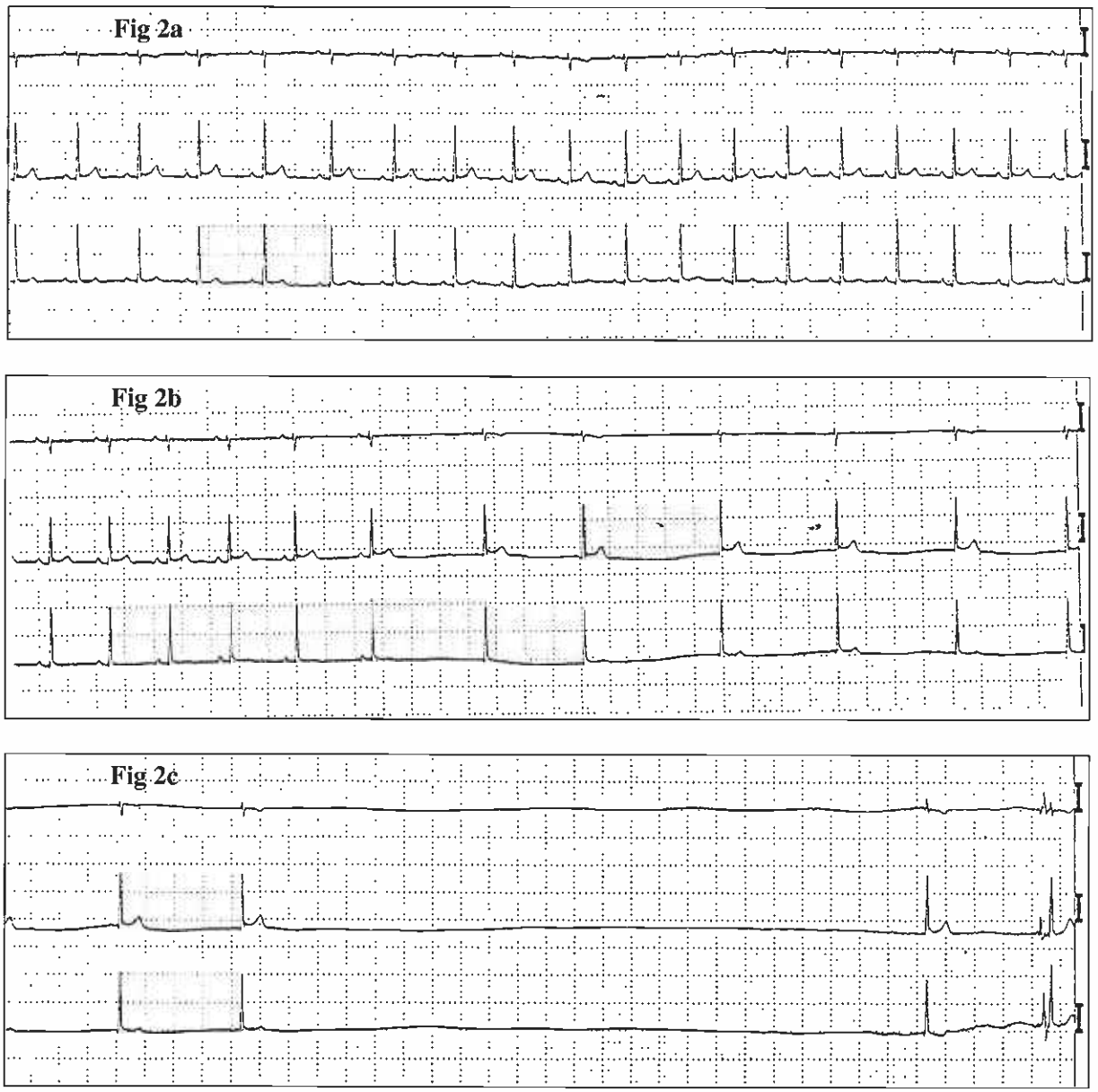


Fig 2a, b and c – A patient with prolonged asystole during baseline tilt. Fig 2a at 18 minutes of baseline tilt shows the patient in sinus rhythm with a heart rate of 76 beats per minute and blood pressure of 112/64 mmHg. In Fig 2b, 15 seconds later, there is junctional rhythm and in Fig 2c, another 15 seconds later, there is asystole which lasts for 9.5 seconds, followed by a junctional escape beat. (scale: 12.5 mm/second, 5mm/mV)



al[25] found that dual chamber pacing could abort syncope in 5 out of 6 patients who had frank syncope during tilt-induced vasovagal reactions and we have had to implant a dual chamber pacemaker in one patient who had recurrent vasovagal syncope with prolonged periods of asystole.

CONCLUSION

The upright tilt table test has become a valuable addition to our diagnostic armamentarium for unexplained syncope. Vasovagal syncope need no longer be a diagnosis by exclusion. The tilt test is a simple, inexpensive, relatively non-invasive test which can objectively document the occurrence of vasovagal reactions in susceptible patients and avoid further more expensive, time-consuming, unfruitful and perhaps invasive investigations in an attempt to prove to the patient that there is no serious underlying cause. It has also helped us to have a better understanding of the physiological basis of vasovagal syncope and in so doing, enabled us to explore and test various therapeutic possibilities. In patients in whom recurrences of syncope are a problem, drug therapy with beta blockers, alpha sympathomimetic agents, or disopyramide have been evaluated. The tilt test can also identify certain patients with the more "malignant" form of vasovagal syncope in whom sudden death has been reported. These patients who have prolonged asystole during vasovagal reactions may benefit from implantation of a permanent pacemaker.

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