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## The response of the tilt table test performed in the afternoon in syncope of unexplained origin.

Surapun Sitthisook\*

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*The tilt table test was performed on 61 patients with unexplained syncope and 13 healthy volunteers in the afternoon after 6 hrs fasting. The test results were positive in 6 patients (9.83%) without isoproterenol infusion and in 21 patients (34.42%) with isoproterenol whereas all of the volunteers were negative. The sensitivity of the tilt table test in unexplained syncope cases was 44% when the test was performed in the afternoon period. Hemodynamically, there was no significant change in systolic and diastolic blood pressure, but increased heart rate occurred in negative response to tilts. The majority (76%) of positive tilts with isoproterenol was mixed cardioinhibition and vasodepression but only a half of the positive tilts without isoproterenol were mixed-type. Three positive tilt patients had malignant vasovagal reaction. Three out of four (75%) micturition syncope had a positive test with isoproterenol.*

**Key words:** *Tilt table test, Syncope, Sensitivity, Hemodynamic response.*

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สุรพันธ์ สิทธิสุข. การตอบสนองของผู้ป่วย อันเอ็กซ์เฟลนด์ ซินโคปีต่อการตรวจ ทิลท์ เทเบิล เทส ในภาคบ่าย. จุฬาลงกรณ์เวชสาร 2537 ธันวาคม; 38(12): 761-770

ได้ทำการตรวจ tilt table test ในผู้ป่วย เป็นลมหมดสติที่ไม่พบสาเหตุจำนวน 61 คน เทียบกับ อาสาสมัครปกติจำนวน 13 ราย โดยทำการตรวจในภาคบ่ายหลังจากให้อาหาร 6 ชั่วโมง การตรวจให้ผลผิดปกติในผู้ป่วย 6 ราย (คิดเป็น 9.83%) โดยไม่ใช้ยา isoproterenol และให้ผลผิดปกติในผู้ป่วย 21 ราย (คิดเป็น 34.42%) โดยใช้ยา isoproterenol ในการตรวจด้วย ส่วนอาสาสมัครให้ผลปกติทุกราย ความไวของ tilt table test ในการตรวจผู้ป่วยเป็นลมหมดสติที่ไม่พบสาเหตุคือ 44% เมื่อทำการตรวจในภาคบ่าย การตอบสนองทาง hemodynamic พบว่า ในรายที่ให้ผลปกติ ไม่พบการเปลี่ยนแปลงของ systolic และ diastolic blood pressure แต่มีการเพิ่มขึ้นของอัตราการเต้นของหัวใจ ส่วนในกลุ่มผู้ป่วยที่ให้ผลผิดปกติจะตอบสนองเป็นชนิด mixed cardio-inhibition และ vasodepression ถึง 76% ในกลุ่มผู้ป่วยที่ใช้ isoproterenol ร่วมในการตรวจ แต่พบการตอบสนองชนิด mixed type เพียง 50% ในผู้ป่วยที่ตรวจโดยไม่ใช้ isoproterenol ผู้ป่วยจำนวน 3 รายมี malignant vasovagal reaction ต่อ tilt test และผู้ป่วย 3 ใน 4 ราย (75%) ของ micturition syncope ในผลผิดปกติเมื่อตรวจโดยใช้ isoproterenol ร่วมด้วย

Syncope is the transient loss of consciousness due to an acute decrease in cerebral blood flow. The patient is able to gain consciousness spontaneously without any intervention. Normally there is autoregulation mechanism to keep cerebral perfusion constant in case that fluctuation in systemic blood pressure occurs in a limited range. During syncope the patient has severe hypotension which is an important clinical clue to differentiate from epilepsy. If a decrease of cerebral blood flow is long enough the patient has a convulsion during syncope so it is prudent to make a definite diagnosis.

Syncope is a common problem accounting for 3% of emergency room visits and 6% of general medical admissions.<sup>(1,2)</sup> Although the patients are thoroughly examined, half of them are classified as experiencing syncope of unknown cause.<sup>(3)</sup> The tilt table test was introduced and became useful as a provocative test for neurally-mediated syncope which was believed to be the most common cause for unexplained syncope. The mechanism of this test is to induce a decrease in venous return during the tilt while there was an increase in sympathetic tone due to the decreased hemodynamic pressure at the baroreceptors. The mechanoreceptor C-fiber at the inferoposterior wall of the left ventricle is then stimulated to trigger the parasympathetic reflex response manifested by hypotension and bradycardia, a typical manifestation of vasovagal or vasodepressor syncope.

Most prior investigators performed the tilt table test with the angle of tilt between 60 and 80 degrees and the duration of tilt between 10 and 60 minutes. Although there was no standardization for the procedure, most of the time the test was performed in the morning after an overnight fasting. The purpose of our study was to observe the

response of the tilt table test when performed in the afternoon after a 6-hour fasting. The reasons we conducted this study were, firstly, to determine the sensitivity of the test when performed in the afternoon when the doctor's schedule was light and the multipurpose tilt table was not in use.

Secondly, as we knew that there was diurnal variation of autonomic tone, we wished to determine by historical comparison, if the response of our tests would be different from the test performed in the morning.

## Methods

We analyzed the tilt table test data of 61 patients with histories of syncopal or near-syncopal attacks who had undergone tests between September 1991 and December 1994 at Chulalongkorn Hospital. All of the patients had no evidence of structural heart disease as determined by history, physical examination and noninvasive cardiac investigations. In addition, we studied a control group of 13 healthy volunteers who underwent a tilt table test without isoproterenol infusion after informed consent signature.

## Head-up tilt test protocol

A multipurpose electronically controlled tilt table was utilized in an undisturbed and quiet environment. All subjects were nonmedicated and at least 6-hours in a fasting state. All procedures were scheduled in the afternoon (12.00-2.00 P.M.). The subjects were progressively tilted at 15 and 30 degrees (each for two minutes) and at 60 degrees for 30 minutes. The subjects were supported by a belt across the torso and by a foot support at the base of the bed. 5% dextrose solution was given to keep a vein open

and for isoproterenol infusion. Automated cuff blood pressure was recorded every minute and lead - II of the surface EKG was continuously monitored. The tilt was terminated when the patient developed syncope, near syncope, or severe lightheadedness. If the test was negative after 30 minutes of 60 degrees tilt, a graded isoproterenol infusion (1-5 ug/min) was administered to achieve at least a 25% increase in supine heart rate. The 60 degrees tilt was then repeated for an additional 10 minutes under the isoproterenol infusion. The tilt was terminated when the patient developed syncope, near syncope, severe lightheadedness or completed the 10 minutes of 60 degrees tilt with isoproterenol infusion.

A positive tilt test was defined as the occurrence of syncope, near-syncope or severe lightheadedness associated with marked hypotension (vasodepressor syncope), bradycardia (cardioinhibitory form) or both in the course of the tilt.

Four groups were defined based on the results of the tilt test:

Group 1 Patients with a history of syncope and a positive tilt test without isoproterenol.

Group 2 Patients with a history of syncope and a positive tilt test with isoproterenol.

Group 3 Patients with a history of syncope and a negative tilt test.

Group 4 Normal control group. No history of syncope and a negative tilt test.

The data are expressed as mean  $\pm$  standard deviation. Comparison between groups was made by paired and unpaired student's t-test or the Fisher exact-test as appropriate. A p-value of  $< 0.05$  was considered significant.

## Results

Twenty-seven of the sixty-one patients (44%) had a positive tilt test. These consisted of six patients (9.83%) positive without isoproterenol and twenty-one patients (34.42%) positive with isoproterenol infusion. The time from the start of the 60 degree tilt to syncope or near syncope was  $14.33 \pm 9.79$  minutes in group 1 and  $4.03 \pm 2.22$  minutes in group 2, and this is a statistically significant difference ( $p=0.05$ ). All of the thirteen healthy control subjects were negative tilt test. Table 1 illustrates the characteristics of the four groups.

**Table 1.** Patient population.

	Group 1	Group 2	Group 3	Group 4
Number	6	21	34	13
Males : Females	4:2	8:13	11:23	11:2
Age(yrs) $x \pm SD$	$37.4 \pm 22.23$	$34.62 \pm 12.57$	$40.53 \pm 14.83$	$29.38 \pm 2.10$

Group 1 = Patients with history of syncope and positive test without isuprel.

Group 2 = Patients with history of syncope and positive test with isuprel.

Group 3 = Patients with history of syncope and negative test.

Group 4 = Normal Control.

The hemodynamic data recorded at baseline and during head-up tilt is summarized in table 2. In those subjects who developed syncope

or presyncope during tilt, data is presented at baseline and immediately before the end point occurred.

**Table 2.** Hemodynamic response to head-up tilt performed in the afternoon in unexplained syncope.

	N		SBP	DBP	HR
Group 1	6	baseline	120.67 ±24.28	71.58 ±14.66	71.08 ±10.84
		before syncope	108.5 ±18.89	68.83 ±15.84	82.17 ±15.10
		during syncope	75.25 ±12.68	39.67 ±15.88	39.33 ± 6.34
Group 2	21	baseline	121.84 ±14.07	75.44 ±10.02	71.64 ±11.10
		60°, 30 min	114.86 ±14.29	73.68 ±12.98	77.45 ±11.44=O
		baseline isuprel	130.73 ±19.81	61.59 ±10.84	106.77 ±13.52
		before syncope	113.78 ±16.95*	55.72 ±11.93*	105.55 ±22.10
		during syncope	73.67 ±11.96+	40.89 ± 9.13+	75.09 ±22.89+
		baseline isuprel	127.07 ±19.15	64.33 ± 9.14	111.92 ±15.68
Group 3	34	baseline	120.99 ±13.95	74.95 ± 8.24	74.08 ±13.99
		60°, 30 min	118.09 ±13.72	77.26 ±11.44	80.38 ±17.24=O
		baseline isuprel	127.07 ±19.15	64.33 ± 9.14	111.92 ±15.68
		60°, 10 min isuprel	127.22 ±16.42	66.70 ± 9.55	120.70 ±20.96=O
Group 4	13	baseline	112.92 ±11.49	69.23 ± 5.10	69.48 ±11.09
		60°, 30 min	114.38 ±10.36	67.85 ± 6.22	75.0 ±12.26=O

x ±SD

\* = P < 0.05 baseline isuprel VS before syncope

+ = P < 0.000005 baseline isuprel VS during syncope

=O= P < 0.05 baseline VS 60°, 30 min

=□= p < 0.05 baseline isuprel VS 60°, 10 min isuprel.

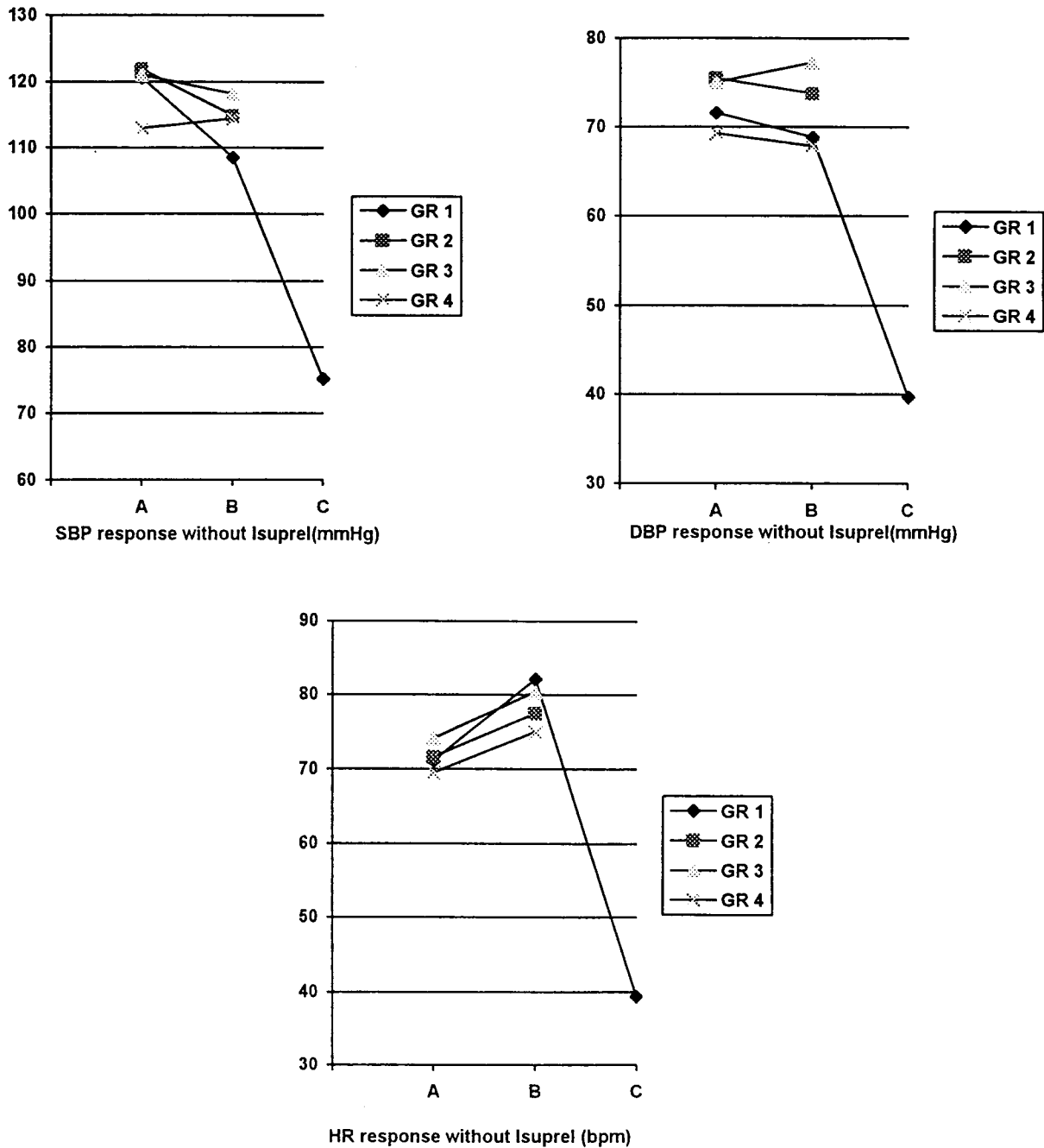
The hemodynamic response in tilt negative subjects was that both systolic and diastolic blood pressure were not significantly changed, but the heart rate increased significantly, including in subjects with isoproterenol infusion.

The baseline hemodynamic data during isoproterenol infusion in supine position revealed increased systolic blood pressure, decreased diastolic blood pressure and increased heart rate as expected. The difference in hemodynamic response between tilt positive subjects, with

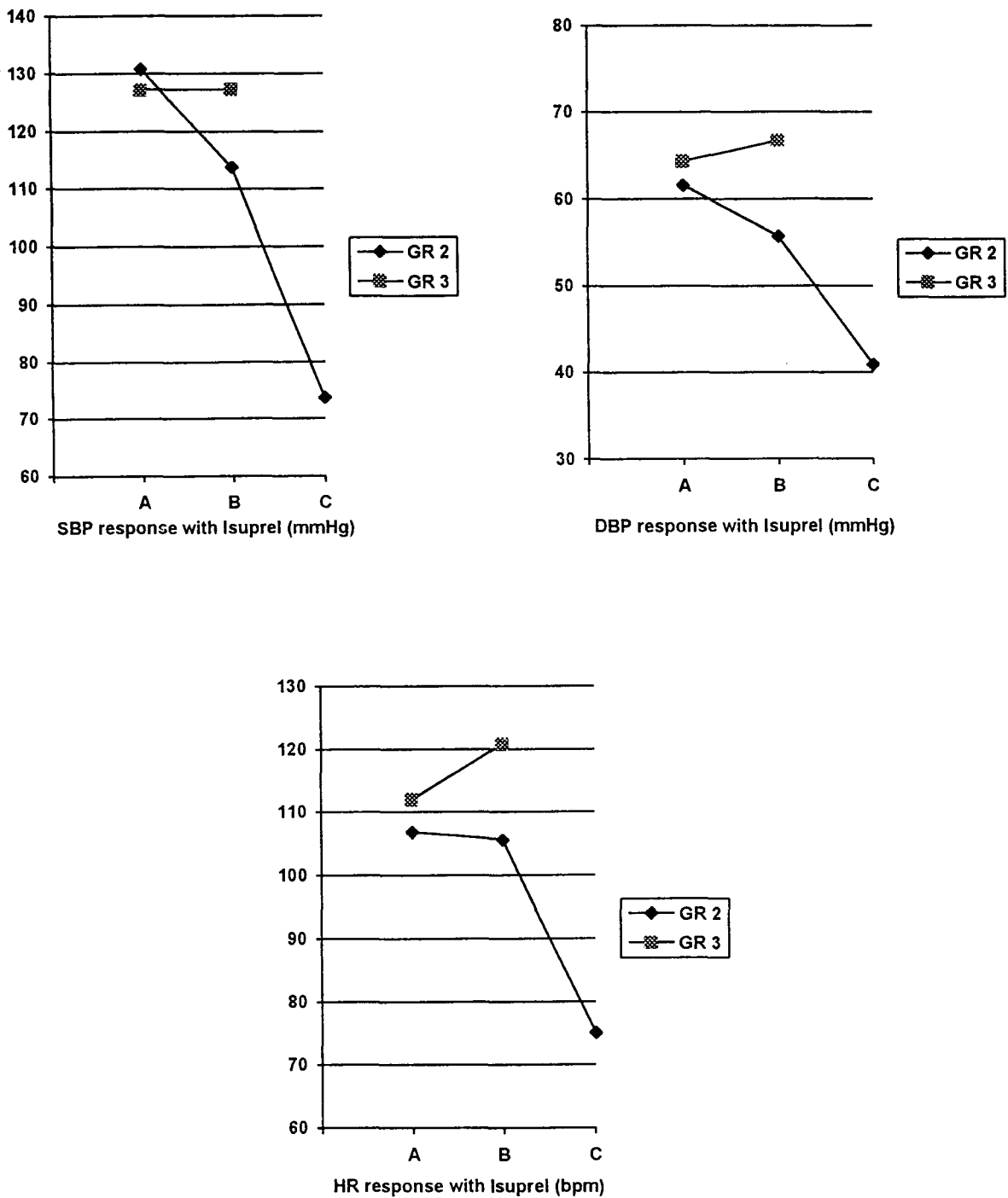
and without isoproterenol, was that the systolic and diastolic blood pressure were significantly decreased before syncope only among positive tilt subjects with isoproterenol.

Of the six positive tilt patients in group 1, there were three cardioinhibitory responses and three mixed-type responses. Of the twenty-one positive tilt patients in group 2, there were five vaso-depression and sixteen mixed-cardioinhibitory-vasodepression responses.

Figs 1 and 2 illustrate systolic blood pressure, diastolic blood pressure and heart rate response to tilt with and without isoproterenol in the four groups respectively.



**Figure 1.** Hemodynamic response to head-up tilt without isoproterenol. The systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) of the four groups are illustrated. A. represents the baseline measurement. B. corresponds to the measurement before syncope in the group with positive tilt test, and at 60 degrees 30 minutes in the groups with negative test. C. corresponds to the measurement during syncope.

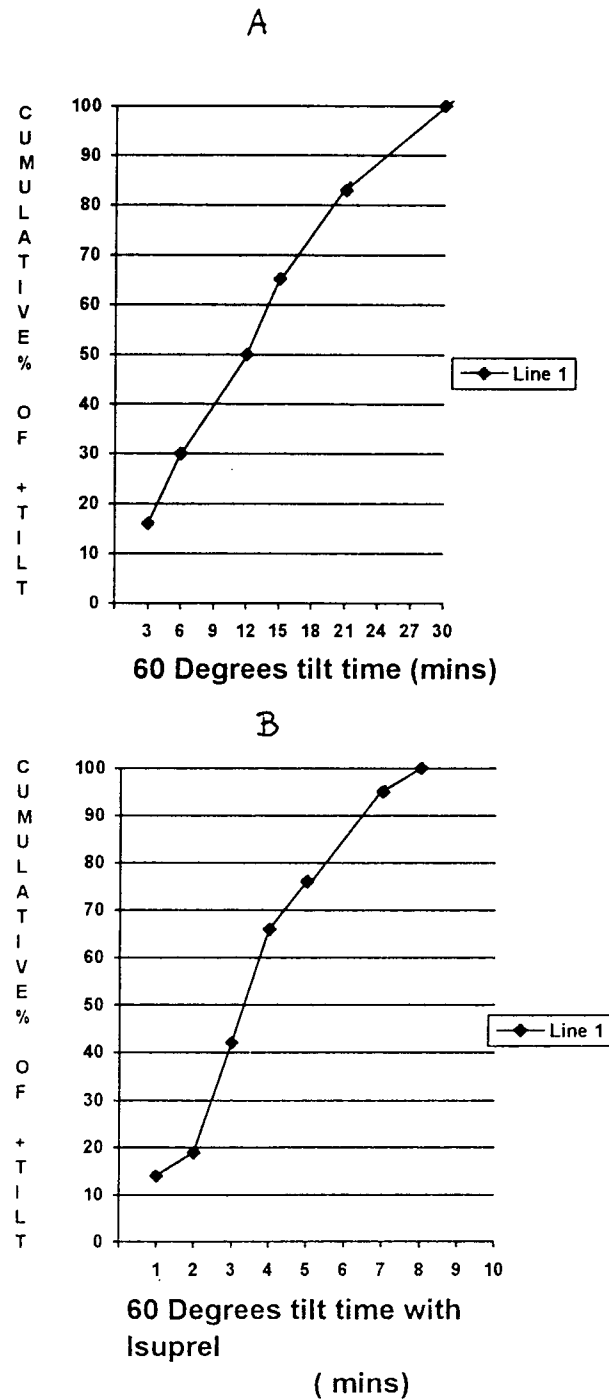


**Figure 2.** Hemodynamic response to head-up tilt with isoproterenol. The systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) of group 2 and 3 are illustrated. A. represents the baseline measurement under isoproterenol infusion. B. corresponds to the measurement before syncope in the group with positive tilt test, and at 60 degrees 10 minutes under isoproterenol infusion in the group with negative test. C. corresponds to the measurement during syncope.



The cumulative percentage of subjects with a positive head-up tilt is analyzed in Fig 3 (group 1 and group 2).

The sensitivity of the tilt table test performed in the afternoon was 44%.



**Figure 3.** Cumulative percentage of positive tilt tests; 3A represents the group without isuprel (group 1), 3B represents the group with isuprel (Group 2). Only subjects with positive tilt test are represented in this graph (n=6 in group 1, n=21 in group 2). Each point may be represented by more than one subject.

## Discussion

Tilting causes 300-800 ml of venous pooling in lower part of the body which reduces venous return and ventricular filling. As a result, the arterial blood pressure falls and the inhibitory drive from the baroreceptors is reduced. The resultant increased left ventricular contractility stimulates mechanoreceptors causing increased efferent vagal tone and the clinical picture of a vasovagal attack.<sup>(4,5)</sup>

In previously published reports, the sensitivity of a head-up tilt test in patients with a history of syncope of unknown etiology varied from 20 to 74%.<sup>(1,6-11)</sup> This enormous variability was possibly due to heterogeneity of patient population, duration of tilt, the angle used for tilt, and the lack of a gold standard diagnostic test for neurally-mediated syncope.<sup>(12)</sup> The use of isoproterenol, a beta agonist used to increase the sensitivity of the test, is based on the hypothesis that increased sympathetic drive precedes the development of vasovagal response and that an increase in myocardial contractility during adrenergic stimulation produces distortion of ventricular mechanoreceptors that mediate efferent cardiac vagal reflexes.<sup>(11)</sup> Additionally, it has been reported that the specificity of head-up tilt is markedly reduced in tilts with saddle support so footplate support is recommended in routine tilt test.<sup>(12)</sup>

This is the first report of tilt tests performed in the afternoon after a 6-hour fasting period. The sensitivity of the tests without isoproterenol infusion is less than tests done in the morning, as previously reported.<sup>(1,6-11)</sup> However, isoproterenol markedly increased the sensitivity of our test. Hemodynamically, we did not have statistically significant increased diastolic blood pressure in

normal response to tilting as expected probably due to only mild vasoconstrictive response to upright posture.

Analysis revealed three patients of malignant vasovagal attacks whom we provided permanent pacemakers. They were symptom free after a one year follow up period.<sup>(13)</sup> Of the four patients with a diagnosis of micturition syncope, three had a positive test with isoproterenol infusion (75% sensitivity).

The positive response of tilts with isoproterenol was mostly mixed cardioinhibition and vasodepression (76%) whereas positive response without isoproterenol was half cardioinhibition and half mixed type. Obviously isoproterenol may add vasodepression reaction which probably causes false positive test as someone's concern.

In conclusion, the head-up tilt tests performed in the afternoon had an acceptable sensitivity (44%) when isoproterenol was used. The tilt test is a noninvasive test which can be performed as a screening test in cases of unexplained syncope before proceeding to invasive testing. The controlled study is required to definitely test the reproducibility and diurnal variation of the sensitivity.

## Acknowledgment

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