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Comparison between Short and Long Protocols of Head Up Tilt Table Test

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ABSTRACT

Background: There are several potential causes of syncope, however vasovagal syncope is quite prevalent. Knowing the root cause of syncope requires a thorough history and a variety of investigative methods. Time and energy could be conserved with a streamlined approach for the head-up tilt table (HUT) test.

Objective: The present study aim was to compare the efficacy of a shorter HUT technique to the longer standard methodology.

Patients and Methods: The study was conducted on 276 patients with history of syncope. In the interest of patient care, all patients were directed to HUT. Complete clinical evaluations were performed on all patients, both generally and locally, in addition to a 12-lead electrocardiogram (ECG) as a baseline. They were classified randomly in 2 groups, the first group (group A) included 150 patients who underwent HUT test by the conventional long protocol which included 15 minutes duration in stage I, and the other group included 126 patients (group B) underwent the same procedure with the modified short-timed protocol which included only 10 minutes duration in stage I.

Results: Our results showed no statistically significant differences between the two groups in terms of test outcomes; nevertheless, there was a statistically significant difference in patient recovery time between the two groups for the shorter-timed procedure (mean 2.64 ± 1.35 minutes) versus the long-timed protocol (4.05 ± 1.19l minutes), with p value <0.001.

Conclusions: When attempting to identify neuro-cardiogenic syncope, using the shorter timed protocol for HUT testing is just as valid as using the longer timed technique. Reduced time and effort spent on the procedure contributed to better patient recovery time and convenience.

Keywords: Syncope, Head up tilt, Tilt protocol, Short protocol, Vasovagal syncope.

INTRODUCTION

Syncope is a temporary loss of consciousness caused by a lack of blood flow to the brain, and it is characterized by a sudden start, a brief duration, and a full and immediate recovery. Syncope's primary pathophysiologic processes are low blood pressure and widespread cerebral hypoperfusion [1].

Cardiac syncope may be due to different possible causes with wide scale of dangerousness. Neuro-cardiogenic type of syncope is still the most common cause among the cardiac causes [2]. A major challenge in management of syncope is risk stratification to decide the possibility of hospital admission aiming of reduction of inappropriate admissions while maintaining the safety of the patients [3].

Syncope and/or hypotension can occur when cardiac output or total peripheral resistance decreases, the two components that make up systemic blood pressure. Nonetheless, the two systems often work together, albeit to various degrees, to bring on syncope. Reflex syncope of the "vasodepressive type" occurs when sympathetic vasoconstriction is withdrawn, generating vasodilation and low total peripheral resistance [4], or structural or functional impairment of the autonomic nervous system. When autonomic dysfunction is present, the body does not respond appropriately to being upright by narrowing its blood vessels in a process called sympathetic vasoconstriction [5]. Insufficient blood flow to the heart can result from a reflex bradycardia, (commonly called cardioinhibitory reflex syncope), cardiac etiologies (structural disease including pulmonary embolism as well as pulmonary hypertension, and arrhythmia,) low venous return(caused by blood pooling in the veins or a lack of blood volume) and, Deficiencies in both chronotropic and inotropic response [6]. Reflex syncope is characterized by two pathophysiological mechanisms: vasodepression, which describes insufficient sympathetic vasoconstriction leading to hypotension, and autonomic instability [1, 2], and "An instance of "cardioinhibition," characterized by bradycardia and/or asystole and indicating a switch to parasympathetic dominance, is described. Reflex syncope can be triggered by a variety of stimuli, and the resulting hemodynamic pattern (cardioinhibitory, vasodepressive, or both) is unrelated to the stimulus (A syncopal episode brought on by micturition may have a cardioinhibitory or vasodepressor presentation).

Orthostatic hypotension is one cardiovascular condition that can lead to orthostatic intolerance (classical, initial or delayed), Orthostatic vasovagal syncope (OVS) or postural orthostatic hypotension syndrome (POTS) [7]. Patients with low-risk symptoms, such as those seen in situational syncope, reflex syncope, or syncope related to orthostatic hypotension (OH), are typically discharged without further intervention [8]. When going from a supine to an upright position, blood flows differently, diverting away from the torso and toward the lower extremities and abdominal cavity, lowering venous return and, thus cardiac output. Syncope can occur if blood pressure drops too low and the body is unable to respond appropriately [9]. Active standing, the head-up tilt table (HUT) test, and 24-hour ambulatory blood pressure

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monitoring are the three methods available today for evaluating the body's reaction to going from a supine to an upright position [10].

Diagnostic criteria for OH include the following: Abnormal Dropping your blood pressure means your systolic readings have decreased by 20 mm Hg or your diastolic readings have decreased by 10 mm Hg from your baseline readings, or your systolic readings have decreased to 90 mm Hg or below [11] upon standing. Clinically, a decrease in diastolic blood pressure on its own is of limited use in the diagnosis of OH. History taking, a thorough physical examination, and HUT test can help determine the likelihood that syncope and orthostatic problems are caused by OH [12].

Certain clinical characteristics are suggestive of OH, such as syncope occurring during standing, absent while lying; preferred morning hours; sleeping down almost relieves symptoms; worsening after eating, exercising, or exposure to high temperatures [13]. HUT test can confirm the diagnosis of reflex syncope and distinguish it from syncope due to neurological reasons [14]. Autonomic failure can be evaluated using this method, and it is often used to reproduce delayed OH (which can be hard to spot with active standing due to its delayed onset) [15] and POTS [16,17]. However, HUT test is not particularly useful for gauging the treatment's success [18]. Moreover, it is generally acknowledged as a helpful technique for demonstrating an individual's susceptibility to reflex syncope, particularly vaso-depressive syncope, and consequently initiating treatment strategies (e.g. physical maneuvers) [19].

Variety of protocols has been proposed for HUT [3,4]. One of the commonly used protocols is the HUT with the nitroglycerine protocol. The suggested mechanism of the test is either induction of venous dilation or stimulation of vagus nerve that cause syncope. Systematic reviews have shown that the nitroglycerine protocol has a 66% overall positive outcome rate in patients with syncope, while the isoproterenol protocol has a 61% positive outcome rate; Those without syncope had a positive rate of 11-14%, and the test could tell those with the condition apart from controls with an odds ratio of 12 [20].

Inducing symptoms, including the classic circulatory pattern of reflex hypotension/bradycardia, OH, and POTS, is the ultimate goal of HUT [13]. A short-timed protocol of HUT could save effort, time, and money.

The aim of the present study was to evaluate the effectiveness of short-timed protocol of HUT versus the long-timed traditional protocol in the assessment of neuro-cardiogenic syncope.

PATIENTS AND METHODS

Two hundred seventy-six people who had a history of syncope participated in the study. In this study, all patients were recommended to undergo a HUT. The study included patients with their age ranged from 18 to 60 years, with no history of cardiac or neurological co-morbidities, no history of hypertension, diabetes mellitus, chronic kidney disease, autonomic dysfunction, or peripheral neuropathy. Patients with cardiac comorbidities, neurological comorbidities, autonomic dysfunction, or peripheral neuropathy were excluded from the study.

All patients underwent: (1) Complete history taking including the frequency of syncopal episodes, presence of syncope versus pre-syncope, whether syncope occurred during standing or in lying position, any predisposing factors, the presence or absence of seizures, duration of the syncopal episodes, the time and manoeuvre for recovery. (2) Complete general and local examination with special emphasis on heart rate and blood pressure including orthostatic blood pressure measurement. (3) 12 leads baseline ECG to exclude cardiac comorbidities like arrhythmia or ischemic heart disease. (4) Echocardiography to exclude structural heart disease.

The study population was classified randomly into two groups, group A included 150 patients underwent HUT test by the conventional long protocol (15 minutes at passive stage; stage I) and the other group, group B included 126 patients underwent HUT by the modified short timed protocol (10 minutes at passive stage; stage I). During stage I the table was tilted to 80 degrees angle with manual meticulous measurement and recording of both blood pressure and heart rate by two experienced doctors with synonymous observation of patient symptoms every 3 minutes, while in stage II (The active stage) the patient was returned to supine position and 5mg of sublingual isosorbide dinitrate was given to the patient, the table was tilted again to 80 degrees angle, with manual meticulous measurement and recording of both blood pressure and heart rate by the same experienced doctors with synonymous observation of patient symptoms, each 1 minute for the first 3 minutes and each 3 minutes in the remaining period so as to accurately detect the patient response. Both groups were compared regarding demographic data, systolic blood pressure, diastolic blood pressure, heart rate, outcome, and recovery time. HUT test was considered positive if the patient developed syncope with significant hypotension from the baseline blood pressure value with less than 10% decrease in the heart rate from its peak at time of syncope (vasodepressor response), if the patient developed significant bradycardia (<40 beats per minute for more than 10 seconds) (cardioinhibitory response) or drop in the heart rate but not less than 40 beats per minute and with fall in the blood pressure before the heart rate falls (mixed response).

Ethical consent:

An approval of the study was obtained from Ain Shams University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association

(Declaration of Helsinki) for studies involving humans.

Statistical analysis

In order to analyze the collected data, Statistical Package of Social Science (SPSS) version 20 was used to execute it on a personal computer. In order to convey the findings, tables and graphs were employed. The quantitative data was presented in the form of the mean, median, standard deviation, and confidence intervals. The qualitative data was presented as numbers and percentages. The student's t test (T) is used to assess the data while dealing with quantitative independent variables. Pearson chi-square (X^2) and chi-square for linear trend were used to assess qualitative independent data. The level of significance was set at a p value of 0.05 or less.

RESULTS

We enrolled 276 patients who were referred to do HUT test as an investigatory tool for diagnosis of syncope. No statistically significant differences in demographic data were found between the two groups (Table 1).

Table (1): Comparison between patients who underwent HUT short protocol versus long protocol, regarding demographic data.

Demographic data	Total (n=276)	Short Protocol (n=126)	Long Protocol (n=150)	p-value
Sex				
Female	184 (66.7%)	90 (71.4%)	94 (62.7%)	0.277
Male	92 (33.3%)	36 (28.6%)	56 (37.3%)	
Age (years)				
Mean±SD	36.43±14.57	37.56±14.37	35.49±14.77	
Range	8-65	8-65	9-65	0.409

n: number, SD: standard deviation

Systolic blood pressure, diastolic blood pressure, and heart rate did not differ significantly before, during, or after the passive period between the two groups (stage I) (Tables 2, 3 and 4).

Table (2): Comparison between HUT short protocol and long protocol according to baseline resting systolic blood pressure and blood pressure during and after the passive stage.

Systolic blood pressure (mmHg)	Total (n=276)	Short Protocol (n=126)	Long Protocol (n=150)	p-value
Resting Mean±SD	110.25±13.81	113.65±12.86	110.40±14.01	0.287
1st 3 min. Mean±SD	108.95±13.51	111.27±13.14	108.00±13.61	0.291
2nd 3 min. Mean±SD	107.03±15.21	109.21±16.47	105.20±13.91	0.124
10^{th} min Mean±SD	105.74±14.88	109.67±14.97	104.53±14.10	0.214
4th 3 min Mean±SD	--	--	102.47±14.96	--
5th 3 min Mean±SD	--	--	102.93±13.18	--
After passive stage Mean±SD	106.37±13.29	108.50±12.46	105.27±12.56	0.183

BP: blood pressure, min: minutes, n: number, SD: standard deviation

Table (3): Comparison between HUT short protocol and long protocol according to diastolic blood pressure (mmHg).

Diastolic blood pressure (mmHg)	Total (n=276)	Short Protocol (n=126)	Long Protocol (n=150)	p-value
Resting Mean±SD	72.83±8.73	73.65±8.09	72.13±9.23	0.311
1st 3 min. Mean±SD	73.19±8.73	73.65±8.67	72.80±8.82	0.571
2nd 3 min. Mean±SD	72.96±8.92	72.98±9.12	72.93±8.82	0.974
10th min Mean±SD	71.65±9.59	72.70±9.47	70.80±9.66	0.251
4th 3 min Mean±SD	--	--	71.80±10.06	--
5th 3 min Mean±SD	--	--	71.47±8.88	--
After passive stage Mean±SD	71.78±8.97	73.50±7.94	71.40±9.54	0.104

BP: blood pressure, min: minutes, n: number, SD: standard deviation.

Table (4): Comparison between HUT short protocol and long protocol according to heart rate (beat/min).

Heart Rate (beat/min)	Total (n=276)	Short Protocol (n=126)	Long Protocol (n=150)	p-value
Resting Mean±SD	80.67±14.75	81.08±13.63	80.32±15.71	0.764
First 3 min. Mean±SD	89.91±17.20	88.86±15.33	90.79±18.69	0.514
2nd 3 min. Mean±SD	93.62±17.80	92.24±16.11	94.77±19.13	0.407
10th min Mean±SD	95.82±17.27	95.66±15.68	95.96±18.57	0.919
4th 3 min Mean±SD	--	--	97.28±18.91	--
5th 3 min Mean±SD	--	--	99.56±18.69	--
After passive stage Mean±SD	85.17±15.26	82.86±9.84	87.12±18.48	0.102

min: minutes, n: number, SD: standard deviation

We continued the HUT test by performing the active stage by giving sublingual nitroglycerine as a step to increase the test sensitivity. Fourteen of our patients developed significant symptoms with decrease in blood pressure or heart rate or both during the passive stage with no need to proceed to the active stage. We continued the HUT test in both groups with manual meticulous measurement and recording of both blood pressure and heart rate by the same experienced doctors with synonymous observation of patient symptoms, we classified and tabulated the measured readings each 1 minute for the first 3 minutes and each 3 minutes in the remaining period to accurately detect the patient response (Table 5, 6, 7 and 8).

Systolic blood pressure, diastolic blood pressure, and heart rate all showed no statistically significant changes between the two groups during the active phase (stage II) (Table 5, 6 and 7).

Table (5): Comparison between HUT short protocol and long protocol according to systolic blood pressure (mmHg).

Systolic blood pressure (mmHg)	Total (n=276)	Short Protocol (n=126)	Long Protocol (n=150)	p-value
First 1 min. Mean±SD	105.50±13.36	109.17±13.19	107.39±12.79	0.262
At 2 min. Mean±SD	97.60±17.61	100.67±16.96	98.00±17.85	0.066
At 3 min Mean±SD	91.03±19.69	92.59±18.81	89.71±20.46	0.415
At 4-6 min Mean±SD	86.59±20.58	86.44±19.41	86.72±21.68	0.943
At 7-9 min Mean±SD	82.23±23.68	77.95±26.15	85.63±21.18	0.131
At 10-12 min. Mean±SD	85.95±25.30	88.68±26.08	84.62±25.14	0.570
At 13-15 min. Mean±SD	98.55±15.20	99.17±15.64	98.27±15.29	0.868
At 16-18 min. Mean±SD	100.14±14.46	100.42±20.17	100.00±11.27	0.936
At 19-21 min. Mean±SD	97.64±14.22	97.08±21.05	97.92±9.77	0.871

min: minutes, n: number, SD: standard deviation

Table (6): Comparison between HUT short protocol and long protocol according to diastolic blood pressure.

Diastolic blood pressure (mmHg)	Total (n=276)	Short Protocol (n=126)	Long Protocol (n=150)	p-value
First 1 min. Mean±SD	71.30±9.08	72.33±8.10	70.42±9.81	0.232
At 2 min. Mean±SD	68.86±10.68	71.47±9.32	69.67±11.30	0.138
At 3 min Mean±SD	64.71±11.26	64.57±12.00	64.84±10.62	0.895
At 4-6 min Mean±SD	62.07±12.30	61.00±12.16	63.06±12.45	0.397
At 7-9 min Mean±SD	60.90±13.92	60.77±13.47	61.02±11.90	0.238
At 10-12 min. Mean±SD	64.00±13.51	62.61±14.63	63.59±11.63	0.192
At 13-15 min. Mean±SD	68.51±9.56	66.25±8.56	69.60±9.99	0.325
At 16-18 min. Mean±SD	70.00±10.07	69.00±10.87	71.40±8.91	0.173
At 19-21 min. Mean±SD	67.78±9.44	65.00±10.87	69.17±8.56	0.217

min: minutes, n: number, SD: standard deviation

Table (7): Comparison between HUT short protocol and long protocol according to heart rate (beat/min).

Heart Rate (beat/min)	Total (n=276)	Short Protocol (n=126)	Long Protocol (n=150)	p-value
First 1 min. Mean±SD	102.53±17.90	103.28±17.05	101.89±18.69	0.658
At 2 min. Mean±SD	101.62±18.64	99.55±15.79	103.37±20.70	0.245
At 3 min Mean±SD	108.80±21.83	110.55±17.17	107.33±25.11	0.417
At 4-6 min Mean±SD	106.87±18.38	107.81±18.42	108.38±29.06	0.271
At 7-9 min Mean±SD	107.51±32.06	104.56±34.89	109.90±29.72	0.444
At 10-12 min. Mean±SD	113.31±27.14	112.83±24.56	113.59±28.86	0.916
At 13-15 min. Mean±SD	112.57±21.71	112.67±18.02	113.53±30.13	0.531
At 16-18 min. Mean±SD	117.51±25.57	114.00±16.51	119.07±28.85	0.574
At 19-21 min. Mean±SD	115.49±25.18	111.67±18.27	117.32±28.06	0.530

min: minutes, n: number, SD: standard deviation.

When comparing test outcomes, response patterns, and the requirement for IV fluids, neither group differed significantly from the other, but there was a statistically significant difference between groups regarding the time needed for complete recovery which was significantly shorter in the short protocol group in comparison to the long protocol group 2.64±1.35 versus 4.05±1.19, with p-value <0.001 (Table 8).

Table (8): Comparison between HUT short protocol and long protocol according to outcome.

Outcome	Total (n=276)	Short Protocol (n=126)	Long Protocol (n=150)	p-value
Result				
Negative	96 (27.5%)	40 (31.7%)	56 (37.3%)	0.612
Positive	180 (72.5%)	86 (68.3%)	94 (62.7%)	
Type of response				
Cardio-inhibitory	8 (4.4%)	0 (0.0%)	8 (8.5%)	0.294
Mixed	58 (32.2%)	40 (31.7%)	20 (21.3%)	
Terminated due to psychic Presyncope	4 (2.2%)	0 (0.0%)	2 (2.1%)	
Vasodepressor	110 (61.1%)	46 (43.4%)	64 (68.1%)	
Need for iv fluids (saline)	74 (26.8%)	32 (25.4%)	42 (28%)	0.881
Time needed for complete recovery (min)				
Range	0.5-6	0.5-5	2-6	<0.001
Mean±SD	3.49±1.43	2.64±1.35	4.05±1.19	

min: minutes, n: number, SD: standard deviation

DISCUSSION

We enrolled 276 patients who were referred to do HUT test as an investigatory tool for diagnosis of syncope, its type and mechanism. We divided the patients randomly to either long or short protocol groups, with no statistically significant differences between both groups regarding demographic data.

Since the beginning of HUT test in 1986, numerous protocols have been presented, varying the initial stabilization phase time, tilt angle, and pharmacological stimulation in order to achieve the desired results (nitroglycerine versus isoproterenol). In our tertiary center the most commonly used protocol is supplying the patients with 5 mg sublingual isosorbide dinitrate after a 15 min unmedicated phase [21, 22]. This is performed in our hospital by manual meticulous measurement and recording of systolic blood pressure, diastolic blood pressure and heart rate in supine and standing position by an experienced medical staff with meticulous monitoring of patient symptoms.

We divided the patients randomly into two groups, group A underwent the traditional long timed protocol and group B underwent the same protocol with shortening the passive time to be only 10 minutes. The mean blood pressure was 113.65(SD 12.86)/ 73.65(SD 8.09) in the group with short protocol and 110.40 (SD 14.01)/ 72.13(SD 9.23) in the group with long protocol, the blood pressure dropped to 109.67 (SD 14.97)/ 72.70 (SD 9.47) in the group with short protocol after 10-minute of passive stage and to 102.93 (SD 13.18)/ 71.47 (SD 8.88) after 15 minutes of passive stage in the patients with long protocol with no statistical significant differences between both groups as regards systolic or diastolic blood pressure after 10 minutes (p values 0.214 and 0.251 respectively). Both groups did not show significant difference as regard heart rate changes in the passive stage (p value 0.919).

Systolic blood pressure of 50–60 mmHg at heart level (which represents 30–45 mmHg at brain level) in the upright posture, will cause loss of consciousness. The HUT test was terminated and considered complete if the patients developed significant symptoms with decrease in blood pressure or heart rate or both during the passive stage according to the standard protocol. Fourteen of our patients had a positive response during the passive stage with no need to proceed to the active stage, six of them were in the short protocol group and the other eight were in the long protocol group. We continued the HUT test in the other 262 patients by performing the active stage by giving 5mg sublingual isosorbide dinitrate as a step to increase the test sensitivity. HUT test was considered positive in our protocol if the patient developed syncope with significant hypotension from the baseline blood pressure value with less than 10% decrease in the heart rate from its peak at time of syncope (vasodepressor response), if the patient developed significant bradycardia (<40 beats per minute) (cardioinhibitory response) or drop in the heart rate but not less than 40 beats per minute and drop in the blood pressure (mixed response). Ninety six (27.5%) of all patients showed negative response with no significant affection of blood pressure or heart rate, 40 (31.7%) patients were in the short protocol and 56 (37.3%) patients were in the long protocol with no significant differences between both groups (p value 0.612), however 180 patients (72.5%) showed positive response [cardio inhibitory 8 (4.4%), mixed 58 (32.2%) or vasodepressor 110 (61.1%)], with no statistical significant differences between the two groups.

Dehghan and Sabri[23] conducted both conventional and modified tilt test protocols after omitting the passive stage completely on 200 subjects. Before beginning the modified tilt test, the patient lies supine and receives a sublingual dose of isosorbide dinitrate; the table is then tilted for up to 25 minutes, or until the test is positive. The conventional tilt test group had a positivity rate of 79.13%, while the modified tilt test group had a positivity rate of 87.06. This statistically significant difference has a p value of 0.04 and may be attributable to the effect of nitrates, but it does raise concerns about the possibility of a false-positive result if the passive stage is omitted entirely. Omitting the passive stage of HUT test was previously evaluated with isoproterenol protocol since 1999. The vasovagal response can be induced more strongly by the single stage isoproterenol tilt test, according to the findings of **Shen *et al.*** [24]**.** A second, smaller study compared the use of HUT test with and without the initial passive phase in 38 patients in an erect position and found that the former provided a more accurate, sensitive, and specific technique of provoking vasovagal outcomes in clinically suspected patients [25].

These results emphasized that the mechanism of vasovagal syncope can be triggered by the provocation with medication that would lead to venous and arterial dilation with pooling of blood and enhancement of the reflex mechanism that are the underlying mechanism for syncope. In our study we found no significant difference in number of patients who needed intravenous fluid to regain their blood pressure and wellbeing, however there was significant difference in the time needed by the patients for complete recovery in short protocol (mean 2.64 ± 1.35 minutes) versus the long protocol (4.05 ± 1.19l minutes), with p value <0.001.

CONCLUSION

The present study showed no significant differences in the HUT outcome in the short and long protocols and this emphasized that the duration of standing and passive time would not significantly affect the pathophysiological mechanisms that initiate the reflex syncope; however the short protocol had shorter recovery time for the patients and would save the time and effort.

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