COMPARISON OF HEART RATE VARIABILITY IN NEGATIVE AND POSITIVE RESPONDERS TO ACTIVE PHASE OF HEAD-UP TILT TEST

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ABSTRACT

Objective: To compare heart rate variability in negative and positive responders to active phase of head-up tilt test.

Study Design: Cross-sectional comparative study.

Place and Duration of Study: Department of Cardiac Electrophysiology, Armed Forces Institute of Cardiology, Rawalpindi from Jan 2016 to Oct 2016.

Material and Methods: Ninety three adult patients of either gender with recurrent unexplained syncope were recruited through convenience purposive sampling. The known cases of diabetes mellitus, cardiac diseases, cardiac arrhythmias and myocardial infarction were excluded from the study. Head-up tilt test was carried out on an electrically driven tilt table. DMS 300-4L Holters were used to obtain ambulatory ECG recordings during head-up tilt test. Cardio scan premier 12 lux software was used for analysis of heart rate variability frequency domain parameters.

Results: Total ninety three patients of unexplained syncope were enrolled out of which, 77 (82.8%) patients responded positively and 16 (17.2%) patients gave a negative response. There was significant variation in heart rate variability frequency domain parameters being reduced in positive responders to active phase of head-up tilt test as compared to negative responders. This difference in mean values of heart rate variability frequency domain parameters between positive and negative responders was statistically significant with *p*-value less than 0.05.

Conclusion: The heart rate variability frequency domain analysis done during initial 20 minutes of passive phase of head-up tilt test can predict the results of tests before the administration of drugs.

Keywords: Head-up tilt test, Heart rate variability, Syncope.

INTRODUCTION

Head-up tilt test (HUTT) is a medical procedure commonly used as a diagnostic test for reflex syncope[1]. It is a provocation test that reproduces the vagosympathetic disturbances observed during syncope[2]. Syncope is transient loss of consciousness due to cerebral hypo-perfusion[3]. Amongst the diverse etiologies of syncope the commonest is vasovagal syncope (VVS) occurring mostly after periods of prolonged standing[4]. Head-up tilt test has emerged as a robust tool for investigating an individual's predisposition to syncope related to orthostatic stress. The test permits the stimulation of upright posture in a vigilantly monitored environment applying orthostatic stress[5]. Inability of the underlying autonomic nervous system to maintain hemodynamics of the body in upright posture results in cerebral hypo-perfusion[6]. Two main responses are seen when a patient undergoes a head-up tilt table test. The first response is the positive response, which is marked by reproduction of symptoms of syncope and the second response is the negative response which shows slight variations in blood pressure but no other abnormality[7]. Heart rate variability (HRV) is a physiological phenomenon resulting from the active modulation of heart rate by the relation of the sympathetic and parasympathetic nervous system[8]. Heart rate variability can be used as a non-invasive marker of autonomic nervous system[9]. Abnormalities of autonomic

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nervous system function play a dominant role in the genesis of syncope. Heart rate variability analysis is a strong tool to explore the interactions between physiological, mental, and behavioral processes, whose relationships can lead to the genesis of syncopal attacks[10]. Therefore, heart rate variability analysis can be applied to evaluate autonomic functions during tests aimed at provoking syncope[11]. Autonomic nervous system is affected by the changes that occur during head-up tilt test in syncope patients. Present study was planned to explore differences between subjects showing positive and negative results to head-up tilt test on the basis of heart rate variability analysis. Heart rate variability can be used in combination with head-up tilt test to foresee the outcome of this test.

PATIENTS AND METHODS

This cross sectional comparative study was conducted at the Department of cardiac electrophysiology, Armed Forces Institute of Cardiology (AFIC) in collaboration with Army Medical College (AMC), Rawalpindi. An official approval was obtained prior to commencement of the study from Institutional Review Board of AFIC and Ethical review committee of AMC, Rawalpindi. Sample size was calculated using WHO sample size calculator. By keeping the values of confidence level (1-alpha) as 95%, anticipated population proportion (p) as 0.4 and absolute precision (d) as 0.1, the sample size was calculated to be 93.

Ninety three patients with complaint of recurrent syncope were recruited through convenience purposive sampling. Patients mainly referred to AFIC for a head-up tilt test by internal medicine specialists and cardiologists were included in the study. The individuals having diabetes mellitus, known cardiac diseases, cardiac arrhythmias and myocardial infarction were excluded. All the patients were subjected to standard ECG and echocardiography to rule out cardiac arrhythmias, heart failure, and any other structural heart diseaseS. The selected patients were informed to come for the test in a 4 hour fasting state as a prerequisite to the test. On arrival written and informed consent was taken from all the participants. A thorough history, especially relevant to syncope and general physical examination was carried out. The patients were told to lie down on the tilt table that is electrically driven and can be tilted upto 60 to 70 degrees. The patients were Holtered with DMS 300-4L Holters from DM systems company Ltd. Heart rate variability was measured in frequency domain for 5 minutes in supine position along with initial blood pressure, heart rate and ECG. Throughout the test, ECG, heart rate and blood pressure readings were monitored. The test consisted of 2 consecutive stages. In stage-I the patients were tilted to an angle of 70 degrees for 20 minutes. During this phase, heart rate variability frequency domain parameters were measured for first 5 and last 5 minutes. In stage-II, 400 µgm of nitroglycerine was administered and tilting continued for another 20 minutes. On development of syncope patients were returned to supine position and test was terminated. Positive responders were those patients who developed either syncope or near-syncope state (pallor, nausea, light headedness and blurred vision), negative response was neither the development of syncope nor pre-syncope. Ambulatory ECG data was transferred to the computer and edited for all the improper beats (ectopic and artefacts) with the help of DMS cardioscan software premier 12 lux version. Heart rate variability frequency domain analysis was done. The parameters analyzed were low frequency (LF), high frequency (HF) and LF/HF ratio and total power (TP). Data were analyzed using computer software IBM SPSS version 23. Mean and standard deviation were calculated for numerical variables like age and frequency domain parameters whereas frequency and percentage was calculated for categorical variables like gender and positive and negative responders of head up tilt test. Non-parametric test (Mann-Whitney U-test) was used to reveal the comparison between negative and positive responders to active phase

of head-up tilt test. Alpha value was kept at 0.05 at confidence level of 95% to control alpha error.

RESULTS

There were 84 (90.3%) male and 9 (9.7%) female patients out of total 93 patients with the mean age of 37.96 ± 16.126 years. Among 93 patients, there were 77 (82.8%) positive responders and 16 (17.2%) negative responders to head-up tilt test. The frequency comparison of positive and negative responders is shown in table-I. Among the 77 (82.8%) positive responders, 2 (2.2%) patients developed syncope during passive phase while 75 (80.6%) patients developed syncope during active phase. The frequency comparison of observed positive passive, positive active and negative responders is given in table-II. The mean values of heart rate variability frequency domain parameters measured in the last 5 minutes of passive phase of head-up tilt test are given in table-III. The mean values of high frequency (HF), LF/HF and total power (TP) parameter are different among the positive and negative responders and these differences are statistically significant (p<0.05).

Table-I: Frequency comparison of positive and negative responders to head-up tilt test.

Responders	Frequency (N=93)	Percentage
Positive	77	82.8
Negative	16	17.2

Table-II: Frequency comparison of positive (active, passive) and negative responders of head-up tilt test.

Responders	Frequency (N=77)	Percentage
Positive Passive	2	2.2
Positive Active	75	80.6
Negative	16	17.2

Table-III: Comparison of frequency domain parameters in positive and negative responders to active phase of Head-Up Tilt Test.

Frequency Domain Variables	Values (mean ± SD)		*p*-value
	Positive Responders	Negative Responders	
HF	78.14 ± 45.01	150.91 ± 68.83	0.000*
LF	357.02 ± 251.37	456.95 ± 246.01	0.070
LF/HF Ratio	5.09 ± 3.20	3.31 ± 2.00	0.027*
TP	846.17 ± 461.50	1459.66 ± 748.63	0.000*

*p-value significant (less than 0.05)

DISCUSSION

The result of our present study demonstrated that, heart rate variability frequency domain analysis carried out during passive phase of head-up tilt test differs amongst the positive and negative responders. Heart rate variability is significantly decreased in positive responders as compared to the negative ones. Results of present study helped us to identify patients that are at risk of developing syncope during active phase of test, even before the administration of the pharmacological agent most commonly nitroglycerine. In the patients developing syncope, the power of high frequency (HF), LF/HF, total power (TP) components changed significantly as the passive head-up tilt test advanced. However, parameters of negative responders did not change significantly during the passive phase of the test. The probable cause of syncope is vasovagal syncope (VVS) occurring because of profound systemic hypotension due to reflex vasodilatation, or vagally driven bradycardia, or both followed by dizziness, presyncope and finally syncope. The results of our study are comparable to the study conducted by Efremov *et al*[12]. They enrolled 64 patients with preceding episodes of loss of consciousness, 20 patients developed syncope during tilt test after administration of nitroglycerine, while the remaining 44 patients stayed negative. The heart rate variability frequency domain parameters measured during the passive phase did not change significantly in negative responders

but showed a significant decrease in positive responders[8]. Duplyakov *et al* enrolled 114 patients with recurrent vasovagal syncope. He suggested that positive responders of head-up tilt test had significantly decreased values of heart rate variability parameters when measured in the initial 5 minutes of passive phase as compared to negative patients. Our results are in synchrony with Duplyakov's study[13]. The mean values of heart rate variability frequency domain parameters were significantly different among positive and negative responders in present study. With respect to the foretelling value of heart rate variability in discriminating positive and negative patients, the most consistent behavior was shown by, HF, TP and LF/HF parameters. In positive responders, the mean values of these parameters were decreased as compared to negative responders. Mehlsen and his colleagues conducted a study in year 2007 on 70 patients. Their results contradicted to the results of our study showing no difference amongst the HUTT positive and HUTT negative patients with respect to heart rate variability. The suggested reason of difference between results could be due to very small amount of data relative to the number of parameters[14]. Furlan *et al* studied RR interval variability in 22 healthy subjects who experienced fainting for the first time and in 22 control subjects. The results showed a significant increase of low frequency (LF) and LF/HF and a concomitant decrease of high frequency (HF) in positive responders of head-up tilt test[15]. The difference in the results could be due to the different methods used for the heart rate variability frequency domain analysis. Heart rate variability analysis was done using autoregressive power spectral analysis by Furlan and his colleague[15]. The fast fourier transformation (FFT) and different orders of Autoregressive models (AR) for heart rate variability frequency domain analysis can give different results.

In our study, we found that changes in individual heart rate variability frequency domain parameter could discriminate between positive and negative responders of HUTT. The predictive value increased remarkably when we used several parameters simultaneously. On the basis of heart rate variability analysis done in the passive phase of head-up tilt test, we remained unable to discover any significant differences amongst the various types of vasovagal syncope. This could be due to small sample size and less patients with each respective type of vasovagal syncope investigated in our study.

CONCLUSION

The heart rate variability frequency domain analysis done during initial 20 minutes of passive phase of head-up tilt test can predict the results of tests before the administration of drugs.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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