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HEART RATE VARIABILITY IN VASOVAGAL SYNCOPE DURING HEAD-UP TILT TEST

Shavana R Rana	Assistant professor, Department of physiology,NAIHS, Kathmandu.
Anirban T Bhattacharya*	Assistant Professor, Department of Physiology, AFMC, Pune *Corresponding Author
Bikalp Thapa	Assistant Professor , Department Of physiology,NAIHS,Kathmandu.
Anuj Chawla	Professor, Department of Physiology, AFMC, Pune

ABSTRACT

BACKGROUND: HRV analysis of vasovagal syncope (VVS) patients have shown variable results. Objective was to study the behavior of cardiac autonomic activity during HUTT and also see if VVS could be predicted during tilt.

MATERIALS AND METHOD: Retrospective HRV analysis of patients presenting with syncope and undergoing HUTT (21 HUTT positives and 21 HUTT negatives) during 5 minutes each of resting position, post tilt and before end of test or syncope/presyncope.

RESULTS: Resting values were comparable. HUTT positives showed a significant rise in LF and a decrease in HF throughout tilt. SDNN and total power decreased throughout tilt from resting position in HUTT negatives only.

DISCUSSION: HUTT positive VVS showed increased sympathetic activity at the occurrence of syncope/pre-syncope and incomplete withdrawal of parasympathetic activity during tilt. These findings support the empty ventricle theory. Significant rise in LF and decrease in HF in HUTT positives during tilt may predict syncope.

KEYWORDS : Vasovagal syncope (VVS), heart rate variability (HRV), head-up tilt test (HUTT)

INTRODUCTION:

Vasovagal syncope (VVS) is a neural mediated reflex syncope that is caused by a sudden decrease in blood pressure, heart rate or both. If severe enough, it can affect the quality of patient's life. The modulation of the autonomic nervous system is believed to play a major role in pathophysiology of vasovagal syncope. However the mechanisms leading to VVS are highly variable and differ among the patients of VVS. It is diagnosed by typical history, in absence of any other known cause of syncope, and a positive response on head up tilt test (HUTT) (1,2,3,4).

Heart rate variability (HRV) has been used to assess the role of autonomic nervous system and to see the interplay between sympathetic and vagal nervous system on heart rate modulation in vasovagal syncope during HUTT (5).

Studies have shown conflicting reports on modulation of heart rate in patients of VVS during HUTT. Morillo et al. showed decrease in LF and LF/HF ratio suggestive of decreased sympathetic tone after 5 min of tilt in positive responders to HUTT (6). However, Mangin et. al have reported a sympathetic preponderance with increased LF/HF during tilt and immediately before syncope in VVS patients (7).

The present study was carried out with the objectives of analyzing the HRV in patients of syncope with a positive and negative response to HUTT and to ascertain whether HRV analysis during head-up tilt could predict the occurrence of VVS.

MATERIALS AND METHOD:

Patients:

42 patients with history of ≥2 episodes of syncope were analyzed retrospectively. Based on the occurrence of signs/symptoms of syncope or pre-syncope during the HUTT, patients were divided into two groups. Group 1- patients who did not develop symptoms during HUTT (negative responders) and Groups 2- who developed symptoms (positive responders). All patients had normal physical examination, 12–lead ECG, Holter ECG, Echocardiography and EEG which ruled out cardiac or neurologic causes of syncope.

Protocol of Head up tilt test:

HUTT (drug free passive tilt testing) was performed in a quiet room between 0830hrs – 1100hrs. The patient remained 10 minutes in supine (resting) position, followed by 70-degree tilt for 45 minutes and then back to supine position for 10 minutes. A continuous ECG monitoring was done. HUTT was stopped if the criteria for onset of vasovagal syncope was fulfilled or at 45 minutes in the absence of syncope.

Spectral analysis of HRV was performed off-line using Fast Fourier Transformation. The ECG data from the recordings was analysed by Acknowledge 3.9, MP100 Biopac software for HRV. HRV of 5 minutes duration was analyzed for 3 phases. HRV during 5 min of resting position (Phase A), 5 min immediately after tilt (Phase B) and 5 min just before end of test or occurrence of syncope/presyncope (Phase C). Time domain and frequency domain components of HRV and Total Power were calculated for all the three phases. Statistical analysis was done using SPSS version 20.

RESULTS:

Age, height and weight were comparable between the two groups.

Table 1: Anthropometric parameters (Group 1 – Negative responders, Group 2 – Positive responders).

	Group	Mean ± SD	p value
Age (years)	1	33.0 ± 12.3	0.134
	2	27.3 ± 11.5	
Height (cm)	1	171.1 ± 8.5	0.781
	2	170.1 ± 10.1	
Weight (kg)	1	67.8 ± 9.5	0.546
	2	65.5 ± 12.8	

Comparison of HRV parameters between different phases of HUTT (Negative responders).

Table 2: HRV components in negative responders to HUTT.

HRV Components	Phase A	Phase B	Phase C	Phase A to B	Phase B to C	Phase A to C
SDNN (msec)	47.8 ± 18.1	39.4 ± 14.9	36.7 ± 14.3	**0.058***	0.238	**0.021***
RMSSD (msec)	32.5 ± 14.2	21.6 ± 13.6	19.6 ± 13.4	**0.014***	0.275	**0.005***
LF (nu)	61.9 ± 17.9	74.8 ± 13.1	80.7 ± 13.5	**0.003***	0.072	**0.002***
HF (nu)	38.0 ± 17.9	25.1 ± 13.1	19.5 ± 13.6	**0.003***	0.083	**0.002***
LF/HF	2.3 ± 1.7	4.9 ± 4.7	7.2 ± 6.2	**0.019***	0.107	**0.024***
Total power (msec2)	2331.8 ± 1671.1	1560.8 ± 1233.6	1361.5 ± 1127.0	**0.029***	0.44	**0.005***

Comparison of HRV parameters between different phases of the HUTT (Positive responders)

Table 3: HRV components in positive responders to HUTT.

HRV Components	Phase A	Phase B	Phase C	Phase A to B	Phase B to C	Phase A to C
SDNN (msec)	49.1 ± 24.1	37.2 ± 18.6	42.6 ± 25.2	**0.008***	0.248	**0.277**
RMSSD (msec)	38.9 ± 26.5	17.0 ± 10.3	16.3 ± 11.8	**0.00***	0.776	**0.001***
LF (nu)	58.0 ± 18.4	78.2 ± 15.7	85.3 ± 9.2	**0.004***	**0.007***	**0.000***
HF (nu)	41.9 ± 18.4	21.7 ± 15.7	14.6 ± 9.2	**0.004***	**0.007***	**0.000***
LF/HF	2.1 ± 1.9	7.0 ± 8.7	8.6 ± 5.6	**0.026***	0.431	**0.000***
Total power (msec2)	2632.4 ± 2895.5	1488.3 ± 1393.5	2416.4 ± 3290.6	**0.04***	0.164	**0.793**

Comparison between positive and negative responders to HUTT in different phases.

No significant differences in any parameter were found between the two groups in supine (resting) position - Phase A.

Further, no significant differences in any parameter were found between the two groups in Phase A to B, Phase B to C and Phase A to C.

DISCUSSION:

HRV at rest was similar in patients of syncope with positive and negative responders to HUTT. However, a significant rise in LF power and a decrease in HF power was seen at the occurrence of syncope during tilt (Phase B to C) in positive responders only, indicating a higher activation of the sympathetic activity during orthostatic stress. Further, the values of SDNN and TP showed a continuous decrease throughout HUTT from resting position (Phase A to C) in negative responders only, indicating a continuous withdrawal of parasympathetic activity in the negative responders which was not seen in the positive responders.

The findings of the present study are in keeping with other studies which report that the autonomic modulation during the resting position remains same in patients of vasovagal syncope with positive and negative responders to HUTT (8,6). The autonomic modulation of heart rate differed in positive and negative responders to HUTT only during orthostatic stress. Patients with vasovagal syncope do not have a stable autonomic response to stress and may have fluctuations in autonomic activity which render them susceptible to syncope (9).

Morillo C et al reported an increase in HF power and decrease in LF power in the first five minutes of tilt in patients of vasovagal syncope. However Ahelan D et al reported a greater increase in sympathetic activity in the first five minutes after tilt in VVS. Our study could not find any differences in HRV between the two groups immediately after tilt (Phase A to B). The possible reasons for the variable findings could include the different degrees of tilt employed, tilt rate and variations in the ambient environment in terms of temperature and circadian influences (6,10).

The finding of a significant rise of LF power and decrease in HF power at the occurrence of syncope during tilt (orthostatic stress) in the positive responders indicate a higher rise of sympathetic activity in this group throughout the duration of tilt. Efremov K et al reported a significant decrease of HF power in the positive responders at the end of 20 minutes of test but variable findings of LF power, while Mangin et al reported a decrease in HF and increase in LF/HF at the occurrence of syncope. Khodor N et al have reported a greater increase in LF power in Cardioinhibitory VVS and a greater parasympathetic activity in Vasodepressor VVS during the duration of tilt. (11,12,7).

The findings of the present study support the empty ventricle theory as the likely pathophysiological mechanism of VVS in positive responders to HUTT. This theory states that an increase in sympathetic activity during orthostatic stress causes vigorous contractions of the hypovolemic ventricle which stimulate mechano-sensitive C fibers from the left ventricle. This may evoke a Bezold-Jarisch like reflex causing hypotension and bradycardia, leading to syncope (13,14).

A sustained decrease in SDNN and TP throughout tilt from resting position (Phase A to C) in negative responders to HUTT suggests a continuous withdrawal of parasympathetic activity in this group. The positive responders to HUTT, showed decreased values immediately after tilt but which increased at the occurrence of syncope. This suggests an incomplete withdrawal of the parasympathetic activity in this group and can explain the occurrence of syncope in these patients. Other studies have also found a rise in TP and RMSSD at the occurrence of syncope. The present study however did not find a difference in the RMSSD in both the groups of patients (15,16).

Our study also tried to explore the possibility of prediction of syncope based on HRV analysis during HUTT. The values of LF and HF might provide some clue. In the positive responders there was a significant rise of LF power and a significant decrease in HF power from the start of tilt till the occurrence of syncope, a finding not seen in the negative responders to HUTT. This might provide a parameter, which could be used as a predictive marker of outcome during tilt testing and could help shorten the duration of the HUTT from the present recommendation of 45 minutes of head up tilt. Some studies have already looked at LF and blood pressure variability to predict syncope. However, no valid parameter exists at the moment (17). The findings of the present study need to be followed up prospectively to explore this possibility.

A limitation of the present study is that the positive responders on HUTT were not divided into subgroups of vasodepressor, cardioinhibitory or mixed type of VVS as the number of subject in each group would have been very small for statistical analysis. However, studying the different sub-groups might have provided different patterns of HRV during the tilt testing and is an area that deserves further study.

The present study shows that resting/ baseline values of HRV are comparable in positive and negative responders to HUTT in patients of syncope. However, autonomic modulation of heart rate is different in those syncope patients who are positive responders to HUTT. These patients showed a greater increase in sympathetic activity throughout the duration of tilt and incomplete withdrawal of parasympathetic activity, which supports the empty ventricle theory of vasovagal syncope. This study also suggests the possibility of using HRV as a predictive marker for outcomes during HUTT for evaluation of syncope.

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