Kathmandu University Medical Journal (2009), Vol. 7, No. 3, Issue 27

Original Article

Heart rate variability: Response to graded head up tilt in healthy men

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Abstract

Background: Heart rate variability is actually a misnomer for R to R variability in cardiac cycle. Variation in successive cycle length is called the heart rate variability (HRV). Head-up tilt is a model of studying cardiovascular haemodynamics, which reflects in heart rate variability (HRV).

Objectives: To study the effect of 10° and 70° head-up tilt on HRV.

Materials and methods: The study was done in the Department of Physiology using graded head up tilt (passive orthostatism). HRV measurement was done at 10° and 70° tilt and compared with supine using standardised methods on 30 consenting healthy males (age 25.37±3.89 years). The HRV variables across postures were compared by ANOVA and Bonferroni test.

Results: The heart rate increased at 70° compared to 10° and supine (70.48±8.17 Vs 70.22±8.67 and 88.51±12.84 bpm, $p<0.001$). The 70° tilt decreased vagal HRV indicators compared to 10° and supine: SDNN (31.13±8.12 Vs 38.07±11.29 and 38.13±10.89 ms, $p<0.05$), RMSSD (20.06 ±8.47 Vs 34.23±14.22 and 36.16±12.22 ms, $p<0.001$), NN50 count (13.03±20.58 Vs 45.07±44.44 and 55.27±44.10, $p<0.01$), pNN50 (3.28±6.08 Vs 14.06±15.65 and 16.65±14.23, $p<0.01$), HF power (197.20±143.76 Vs 218.17±155.85 and 216.87±150.98 Hz, $p<0.05$), HFnu unit (24.28±14.16 Vs 45.48±16.34 and 47.67±19.89, $p<0.001$).

The 70° tilt increased LF power% (197.20±143.76 Vs 218.17±155.85 and 216.87±150.98, $p<0.001$). LFnu unit (75.72±14.76 Vs 54.52±16.34 and 52.32±19.89, $p<0.001$), LF: HF (4.96±4.08 Vs 1.53±1.138 and 1.69±1.67, $p<0.001$) compared to 10° and supine.

Conclusion: At 70° tilt, HRV measures, reflecting vagal contribution to cardiac-cycle length, decreased with reciprocal increase in sympathetic activity compared to 10° or supine leading to increase in sympathetic predominance. A 10° tilt, which is almost equivalent to lying down with pillow, did not change HRV from supine.

Key words: Cardiac cycle, cardiovascular haemodynamics, head-up-tilt, heart rate variability, sympathetic activity, parasympathetic activity

It is commonly perceived that a regular heartbeat is a sign of good cardiac health. However, sinus rhythm, the rhythm of healthy heart, or the successive cardiac cycle length is characterised by significant variability [1]. Therefore, normal heart rate is not characterised by clockwise regularity. In fact, preferably regular cardiac cycle length may signify disease condition [2, 3]. Variation in successive cycle length is called the heart rate variability (HRV). The heart rate fluctuates with phase of respiration: cardio-acceleration during inspiration and cardio inhibition during expiration[4]. The relationship between heart rate (HR) and heart rate variability (HRV) are not simple but, both depend on autonomic nervous system; so they are not independent variables. The quantification of HRV is influenced by HR level [5]. So, heart rate and heart rate variability variables represent quite different characteristics of autonomic nervous activity [6].

Measurement: Time domain and frequency domain analysis[7].

Time domain analysis

In a continuous electrocardiograph (ECG) record, successive QRS complex (R peaks) detected and intervals between are called normal to normal (NN) intervals.

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Statistical methods: The most commonly used measure derived from interval differences include RMSSD (the square root of the mean squared differences of successive NN intervals), NN 50, the number of interval differences of successive NN intervals greater than 50 ms, and pNN50 (percentage NN50 count). **Geometrical methods:** The geometrical method uses the sequence of RR intervals to construct a certain geometrical forms and extract the assessment of HRV from this. e.g. Lorenz plot or Poincare plot SD1, which represents the short term HRV and SD2, which represents long term HRV[8].

Frequency domain (Power spectrum) analysis

In the frequency domain measure, power spectral densities of R-R intervals are plotted and different frequency components are identified. It includes the high frequency (HF) components (0.15-0.40 Hz) its power, percentage and normalized unit value that represents vagal modulation of HRV; and low frequency (LF) components (0.03-0.15 Hz) and its power, parentage and normalised unit value that represents sympathetic modulation [9]. LF/HF ratio represents sympathovagal balance[7].

Head up tilt

Head up tilt is one of the experimental models of orthostatic test commonly used for autonomic test including HRV. On moving from supine to erect position there is large gravitational shift of the blood away from the chest to the distensible venous capacitance system below the diaphragm. So during head up tilt, a hydrostatic venous pooling in the extremities occurs owing to gravity [10]. In addition, with prolonged standing, the high capillary transmural pressure in dependant parts of the body causes filtrations of protein free fluid in to the interstitial spaces. It is estimated that this results in 15-20% (700 ml) decrease in the plasma volume in 10 minutes in healthy adult humans[11]. As a consequence of this, venous return to heart is reduced resulting in the rapid diminution of cardiac filling pressure and, thereby decrease in stroke volume. Despite decreased cardiac output, a fall in mean arterial pressure is prevented by a compensatory vasoconstriction of the resistance and capacitance vessels in the splanchnic, musculo-cutaneous, and renal vascular beds within a minute. Vasoconstriction of the systemic blood vessels is the key factor in the maintenance of arterial blood pressure in the upright posture. There is pronounced HR increase to maintain cardiac output[11]. These rapid short terms adjustment to orthostatic stress is mediated exclusively by the autonomic nervous system. During prolonged orthostatic stress, additional adjustments are mediated by the hormonal limb of the neuroendocrine system [11]. The static increase in skeletal muscle tone induced by the upright posture opposes the pooling of the blood in the limb veins even in the absence of movement of the subjects [12]. However, this mechanism does not operate in head up tilt. Failure of above discussed compensatory adjustments to orthostatic stress is thought to play a predominant role in the large number of patients with syncope. This forms the basis for the use of tilt testing in the evaluation of patients with syncope. There is a large body of literature on the mechanism involved in vasovagal syncope induced by tilt testing. Yet, many unanswered questions remain regarding the multiple potential caused and underlined physiologies. In the normal subject, passive head up tilt virtually always leads a reduction in vagal and increase in sympathetic modulation to heart rate.

Most of literature report tilts between angles of 45º to 90º. However, tilt at 10º which is analogous to usual day to day activity, lying down with a pillow or back rest for patients is rare in the available literature. Therefore, this study was aimed at exploring effect on graded head up tilt.

Materials and methods

This self-controlled experimental study was conducted in 30 consenting healthy adult men (18-35 years) in the Human Physiology Lab of Department of Physiology, BPKIHS. The subjects were selected using convenient sampling techniques, according to following inclusion and exclusion criteria. **Inclusion criteria:** I. subjects with low nicotine [13] and alcohol dependence[14] (i.e. with nicotine dependence score $\leq$ 4 and alcohol disorder identification (AUDIT) <8. II. Mediation free subjects with the supine BP< 140/90 mmHg and the body mass index (BMI) $\leq$ 25. **Exclusion criteria:** subjects with past history of syncope and with the presence of diabetes mellitus, cardiovascular disorder, drug dependence and other diseases that is likely to affect autonomic function.

Recording procedure: The subjects were instructed not to take tea or coffee at least for 4 hours before test. Alcohol was forbidden 24 hours prior to test. The recording was done in morning hours between 8:00 to 12:00 hours after 15 min of supine rest. The resting ECG with spontaneous respiration at three positions first at supine followed by 10º and 70º were recorded for 5 minutes in the computer. The ECG signals for HRV were captured using Coulbourn Instrument and its software Windaq pro/pro+. From this software R-R intervals were obtained, which were manually checked and edited. Then from R-R intervals different parameters of time and frequency domain measure of HRV were calculated by using HRV analysis software 1.1[15].

Statistical analysis: Descriptive and inferential statistics of all the variables of the time domain and frequency domain measure of HRV were done along with age, BMI, respiratory rate, blood pressure. Multiple comparisons among the variables were analyzed by one way ANOVA and Bonferroni tests of multiple comparisons using software SPSS version 10.2.

Results

The mean age of the subjects was 25.37±3.89 years and their BMI ranged from 18.11 to 24.72 kg/m^2 (mean= 20.77±2.1 kg/m^2)

Effect of graded head up tilt on cardiopulmonary variables

No significant difference in respiratory rate and systolic blood pressure in response to 10º or 70º tilt were observed in the present study. The diastolic blood pressure was significantly increased in response to 70 degree tilt compared to 10 degree (81.07±6.94 vs. 75.87±8.10 mmHg, p< 0.05) tilt and supine (81.07±6.94 vs. 74.13±7.3 mmHg, p<0.01). The difference in heart rate was not significant in response to 10 degree head up tilt. Whereas, in response to 70 degree tilt as compared to supine, it increased significantly (88.51±12.84 vs. 70.48±8.17 bpm, p<0.001), the increases in heart rate at 70º was also significant compared to 10º tilt (88.51±12.84 vs. 70.22±8.67 bpm, p<0.001).

Effect of graded head up tilt on HRV

The 70º tilt significantly decreased the following vagal HRV indicators compared to 10º and supine: RMSSD, NN50, pNN50, SDNN. (Table 2)

The 70º tilt significantly decreased HF power, HF unit compared to 10º and supine where as the same 70º tilt increase LF power %, LF normalised unit, and LF: HF ratio compared to 10º and supine. (Table 3).

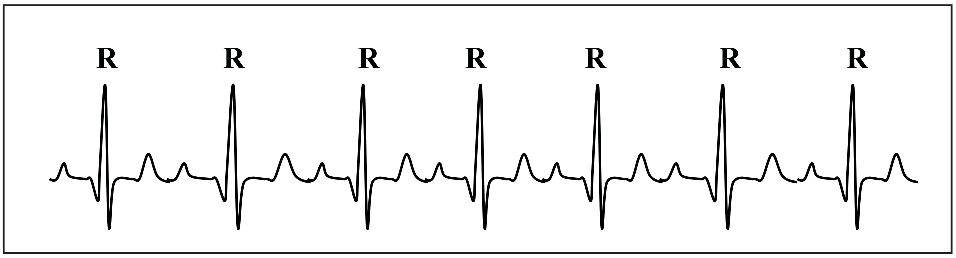

Fig 1: ECG graph showing R-R intervals

Table 1: Cardiopulmonary variables

Variables	Supine	At 10˚ tilt	At 70˚ tilt	P value
SBP, mmHg	118.60±8.98	118.07±9.50	121.20±9.46	NS
DBP, mmHg	74.13±7.30	75.87±8.10	81.07±6.94	p<0.05 (70˚ vs. 10˚) p<0.01(70˚ vs. supine)
Heart rate, bpm	70.48±8.17	70.22±8.67	88.51±12.84	NS (10˚ vs. supine) p<0.001 (70˚ vs. Supine) p<0.001 (70˚ vs. 10˚)
Respiratory rate, per minute	18.03±2.04	18.27±2.58	19.20±3.17	NS

SBP: Systolic blood pressure, DBP: diastolic blood pressure, bpm: beats per minute.

Table 2: Time domain variables

Variables	Comparison among variables with mean ± SD		P value
Mean RR (ms)	Supine = 831.23±162.30	At 10° tilt = 869.17±103.27	NS
		At 70° tilt = 687.07±94.81	p<0.001
SD of RR (ms)	Supine = 38.13±10.89	At 10° tilt = 38.07 ± 11.29	NS
		At 70° tilt = 31.13 ± 8.12	p<0.05
RMSSD (ms)	Supine = 36.16±12.22	At 10° tilt = 34.23±14.22	NS
		At 70° tilt = 20.06 ±8.47	p<0.001
NN50 count	Supine = 55.27 ± 44.10	At 10° tilt = 45.07 ± 44.44	NS
		At 70° tilt = 13.03±20.58	p<0.001
pNN50	Supine = 16.65 ± 14.23	At 10° tilt = 14.06±15.65	NS
		At 70° tilt = 3.28 ± 6.08	p<0.001
SD1	Supine = 25.93±8.72	At 10° tilt= 24.55±10.14	NS
		At 70° tilt= 14.73±6.14	p<0.001
SD2	Supine= 56.40±18.23	At 10° tilt= 57.33±18.34	NS
		At 70° tilt= 49.18±13.24	NS

Mean RR: Mean of RR intervals, SD of RR: Standard deviation of RR intervals, RMSSD: The root mean square of differences of successive RR intervals, NN50: No. of RR intervals that differ by more than 50 ms, pNN50: The percentage value of consecutive RR intervals that differ by more than 50 ms.

Table 3: Frequency domain variables

Variables	Comparison among variables with mean ± SD		P value
VLF peak, Hz	Supine = 0.023 ± 0.008	At 10° tilt=0.02 ±0.07	NS
		At 70° tilt= 0.023±0.006	NS
VLF power, ms^2	Supine = 96.97 ± 81.38	At 10° tilt= 121.93±117.32	NS
		At 70° tilt= 67.9±50.36	NS
VLF power %	Supine =18.88 ± 7.87	At 10° tilt= 23.76±10.59	NS
		At 70° tilt= 21.25±11.13	NS
LF peak, Hz	Supine= 0.09±0.33	At 10° tilt0.083±0.03	NS
		At 70° tilt= 0.082±0.15	NS
LF power, ms^2	Supine= 216.87±150.98	At 10° tilt= 218.17±155.85	NS
		At 70° tilt= 197.20±143.76	NS
LF power %	Supine = 41.61±14.29	At 10° tilt = 40.73±11.58	NS
		At 70° tilt= 59.52 ± 14.50	p<0.001
LF nu	Supine = 52.32±19.89	At 10° tilt= 54.52±16.34	NS
		At 70° tilt= 75.72±14.76	p<0.001
HF peak, Hz	Supine= 0.26 ±0.72	At 10° tilt= 0.25±0.067	NS
		At 70° tilt= 0.24±0.69	NS
HF power, ms^2	Supine= 207.67±181.22	At 10° tilt= 189.57±167.81	NS
		At 70° tilt= 72.70±101.17	p<0.01
HF power %	Supine= 39.57±18.54	At 10° tilt= 35.49±15.75	NS
		At 70° tilt= 19.31±13.25	p<0.001
HF nu	Supine = 47.67±19.89	At 10° tilt= 45.48±16.34	1.000
		At 70° tilt= 24.28±14.16	p<0.001
LF/HF	Supine = 1.69±1.67	At 10° tilt= 1.53±1.138	NS
		At 70° tilt= 4.96 ±4.08	p<0.001

VLF: very low frequency, LF: low frequency, HF: high frequency, nu: normalized unit

Discussion

Heart rate variability, which routinely used in the assessment of haemodynamics in the western countries is a tool established in 1980s for assessment of autonomic regulation of cardiac rhythm [7]. It can delineate sympathetic and parasympathetic contribution to heart rate regulation, thus making it very sensitive to diagnose autonomic neuropathy in its sub-clinical stage in diabetes mellitus. The HRV has special significance in risk stratification of post-myocardial infarction. It is an independent predictor of sudden cardiac death.

Head up tilt (orthostatic test) is the experimental procedure of passive standing resulting in the gravitational shift of the blood to lower extremities, which results in reduced venous return to the heart and, thereby decreasing stroke volume.

This study attempts to explore the HRV response to graded 10º and 70º tilts from supine position. The study showed no significant change in cardiovascular parameters at 10º tilt of head up tilt compared to supine. So, cardiovascular response at supine and 10º tilt is statistically similar. But, cardiovascular parameters changed in response to 70º tilt compared to supine and 10º. It is also known from the literature that there is no change in systolic blood pressure in response to tilt [36]. This is consistent with our study that we did not find significant difference in systolic blood pressure in response to 10º or 70º of head up tilt. The heart rate in case of higher degree of tilt involves an early rise due to vagal withdrawal and more delayed increase over first two minutes caused by enhanced sympathetic activity. The heart rate increased at 70º in our study.

Effect of graded head up tilt in time domain measure of HRV

There was corresponding decrease in HRV measure, believed to be vagal: SDNN, RMSSD, NN50, pNN50 and SD1. Among the time domain measure, mean RR interval was significantly decreased in response to 70º tilt as compared to 10º tilt or supine. Literature suggests non significant decrease in SDNN intervals with passive tilt [15]. However, in our study the SDNN interval decreased significantly in response to 70º tilt as compared to 10º tilt or supine. The difference was probable due to method applied; most of the tilt tables used was of foot supporting type of tilt table compared to table with only support on the centre not the foot, which we have used. So, no skeletal muscles were involved to support venous return in our ser up of passive standing and hence, the difference was much pronounced. The RMSSD is one of the most common parameters based on interval differences that correspond to short term HRV changes and are not dependant on day and night variations [16]. It was significantly decreased in response to 70º of head up tilt as compared to 10º tilt or supine. The NN50 count decreased significantly in response to 70º tilt compared to 10º or supine. Similarly, significant decrease in pNN50 was observed in response to 70º of tilt compared to 10º or supine. This pNN50 is one of the most common parameters that correspond to short term HRV changes. Among the geometrical methods, Poincare plot SD1, that represents the short term HRV was significantly decreased in response to 70º tilt as compared to 10º or supine, whereas the Poincare plot SD2, that represents the long term HRV, remained unchanged among the different degree of tilt.

Effect of graded head up tilt on frequency domain measure of HRV

It is known that in normal subjects, head up tilt leads to decrease in high frequency components of HRV that that represents the vagal modulation to heart[15, 17]. At the same time, it leads to increase in low frequency components [18] that represent the sympathetic modulation to heart. So, head up tilt leads to vagal withdrawal [18]. In our study, HF peak did not change in response to 10º or 70º tilt from supine but the HF power, its percentage value and the HF normalized unit decreased in response to 70º tilt as compared to 10º tilt and supine. However, there was no significant difference in LF peak, and its power in response to tilt to 70º, where as the LF power percentage increased in response to 70º as compared to 10º and supine. In the same way, the LF normalized unit also increased in response to 70º tilt as compared to 10º and supine. LF to HF ratio has been considered as sympathovagal balance, which changes in response to head up tilt angle above 30 degree [19]. The LF: HR ratio increased significantly at 70º compared to 10º or supine. Very low frequency components remained statistically similar at supine, 10º and 70º. It was interesting to note that changes in HRV in response to tilt occurred without change in respiratory frequency.

Strength and limitation of the study

In cardiovascular evaluation, different degrees of tilt are applied. However, tit at 10º has rarely been found in the available literature. Therefore, a 10º tilt is one of the frequent positions used in everyday practice. Hence, it was worth studying HRV changes in this position. But it was found to be similar to supine posture in terms of HRV.

This study has some limitations, the major of which is the limitation of time, due to which this study could not be carried out on a large sample size, besides this study was carried out only on males. So result of the study cannot be generalised on both sexes.

Conclusion

At 70º of head up tilt, HRV measures reflecting vagal contribution to cardiac-cycle length decreased with reciprocal increase in sympathetic activity compared to 10º tilt or supine leading to increase in sympathetic predominance. LF to HF ratio, which reflects the sympathovagal balance, was found to be increased at 70º tilt. So with tilt of higher angle there is increase in sympathetic activity and decrease in parasympathetic activity. The 10º tilt, which is almost equivalent to lying down with a pillow, did not change HRV from supine. So, 10º tilt is physiologically similar to supine position. It can also be said that passive inclination to 10º tilt does not cause significant haemodynamics change to produce appreciable changes in blood pressure and HRV.

Acknowledgements

Authors like to thank all the family members of Department of Physiology, BPKIHS for providing opportunity to carry out this research work. Authors are deeply indebted to all the volunteers who participated in the study.

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