Chronobiology of Rate Pressure Product in Young Adults

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Abstract: ***Cardiac events are known to precipitate at specific hours of the day implying that a circadian rhythm of myocardial oxygen demand may exist. Rate - pressure product (RPP) is regarded as a surrogate measure of myocardial oxygen demand and can be obtained without any invasive procedure. Hence the project was designed to study the circadian rhythmic pattern of RPP in healthy individuals and its gender variability in Indian population. Blood pressure was monitored at 2 hourly intervals for 24 hours in 55 male and 70 female healthy subjects between 18 to 25 years of age without any acute or chronic illness. Independent sample't' test were performed for descriptive analysis. Repeated measures post hoc Tukey ANOVA test was performed for comparison of RPP within the groups. RPP values were seen to be minimum at 2 am in males (5332 ± 924) and at 4 am in females (6567 ± 1092) and maximum at 2 pm in males (8206 ± 1296) and at 8 pm in females (9928 ± 1709). At all the observed time intervals RPP values were higher in females. There exist a definite pattern of circadian rhythm in RPP with peak values attained during daytime and least values during early morning hours. Also the rhythm and amplitude of RPP is different in both genders.***

Keywords: circadian rhythm, chronotherapy, rate-pressure product.

1. Introduction

Rate pressure product (RPP), also known as double product or pressure pulse product is calculated as heart rate multiplied by systolic blood pressure. (RPP = Heart rate × Systolic blood pressure). This may easily be obtained by recording heart rate and systolic blood pressure. As the systolic blood pressure is a key determinant of cardiac after load the same may determine the myocardial oxygen uptake. The RPP is regarded as an indirect measure of myocardial oxygen demand and is being used more often in modern medicine. [1,2] This parameter has been used extensively in recent years to assess cardiac work load, risk of left ventricular hypertrophy, and efficacy of antihypertensive therapy. [2] Many diseases impact the expression and /or features of the circadian rhythm for blood pressure.[3]

Heart rate and blood pressure both exhibit a strong circadian pattern with values for blood pressure and heart rate typically peaking in the early morning period.[2] This appears to be mediated by autonomic nervous system which itself is under regulatory control of the Suprachiasmatic nucleus of hypothalamus – 'the master oscillator'. This master oscillator also generates circadian rhythmic patterns for other biological events. It is increasingly being appreciated that many diseases have a pattern associated with circadian rhythms of various biological functions of the body, more so the cardiovascular diseases. [4,5,6] The existence of circadian rhythms in heart rate and blood pressure means that the rate-pressure product would also show a similar rhythm.

Many diseases impact the expression and /or features of the circadian rhythm for blood pressure.[3] Blood pressure and rate pressure product have shown peak values during early hours of day in people suffering from cardiovascular diseases rendering them vulnerable to the rupture of atherosclerotic plaque and sudden cardiac event.[7] Vast data suggest that many hemodynamic, environmental, and hematological factors for cardiovascular diseases clustering in the early morning hours are associated with awakening. [8]

Hermida RC [2](2000) observed the diurnal variations in rate pressure product and also its gender variability. Atkinson G [7](2010) in their study revealed that blood pressure and rate pressure product showed marked morning surges when people were studied in free living conditions. Dodt C[9] (1997) observed variable levels of catecholamines in blood with varying rate pressure product during different hours of the day. We did not come across studies of circadian rhythm of blood pressure and heart in Indian populations**.** Thus the project was planned to study the pattern of RPP in young healthy subjects and its gender differences.

2. Materials and Methods

The study was conducted on a total of 125 healthy medical students, young males (n=55) and young females (n=70) in the age group of 18-25 years. The number of prospective candidates contacted was 142 – i.e. 64 males and 78 females, but due to exclusion criteria only 55 males and 70 females could be considered for the study.

2.1 Exclusion criteria used include – Smokers, Acute or chronic respiratory and/ or cardiac illness, taking any medicines affecting heart or circulation, subjects below 18 and above 25 years of age, subjects not willing to participate in the study.
2.2 Inclusion criteria used include – Young healthy subjects (males and females) in age group 18 to 25, sharing similar environment and food, subjects willing to participate in the study. The young population was hailing from same class and society, and sharing similar environment and food conditions in the hostel accommodation and were performing there usual day to day activities. An informed consent was obtained from all the volunteers and the experimental protocol was explained to them. The

study plan was approved by ethics committee of the institution.

2.3 Anthropometric measurements and calculations:

Height in cm and weight in kg was measured. Body mass index was calculated using the formula: BMI=Weight (Kg) / Height $(M)^2$,Waist circumference (WC) was measured in orthostatic position at the midpoint between the iliac crest and the lowest rib. Hip circumference was measured at the level of the tronchanter major. Waist (cm) /Hip (cm) ratio is the division of above two measurements.

2.4 Blood pressure and Heart rate recording:

A two hourly heart rate and blood pressure observations (systolic and diastolic) were recorded in supine position after a relaxation of at least ten minutes, starting at 12.00 midnight for 24 hrs with the help of OMRON automatic blood pressure monitor HEM-7111, Omron health care Ltd, Singapore. This involved tying the cuff over the arm according to the standard instructions given with the instrument. The arm was put through the cuff loop so that the air tube ran down the inside of the forearm and was in line with the middle finger. The bottom of the cuff was approximately 1 – 2 cm above the elbow. After correct positioning the cuff the fabric fastener was closed firmly. The same instrument also recorded the heart rate. During daytime the subjects participated in their routine activities and were instructed to report half an hour before the stipulated blood pressure recording time. The blood pressure was recorded in supine position in a specified room in their respective hostel where ambient temperature was maintained at 25 ^{0}C; so that the heart rate should not vary according to change in temperature. During night the subjects rested in the same room with the cuff tied to their arm without any discomfort and appropriate recordings were made at stipulated time intervals. The equipment was standardized by comparing blood pressure recordings with that of conventional mercury sphygmomanometer in 10 subjects each of both the genders and no significant statistical difference was noted in the mean recordings between the two methods i.e. OMRON automatic blood pressure monitor & Mercury sphygmomanometer. The instrument was accuracy of ± 3 mm of Hg for pressure and ± 5% of reading for heart rate. To complete the study over a period of two months a total of ten instruments were used five for males and five for females. Each was calibrated and compared with conventional mercury sphygmomanometer.

3. Statistical Analysis

Data was compiled using Microsoft office 2003 Excel software. All the data were expressed as arithmetic Mean ± SD. Statistical analysis was done with SPSS version 12. The tests used were, Independent sample Student's - t test to compare the means; and Repeated measures post hoc Tukey ANOVA test for comparison of RPP values within the male group and female group separately for a pre specified P value of 0.05.

4. Results

Table 1: Anthropometric profile of study population

Parameter	*Males (n=55) Mean ± SD*	*Females (n=70) Mean ± SD*	*'P' value*
Age	18.8 ± 0.8	18.6 ± 0.7	0.071
Weight	58.9 ± 9.4	54.3 ± 9.3	0.008
Height	1.6 ± 0.1	1.5 ± 0.1	0.000
WHR	0.8 ± 0.04	0.7 ± 0.1	0.000
WC	68.5 ± 6.5	70.4 ± 9.7	0.193
BMI	22.0 ± 3.3	23.6 ± 4.1	0.020
BSA	1.6 ± 0.2	1.5 ± 0.1	0.000

Table 1 depicts anthropometric profile of the study group. Statistically significant difference exists in weight, height, WHR, BMI & BSA between the genders.

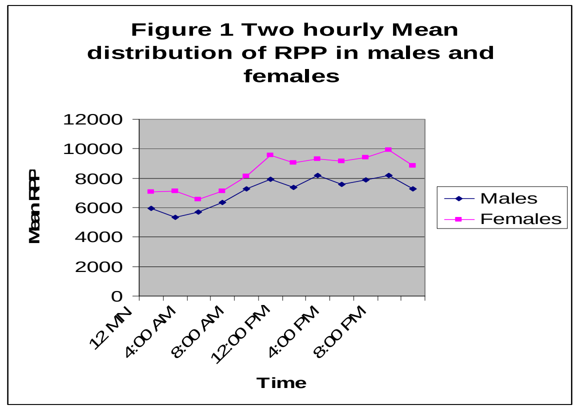

Figure 1: Distribution of RPP values at 2 hourly intervals in male and female groups. The values in females are higher than males at all time intervals

Table 2: Comparative circadian variations in RPP among male and female groups

Circadian durations	*Males (n=55)*	*Females (n=70)*	*'P' value*
12 MN	5962 ± 993	7090 ± 1239	0.000
2 AM	5333 ± 924	7113 ± 1214	0.000
4 AM	5671 ± 1195	6567 ± 1093	0.000
6 AM	6339 ± 1201	7115 ± 1691	0.005
8 AM	7274 ± 1475	8143 ± 1852	0.005
10 AM	7937 ± 1423	9537 ± 1601	0.000
12 PM	7397 ± 1188	9033 ± 1491	0.000
2 PM	8207 ± 1297	9313 ± 1772	0.000
4 PM	7555 ± 1493	9166 ± 1705	0.000
6 PM	7890 ± 1454	9394 ± 1656	0.000
8 PM	8202 ± 1625	9928 ± 1709	0.000
10 PM	7273 ± 1492	8856 ± 1375	0.000

Table 2 displays comparative 2 hourly RPP profiles of male and female groups using unpaired student's 't' test. There is highly significant difference at all 2 hourly observations of RPP between male and female groups. The lowest values are observed at 2 am and 4 am in males and females respectively; whereas highest values are observed at 2pm and 8 pm in males and females respectively.

Repeated measures post hoc Tukey ANOVA test for a prespecified P value of 0.05 was performed for male group and female group individually and the observed values were statistically highly significant. The 2 hourly RPP values from 8 am to 10 pm in both the genders were significantly different from other values.

5. Discussion

The main outcome of the study was that,

1) RPP values followed a circadian rhythm.
2) RPP values were seen to be minimum at 2 am in males (5332 ± 924) and at 4 am in females (6567 ± 1092) and maximum at 2 pm in males (8206 ± 1296) and at 8 pm in females (9928 ± 1709).
3) At all the observed time intervals RPP values were higher in females.

Similar findings in terms of increase in RPP; although highest in the afternoon, 7 hours after commencement of morning activity and least at 3 hours before awakening was reported by Hermida et al (2001)[2] in their study on 125 men and 75 women.

As observed by Anwar & White[10], and Neutel & Smith[11] in their study of normotensive and hypertensive subjects, BP was at its highest level during the daytime (from about 10 a.m. to 6 p.m.), and then declined to reach a trough value between midnight and 3 a.m. Later BP rose steadily over the early morning hours. Anwar & White [10] observed further that an abrupt and steep acceleration in BP occurred at approximately 6 a.m., which was coincident with arousal. This morning BP surge continued for 4-6 hours after awakening and is characterized by an increase in systolic BP of approximately 3 mmHg per hour and in diastolic BP of 2 mmHg per hour. The morning rise in blood pressure and its continued increment for 4-6 hours after awakening was also reported by Millar-Craig et al [12] and White. [13]

In the present study RPP values were significantly higher in females than males at all time intervals. Similar such observations were made by Hermida et al [2] where 24 hour mean RPP in men was significantly lower than that of women, stating sympathetic activity to be more pronounced in females than males, but this is in contrast to many other researchers who have concluded that there is parasympathetic dominance in females and not males. [14, 15].

The existence of a circadian rhythm in RPP could be explained according to catecholamine levels in the blood. RPP begins to increase with increased catecholamine in blood seen upon assumption of morning activities, remains at high levels during the day with peak reaching toward the end of the day and tended to fall during night after sleep.[16] The existence of different rhythms in the pattern of RPP in the two genders may be due to various reasons - difference in the autonomic nervous system development, effects of prevailing levels of sex hormones, differences at the level of reflex arc (receptors, neurotransmitter content & its metabolism, reflex transmission) [9] [17] .

6. Conclusion

There exists a definite circadian rhythm in RPP in young Indian adults with peak values attained during daytime and least values during early morning hours. Also the rhythm and amplitude of RPP is different in both genders.

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