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Short Communication

Rate Pressure Product in Diabetic Cardiac Autonomic Neuropathy at Rest and Under Stress

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ABSTRACT

Introduction: Rate pressure product, a non invasive indicator of myocardial oxygen demand tends to increase with stress. This determinant is less studied in diabetic cardiac autonomic neuropathy patients both at rest and after stress. An insight into this determinant of myocardial oxygen demand in diabetic cardiac autonomic neuropathy patients may explain sudden adverse cardiovascular events in such patients.
Methods: Case control study (n=45) was done on thirty age matched (40-60 yr) type 2 diabetics with/ without diabetic cardiac autonomic neuropathy and fifteen controls for rate pressure product.
Results: Results demonstrated (ANOVA and paired 't' - test, 'SPSS' software) that resting rate pressure product was significantly increased in cardiac autonomic neuropathy patients ($p< 0.05$) and out of normative zone (>12) pushing these patients into risk zone for adverse cardiovascular events. The stress rate pressure product was similar to resting showing little or no increment demonstrating a non significant result ($p>0.01$)
Conclusion: Diabetic cardiac autonomic neuropathy significantly increases resting rate pressure product and inversely affects stress related increment for same.

Keywords: Rate pressure product, Myocardial oxygen demand, Diabetic cardiac autonomic neuropathy,

INTRODUCTION

Rate Pressure Product is also known as Robinson Index. [1] Rate Pressure Product or the double product is the product of heart rate and systolic blood pressure. [2] It is an easily measurable index which correlates well with myocardial oxygen demand and defines the response of coronary circulation to myocardial metabolic demands. [3]

Heart, being a muscular organ, its regular functioning needs steady supply of oxygen and nutrients; if this supply is deficient, there are all chances of heart failure to occur. [4] The importance of this is more applicable in stressed conditions than in resting conditions.

Stress in any form – either mental or physical affects the cardiovascular system. RPP tends to increase with stress. In this contest, RPP is useful in determining the physical fitness of a person in rest as well as in stressed conditions.

So, this study was done to review the RPP values in normal and diabetic patients with and without cardiac autonomic neuropathy in resting and stressed conditions.

MATERIALS & METHODS

Study was done on total 45 subjects of either sex between 40-60 years taken from a tertiary health care centre in North

India - 30 patients with type 2 diabetes mellitus with a duration of diabetes of 8-12 years and 15 healthy controls. This study was approved by the Institutional Ethical Committee of our Hospital in accordance with the Helsinki Declaration of 1975.

Fasting / Random capillary glucose was measured using glucometer. Details of history and examination were recorded on a proforma. Informed consent was taken from all subjects before the recording the blood pressure and heart rate.

Resting blood pressure and heart rate were recorded in all the subjects supine, at complete physical and mental rest. Blood Pressure was recorded using sphygmomanometer and heart rate calculated from lead II on cardiofax ECG machine (Medicaid Systems).

Heart Rate = $\frac{60*25}{\text{R}-\text{R interval}}$

Blood pressure and heart rate were also recorded in all the subjects after subjecting to stress (cold pressor test).

Rate Pressure Product was calculated as a product of heart rate and systolic blood pressure. RPP = Systolic Pressure in mm Hg x Heart Rate in beats/min x 10-2 [5]

Subjects: They were divided into 3 groups of 15 subjects each.

Group A: Patients having type 2 diabetes with clinically evident diabetic cardiac autonomic neuropathy. Autonomic neuropathy was clinically assessed as postural fall in systolic BP > 30 mm Hg.

Group B: Patients having type 2 diabetes without diabetic cardiac autonomic neuropathy. Exclusion Criteria for patients: Ischemic Heart Disease, Congestive heart failure and Cardiac arrhythmias. Patients on α blockers, β blockers, calcium channel blockers, diuretics, antiarrhythmics, antipsychotics were excluded from study.

Group C: 15 healthy age-matched controls (free from any systemic illness) were taken.

Statistical Analysis Statistical analysis was done using ANOVA, and paired t - test ('SPSS' software) with statistical significance set at $p < 0.05$ and $p < 0.01$ respectively.

RESULT

The results of one-way analysis of variance indicated that the mean level of RPP varied significantly among three groups. (Table1a)

The multiple comparisons of three groups were carried out by using Post-hoc ANOVA. The mean difference of RPP of three groups i.e. Group A, Group B and Group C was reported to be differ significantly from each other. (Table 1b)

Table 1a: Comparison of REST RPP among three groups- result of one-way ANOVA

Group	N	Mean	SD	SE	F-ratio	Sig.
Group A	15	134.4	8.04	2.076	42.18	0.00
Group B	15	121.3	16.13	4.164		
Group C	15	91.6	13.79	3.560		

Table 1b: Multiple Comparison of REST RPP among three groups - Post-hoc ANOVA

Variable (I)	Variable (J)	Mean Difference (I-J)	Std. Error	Sig.
Group A	Group B	13.13467*	4.78	0.03
	Group C	42.87133*	4.78	0.00
Group B	Group A	-13.13467*	4.78	0.03
	Group C	29.73667*	4.78	0.00
Group C	Group A	-42.87133*	4.78	0.00
	Group B	-29.73667*	4.78	0.00

* The mean difference is significant at the 0.05 level.

The results of one-way analysis of variance indicated that the mean level of RPP varied significantly among three groups (Table 2a).

The multiple comparisons of three groups were carried out by using Post-hoc ANOVA show that the mean difference of RPP of Group A and Group C was reported to be differ significantly from each other, while the mean difference of RPP in case of Group A and Group B was found to be differ non-significantly from each other. (Table2b)

Table 2a: Comparison of Stress RPP among three groups- result of one-way ANOVA

Group	N	Mean	SD	SE	F-ratio	Sig.
Group A	15	134.5	7.97	2.262	18.56	0.00
Group B	15	139.2	16.53	4.268		
Group C	15	113.5	10.75	2.775		

Table 2b: Multiple Comparison of STRESS RPP among three group-Post-hoc ANOVA

Variable (I)	Variable (J)	Mean Difference (I-J)	Std. Error	Sig.
Group A	Group B	-4.62	4.48	0.93
	Group C	21.01*	4.48	0.00
Group B	Group A	4.62	4.48	0.93
	Group C	25.63*	4.48	0.00
Group C	Group A	-21.01*	4.48	0.00
	Group B	-25.63*	4.48	0.00

* The mean difference is significant at the 0.05 level.

Non significant increment was found in rate pressure product of diabetic cardiac autonomic neuropathy patients after stress (p>0.01).

Table 3: Group-wise comparison of REST RPP and STRESS RPP- result of paired t-test

Group	REST RPP (n=15)	STRESS RPP (n=15)	Mean Difference	95% Confidence Interval of the Difference		t-statistics	P-value
	Mean ± SD	Mean ± SD		Lower	Upper		
Group A	134.4±8.04	134.5±7.97	0.10	-0.29	0.11	1.00^{NS}	0.33
Group B	121.3±16.13	139.2±16.53	17.85	-23.47	-12.23	6.81*	0.00
Group C	91.6±13.79	113.5±10.75	21.96	-31.17	-12.75	5.12*	0.00

NS: Non-significant

* Significant at one per cent level of probability.

Resting rate pressure product was highest in neuropathy patients, out of normative range, already into the risk zone.

Stress rate pressure product was also in risk zone for non neuropathy patients.

DISCUSSION

The present study was carried out with the aim to determine the values of rate pressure product in resting and stressed conditions in diabetics with and without cardiac autonomic neuropathy compared to controls.

Diabetic cardiac autonomic neuropathy patients had a significantly higher Rate Pressure Product at rest compared to non neuropathy counterparts as well as controls (p<0.05). Foo K, et al, confirmed independent association of diabetes with RPP which was estimated to be 9% higher than in patients without diabetes. [6] Our study confirms the same in diabetic cardiac autonomic neuropathy patients also.

Under resting conditions, safer RPP should range between 7.00 and 9.00 in normal subjects. According to Sarnoff (1958) and Fletcher (1979) et al, any total value of RPP more than 10,000 (10.00) is a clear indicator of increased risk for heart disease. [7, 8]

Pepper MG and Crawley BE have calculated mean normative values of RPP to be <12 (heart rate between 60-120 beats per minute and Systolic blood pressure between 100-140 mm Hg, RPP = HR X SBP/1000). [9]

According to White WB, RPP of 12 or below 12 with the HR of 60 to 120 bpm and SBP of 100 to 140 mm Hg is considered to be normal without any existing or future risk of cardiovascular complications in normal. [10]

The resting rate pressure product was found to be highest, out of normative range, (RPP ≥12.00 or 120) in diabetic cardiac autonomic neuropathy patients. Resting tachycardia could potentially be contributing to significantly heightened rate pressure product in such patients.

Another observation was that a type 2 diabetic with resting RPP converting from a value <12 towards a value >12 should be suspected of developing cardiac autonomic neuropathy.

Zones of Rate Pressure Product have been put forth by Sembulingam et al, in normal young adults. Normal Subjects with Rate Pressure Product ranging between 12-17 fall in the risk zone in normal subjects. [11] Diabetic Cardiac Autonomic Neuropathy patients in the study were found to be already in risk zone. Such patients were at a higher risk of adverse cardiovascular events.

According to Sangeetha Nagpal et al., most of the normal individuals develop a Rate Pressure Product of 20 to 35 mm Hg ×

beats/min × 10–3 without any discomfort which is an indication of normal ventricular function. At the same time, low Rate Pressure Product value suggests the restricted coronary blood supply with inadequate ventricular function. However, Rate Pressure Product of more than 22 is considered to be a prelude of myocardial ischemia and angina. [12]

Diabetic Cardiac Autonomic Neuropathy patients had little or no increment in RPP when subjected to stress. This was because a sympathetic dysfunction was present in such patients. A similar result by Khoshdel, et al, demonstrated that diabetics had an impaired change in heart rate, systolic blood pressure and diastolic blood pressure in response to exercise. [13] Since already RPP at rest was high, so there was little capacity of the body to increase it further and improve myocardial perfusion. Non neuropathy patients entered into risk zone under stress.

The change in rate pressure product was lowest or absent in diabetics with cardiac autonomic neuropathy ($p>0.01$). These results suggest an uncoupling between myocardial metabolic demand and supply in diabetic cardiac autonomic neuropathy patients when subjected to sympathetic stimulation/stress. Fixed Rate pressure product or Failure of Rate Pressure Product to increase to meet the body demands at times of physical and emotional stress makes such patients vulnerable to adverse cardiovascular events.

The inverse association of Rate Pressure Product to hemodynamic response supports the early development of arterial and ventricular stiffness in Diabetes Mellitus, unrelated to other likely risk factors such as hypertension and hyperlipidemia. This renders such patients vulnerable to various cardiac risks like left ventricular dysfunction, cardiac arrhythmias, silent myocardial infarction, cardiac arrest and sudden death on exposure to current life stress episodes.

CONCLUSION

Resting Rate Pressure Product was heightened and response to stress blunted in diabetic cardiac autonomic neuropathy patients. Limitation of the study was lower number of patients. Future studies with more number of patients will help to further highlight the role of rate pressure product in predicting the extent of cardiac risk in such patients.

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