

Parasympathetic Nerve Function Status in Female with Rheumatoid Arthritis

Kawser Jahan¹, Noorzahan Begum², Sultana Ferdousi³

Abstract

Background: Sudden cardiac death in patients with Rheumatoid Arthritis has been attributed to the decreased vagal drive to the heart. **Objective:** To assess cardiac parasympathetic nerve function status in patients with Rheumatoid Arthritis (RA). **Methods:** This cross sectional study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka from January to December 2010. Sixty female RA patients aged 18-50 years were included in the study group. They were enrolled from the Out Patient Department of Rheumatology Wing of the Department of Medicine, BSMMU, Dhaka. For comparison age matched thirty apparently healthy females were also studied as control. To assess parasympathetic nerve function status, all the subjects were examined by three noninvasive cardiovascular reflex tests such as heart rate response to valsalva maneuver (Valsalva ratio), heart rate response to deep breathing and heart rate response to standing (30th:15th ratio). For statistical analysis independent sample t test was used. **Results:** Mean values of Valsalva ratio, deep breathing test and 30th:15th ratio were significantly ($p < 0.001$) lower in rheumatoid arthritis patients compared to those of healthy control. **Conclusion:** From this study it may be concluded that lower cardiac parasympathetic nerve activity characterized the autonomic nerve dysfunction in patients with Rheumatoid Arthritis.

Key words: Rheumatoid Arthritis, Parasympathetic nerve function, Cardiovascular reflex test.

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Introduction

Rheumatoid arthritis (RA) is a connective tissue disease which in addition to joints also affects different organs including heart. In a recent research, Johns Hopkins specialists found link between rheumatoid arthritis and heart health.¹ Higher cardiovascular mortality in patients with rheumatoid arthritis has been documented in different epidemiological studies.²⁻⁴ The increased incidence of sudden cardiac death in these group of patients may be related to the decreased vagal drive to the heart.⁵ In RA,

peripheral and central nervous system involvement have been well documented but involvement of autonomic nervous system has rarely been studied and has shown conflicting results.⁶

In 1992, Ewing et al. proposed 3 cardiovascular reflex tests to assess parasympathetic nerve response activity. These include Valsalva maneuver, deep breathing test and heart rate response to standing⁷.

Diminished cardiac autonomic nerve function in rheumatoid arthritis was observed by various

researchers of different countries⁸⁻⁹. Lower values of heart rate response to valsalva maneuver, heart rate response to deep breathing and heart rate response to standing (30th:15th ratio) were reported in patients with RA in comparison with those of healthy control.¹⁰⁻¹³ Opposite finding was also reported by some investigators who did not find any cardiovascular autonomic abnormality in patients with rheumatoid arthritis when compared with those of healthy control¹⁴.

Again, higher HR response to standing was observed by some investigators in patients with RA when compared with those of healthy control.⁶

Cardiovascular reflex tests are non-invasive popular and widely used tests for assessing parasympathetic and sympathetic response in different countries. This study has been designed to evaluate parasympathetic nerve function status in patients with RA.

Methods

Sixty diagnosed Rheumatoid arthritis female patients (Group B), 18 to 50 years of age participated in this cross sectional study under the supervision of the department of Physiology, BSMMU from January to December 2010. They were diagnosed according to American College of Rheumatology (ACR) classification.¹⁵ Thirty age and BMI matched apparently healthy females were taken as control (Group A). Before

recruitment, the objectives of the study were explained to all the subjects and their voluntary participation was encouraged. A written informed consent was taken from each subject. The protocol of this study was approved by the Ethical Review Committee of BSMMU. RA patients with history of hypertension, heart disease, diabetes mellitus, renal diseases and psychic disorders were excluded from the study. Random blood sugar level and serum creatinine level were measured to exclude diabetes mellitus and renal failure. Resting pulse rate and supine resting blood pressure of all the subjects were also measured. Parasympathetic nerve function of all the subjects was assessed in the autonomic nerve function laboratory of Dept of Physiology of BSMMU by the conventional tests i.e heart rate response to valsalva maneuver, heart rate response to deep breathing and heart rate response to standing. Data were expressed as mean \pm SD. Independent sample t test were used for statistical significance.

Results

The mean resting pulse rate ($p < 0.05$) and DBP ($p < 0.001$) were significantly higher and mean SBP was higher ($p < 0.05$) in RA patients. (Table I) The mean values of Valsalva ratio, Heart rate response to deep breathing, 30th:15th Ratio were significantly (< 0.001) lower in RA patients compared to control. (Table II).

Table I: Baseline characteristics in different groups. (n=90)

Variables	Group A (n=30)	Group B (n=60)	P values
Age (years)	36.50 \pm 11.50	37.09 \pm 11.10	0.803 ^{ns}
BMI (Kg/m ²)	23.88 \pm 2.27	23.94 \pm 1.68	0.876 ^{ns}
Pulse (beat/min)	80.29 \pm 10.62	85.34 \pm 11.22	0.03*
SBP (mm of Hg)	114.37 \pm 11.79	116.19 \pm 11.30	0.451 ^{ns}
DBP (mm of Hg)	68.70 \pm 7.59	73.77 \pm 7.01	0.001***

Data are expressed as mean \pm SD. Statistical analysis was done by Independent sample t-test. Group A: Apparently healthy people. Group B: Patients with Rheumatoid arthritis, BMI=Body Mass index, SBP=Systolic blood pressure, DBP=Diastolic blood pressure. **= $p < 0.01$, * = $p < 0.05$, ns= $p > 0.05$, n=number of subjects. ns=nonsignificant

Table II : Parasympathetic nerve function variables in different groups (n=90)

Parasympathetic nerve function variables	Group A (n=30)	Group B (n=60)	P value
Valsalva ratio	1.32 ± 0.12	1.18 ± 0.14	0.000***
Heart rate response to deep breathing	21.27 ± 3.49	12.27 ± 3.48	0.000***
30 th : 15 th Ratio	1.17 ± 0.10	1.10 ± 0.07	0.000***

Data were expressed as mean±SD. Statistical analysis was done by Independent sample t-test. Group A=Control. Group B= Patients with Rheumatoid Arthritis.

30th:15th ratio = Heart rate response to standing

***=p<0.001, n = number of subjects.

Discussion

In the present study, findings of autonomic nerve function parameters in healthy control group were almost within normal ranges and were also similar to the published reports from different countries^{6, 10, 11, 13} and also from our country.¹⁶⁻¹⁹

Significantly higher resting pulse rate, diastolic blood pressure may be attributed to the higher sympathetic nerve activity which is consistent with observation by some other researchers.²⁰

Lower values of heart rate response to valsalva maneuver in the present study indicate decreased parasympathetic activity in RA which is consistent to observations reported by some investigators.¹⁰⁻¹³ Toussirot *et al.*²¹ revealed a significant difference between the series of RA patients and the control for the Valsalva maneuver. Results the of Heart rate response to deep breathing and 30th:15th ratio in RA patients in this study demonstrate lower vagal activity at cardiac level. A lower value of breathing test in RA patients are reported by some investigators.^{6, 10-13}

Several studies also reported lower values of 30th:15th ratio in RA patients.¹¹⁻¹⁴ But there are conflicting reports on this parameter. Sandhu and Allen¹³ in 2004 observed lower value of 30th:15th ratio whereas others rather found higher values.⁶ Leden *et al.*⁸ also found abnormal heart rate response to standing in patients with Rheumatoid Arthritis.

Milovanoviæ *et al.*²² studied abnormal autonomic nerve function status in patients with RA. But they did not publish the values of valsalva maneuver, Deep breathing test or 30th:15th ratio. However, they mentioned that 27.8% of the RA patients had abnormal valsalva ratio, 41.2% had positive deep breathing test and heart rate response to standing was positive in 71.4% of the patients.

Exact mechanisms for the attenuated cardiac parasympathetic activity in RA patients are not yet clear. Various suggestions are proposed by different investigators. According to them, deposition of immune complex, amyloid deposition, autoantibody production against nerve growth factor, cervical ganglia and vagus nerve may be considered as factor for this autonomic nerve function impairment in patients of the present series.^{6, 11-12}

The results of the present study suggests attenuated cardiac vagal modulation in Rheumatoid arthritis and the above mentioned factors may be the consequence of inflammatory process of Rheumatoid arthritis. This finding is well correlated with those published in our previous report²³

Conclusion

From this study, it may be concluded that cardiac autonomic nerve impairment occurs in rheumatoid arthritis which is characterized by reduced vagal activity.

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