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RESEARCH ARTICLE

Assessment of cardiac sympathovagal activity in the patients suffering from ankylosing spondylitis

Atanu Roy[1], Sanjeev K. Singh[2]

[1]Department of Physiology, All India Institute of Medical Sciences, New Delhi, India, [2]Department of Physiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

Correspondence to: Sanjeev K. Singh, E-mail: drssks@gmail.com

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ABSTRACT

Background: Ankylosing spondylitis (AS) is an autoimmune disease which leads to the involvement of skeletal, cardiac, nervous tissues, and other systemic diseases. **Aims and Objectives:** This study was conducted to assess the cardiac sympathovagal responses in the AS patients using Valsalva maneuver (VM) and tilt-table test (TTT). **Materials and Methods:** A total of 30 AS patients having Bath AS Disease Activity Index of ≥4 were included in this study. The same numbers of age- and sex-matched controls were also selected. The blood pressure (BP) and electrocardiogram were recorded during VM and TTT. The Valsalva ratio and 30:15 ratio were calculated. **Results:** During VM, there is a statistically significant decrease in the Valsalva ratio in the cases ($P < 0.05$). After TTT, there is a significant decrease in 30:15 ratio and significant increase in systolic BP (SBP) in the cases ($P < 0.05$). **Conclusion:** The Valsalva ratio in the cases is decreased indicating the parasympathetic loss which is further supported by the decrease in 30:15 ratio observed after TTT. The increase in SBP in cases also supports the shifting of sympathovagal balance toward the sympathetic side.

KEY WORDS: Valsalva Maneuver; Tilt-Table Test; Ankylosing Spondylitis; Autonomic Nervous System

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory disease involving the spine and sacroiliac joints most commonly. Fatigue, spinal pain, joint pain/swelling, local tenderness, and morning stiffness are the diagnostic presenting symptom of the AS. Some extra-articular manifestations are also observed in AS such as neurological involvement[1] and heart diseases.[2] The cardiac complication of AS is well known which is often associated with aortic regurgitation, conduction defects, and arrhythmias.[2] Since, AS is autoimmune in origin, therefore, the involvement of nervous system is also expected. Abnormalities of both the central and peripheral nervous system are described in inflammatory rheumatic diseases such as autoimmune diseases, rheumatoid arthritis, and systemic lupus erythematosus.[3] However, only some studies have shown the involvement of autonomic nervous system with the conflicting results with different degrees of involvement.[4,5]

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It is well known that autonomic nervous system regulates the visceral functions such as heart rate (HR), intestinal motility, urination, sexual activity, and many other visceral functions. As the human body tries to adjust according to the changes in the environment, it is constantly being exposed to various forms of stresses. Therefore, if there is any abnormality in the functions of the autonomic outflow, it will affect the visceral functions which may be presented as abnormal gastric, urinary, and sexual functions.

Prolonged pain of musculoskeletal origin causes changes in the sympathetic and parasympathetic functions. Sympathetic hyperactivation has already been shown in fibromyalgia,[6] migraine,[7] and chronic neck and shoulder pain.[8] The sympathetic and parasympathetic systems work together to maintain the harmony of the human physiology, but this state can be disrupted by the chronic pain. The autonomic nervous system governs the cardiovascular system and this principle has led to various studies showing relations between autonomic dysfunctions and chronic pain.[9,10] Since any alterations in the autonomic nervous system bring about the changes in the cardiovascular parameters such as blood pressure (BP) and HR, therefore, Valsalva maneuver (VM) and tilt-table test (TTT) were performed to evaluate the cardiac sympathovagal activities in the patients suffering from the AS.

MATERIALS AND METHODS

The present study was conducted after obtaining approval from the Ethical Committee (Ref No. Dean/2014-15/EC/512), Institute of Medical Sciences, Banaras Hindu University, Varanasi, to understand the autonomic reactivity in the patients suffering from AS using VM and TTT. All the patients (mean age 34 ± 2.11) were informed about this study and were enlisted after their written consent. Age- and sex-matched controls (mean age 35 ± 2.61) were also included in this study for the various comparisons.

Selection of Cases and Controls

The patients suffering from AS satisfying the Modified New York Criteria for AS[11] were included in this study. The disease activity was measured by the Bath AS Disease Activity Index (BASDAI). This index consists of 1-10 scale (one indicates no problem and ten indicates the maximum problem) and the scores are given according to their answers after asking the five questions regarding the five major symptoms of the AS. These five symptoms are fatigue, spinal pain, joint pain/swelling, local tenderness, and morning stiffness. The patients suffering from AS having BASDAI score of >4 were included in this study. The history of chronic diseases such as hypertension, diabetes mellitus, hyper/hypothyroidism, and uremia or the use of any medication such as diuretics, calcium channel blocker, neuroleptics, antiepileptic, antidepressant, and α/β blockers was considered as exclusion criteria for the selection of patients. Only female patients were selected to avoid the gender-related differences in the response. The age- and sex-matched healthy persons were selected for the comparisons of various parameters and were defined as controls. 30 female patients were selected from the Pain Clinic, Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, based on the exclusion and inclusion criteria as described above. Non-random method was adopted for the selection of the cases during 1 year. Same numbers of controls were also selected in this study for the comparisons of the various parameters.

Study Plan

All the patients were advised to avoid the foods and drinks containing caffeine, nicotine, and alcohol at least 12 h before the test. They were also advised to avoid the strenuous activities such as swimming, running, jumping, and any kind of sports at least 2 h before the recordings. The patients were advised to take light meal containing less fat with 6-8 h of deep sleep in the previous night. All tests were performed before 12 noon after a light breakfast. The temperature of the laboratory was maintained at 25 ± 2°C, with minimum light, and noise. The patients were briefed about the various procedures to be done during the test. They were allowed to lie down on the bed and were given 10-15 min of rest before the onset of recordings. The BP was measured using digital BP apparatus (Omron Healthcare Company Limited, Japan) and electrocardiogram (ECG) and respiration (using stethograph) were recorded by Polyrite D (RMS, Chandigarh, India). Furthermore, HR, Valsalva ratio, and 30:15 ratio were computed from the ECG.

Valsalva Maneuver

An abrupt transient voluntary elevation of intrathoracic and intra-abdominal pressures against the closed glottis is known as VM. For this purpose, the patient blows into the mouthpiece of an aneroid manometer up to 40 mmHg for 15 s. Interpretation of the test is more accurately performed by Valsalva ratio; it is the ratio of the longest R-R interval within 20 beats of maneuver to the shortest interval during the maneuver. In this study, a plastic disposable mouthpiece was placed in the tube of aneroid sphygmomanometer with the patient in sitting position and ECG leads were connected in standard limb lead-II configuration. The patient breathes into a disposable plastic mouthpiece attached to aneroid manometer to maintain pressure at 40 mmHg for 15 s. ECG was recorded up to 45 s after the maneuver and Valsalva ratio was computed manually. This procedure was performed thrice and the average of the ratio from the 3 Valsalva tests was considered as the final result.

Tilt Table Test

The BP, HR, and respiratory changes were recorded after 10-15 min of rest while patients were lying on the tilt table horizontally. The tilt table is self-designed, manually driven, and made by a local carpenter which enables the patients to change the posture at 90° vertical within 3-4 s. This is the advantage of our tilt table over the electric motor-driven tilt table which takes 10-15 s time in changing the posture which may allow the person for the cardiovascular adjustment.

In TTT, the HR changes and systolic BP (SBP) changes occurring due to the postural changes were recorded. The posture was changed from lying to standing expecting for maximum orthostatic effects on the cardiovascular system. The 30:15 ratio was calculated after the tilting of table at 90° for the assessment of HR functions. Difference in SBP between lying and after standing for 1 min was recorded and the values were interpreted. Any decrease in SBP <10 mmHg was considered as normal, between 11 and 20 mmHg as borderline, and >30 mmHg as abnormal value.

Statistical Analysis

Data are presented in the form of mean ± standard error mean. Statistical analysis is done using GraphPad Prism version 6. Unpaired student's *t*-test was used wherever required. The $P < 0.05$ is considered as statistically significant.

RESULTS

Valsalva Maneuver

The international normative Valsalva ratio (longest to shortest R-R interval) during VM is ≥1.21 and considered abnormal if it is ≤1.21. In this study, the mean Valsalva ratio of cases is 1.10 ± 0.05 versus Valsalva ratio in controls of 1.30 ± 0.07. When compared, it was found significantly lesser than the control ($P < 0.05$; Figures 1 and 2).

When Valsalva ratio of controls was compared with the international normative values of Valsalva ratio (≥1.21), it was greater but not significant.

Tilt Table Test (Lying to Standing)

HR Changes (30:15 Ratios)

The international normative HR changes (30th: 15th beat R-R ratio) from lying to standing is ≥1.04, borderline between 1.01 and 1.04, and abnormal if ≤1.00. In this study, the mean HR changes of cases are 0.92 ± 0.02 and mean HR changes of controls are 1.05 ± 0.03, when compared, it was found significantly lesser than the control ($P < 0.05$; Figures 3 and 4). When mean HR changes of control were compared with the international normative values (≥1.04) of HR changes, it was found similar.

Changes in SBP

The international normative SBP change from lying to standing is ≤10 mmHg, borderline between 11 and 20 mmHg, and abnormal if ≥30 mmHg. In this study, the changes in mean SBP after the change of posture (from lying to standing) of cases is 10.04 ± 0.89 mmHg and controls is 7.06 ± 0.76 mmHg. When compared, it was found significantly greater than the controls ($P < 0.05$; Figures 3 and 4). The SBP changes of female cases were compared with international normative value and were found within the normal limit.

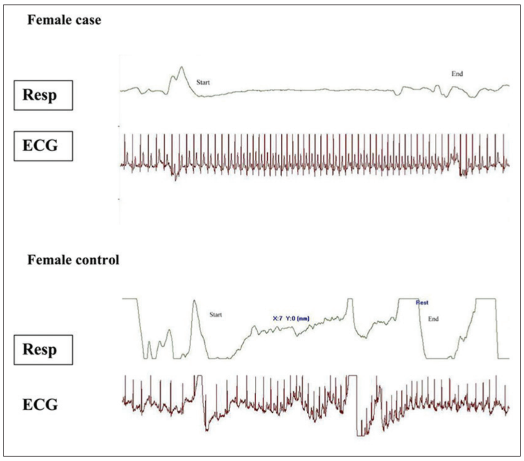

Figure 1: Original tracings showing Valsalva maneuvers in the ankylosing spondylitis cases and age- and sex-matched controls. Speed = 15 mm/s, sensitivity = 500 μv for respiration, and 50 μv for electrocardiogram

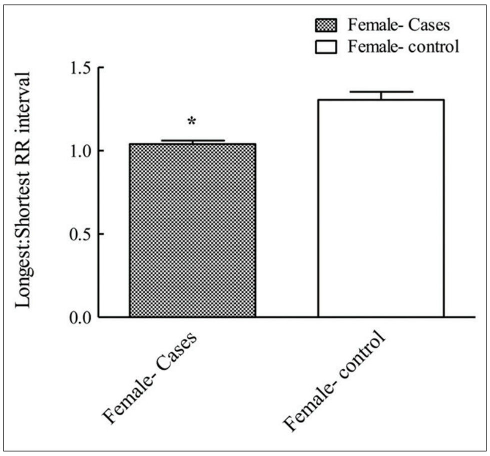

Figure 2: The histograms showing longest:shortest R-R interval (Valsalva ratio) during Valsalva maneuver in ankylosing spondylitis cases and age- and sex-matched controls. Data represents the mean ± standard error mean value of cases and controls. An asterisk "*" indicates $P<0.05$ as compared to the controls

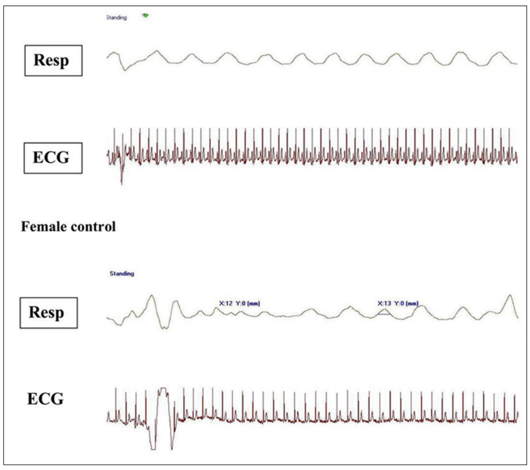

Figure 3: Original tracings showing heart rate changes during tilt-table testing in ankylosing spondylitis cases and age- and sex-matched controls. Speed = 15 mm/s, sensitivity = 500 μv for respiration, and 50 μv for electrocardiogram

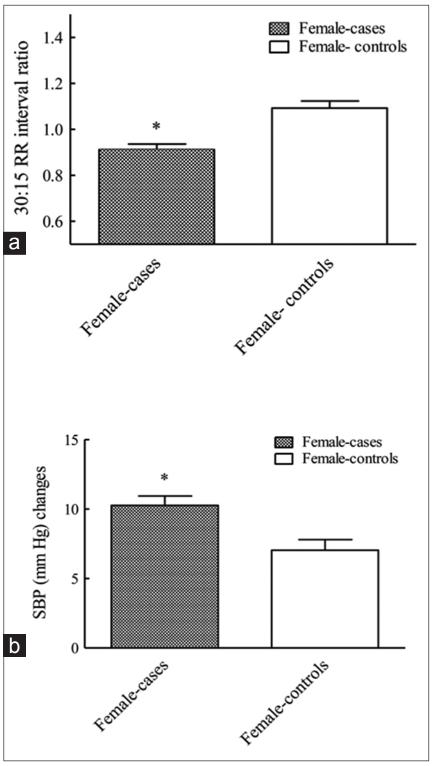

Figure 4: (a) The histograms showing heart rate changes (30:15 ratio) during tilt-table test (TTT) in ankylosing spondylitis (AS) cases and age- and sex-matched controls, (b) the histograms showing systolic blood pressure change during TTT in AS cases and controls. Data represents the mean ± standard error mean value of cases and controls. An asterisk "*" indicates *P*<0.05 as compared to the controls

DISCUSSIONS

AS is a chronic inflammatory disease which involves skeletal and extra-articular organs such as the lungs, eyes, heart, and neurological system.[5,12,13] The young adults between 20 and 40 years of age are most commonly affected with this disease[11] in contrary to the normal belief of involvement of older age group. The most common cardiac involvement in AS is aortic regurgitation, myocarditis with conduction disturbances, myocardial fibrosis causing abnormalities of left ventricular relaxation, and pericarditis.[14]

These patients exhibit the five major symptoms such as fatigue, spinal pain, joint pain/swelling, local tenderness, and morning stiffness which cause pain and severe discomfort to the patients. It is established that prolonged pain and discomfort causes alteration in the autonomic outflow. The autonomic nervous system governs the cardiovascular system and this fact has resulted to various studies showing relations between autonomic dysfunction and chronic pain.[9,10] Since any alterations in the autonomic nervous system bring about the changes in the cardiovascular parameters such as BP and HR, therefore, VM and TTT were performed in this study to evaluate the autonomic reactivity. The increase in HR during exercise is due to the activation of the sympathetic nervous system with simultaneous suppression of the parasympathetic nervous system.[15] The fall in HR immediately after exercise is considered to be the parasympathetic reactivation together with sympathetic withdrawal.

During VM, intrathoracic pressure is increased and the overall parasympathetic outflow of the body is decreased. As the increased intrapulmonary pressure causes the excitation of stretch receptors in the lung and nerve impulses generated converges on the cardioinhibitory area in the medulla. As a consequence, the parasympathetic outflow to the visceral organs is decreased. Since heart is also receiving the parasympathetic innervations; therefore, the decreased parasympathetic supply leads to decreased R-R interval and thereby resulting tachycardia.

In this study, the AS cases had significantly lower Valsalva ratio as compared to the age- and sex-matched controls indicating parasympathetic loss. It is well established that decrease in Valsalva ratio indicated parasympathetic loss. The decrease in parasympathetic activity may be due to sustained stimulation of the nociceptors which might be the cause for the shifting of sympathovagal balance toward sympathetic side in the patients suffering from the AS.

The assumption of the standing position after supine rest for 30 min results in venous pooling of blood and a transient decrease in cardiac output eliciting reflex activation of the sympathetic nervous system and a withdrawal of cardiac parasympathetic tone. This is reflected by characteristic changes in HR which increases abruptly toward a primary peak at around 3 s and secondary peak at around 12 s. It then declines to a relative bradycardia at about 20 s and then gradually increases again.[16]

In TTT, the HR changes and SBP changes from lying to standing were observed. In the cases, 30:15 ratio was found significantly lesser than the controls. This is indicative of decreased parasympathetic reactivity in the AS cases in comparison to the controls. In this study, the HR changes occurring after TTT is similar to the HR changes occurring during VM which is further supporting that there is a decrease in parasympathetic reactivity in the patients suffering from AS. The above findings are consistent with the work performed on the chronic pain using handgrip test and deep-breath test elsewhere.[17] However, the sample size is the limitation of this study; because of non-availability of the sufficient number of AS patients. Furthermore, planning of the interventional study could have been more informative in this type of study.

CONCLUSION

The value of Valsalva ratio is decreased in the AS patients in comparison to the controls indicating the parasympathetic loss which is further supported by the decrease in 30:15 ratio observed after the TTT. The increase in SBP in cases also supports the shifting of cardiac sympathovagal balance toward the sympathetic side in the AS patients.

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