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To study the cardiac autonomic functions in leprosy patients, a hospital based study- an original research article

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ABSTRACT

Aims and Objectives

The aim of this study was to evaluate cardiac autonomic functions in leprosy patients and to compare the same between paucibacillary, multibacillary leprosy patients and with the normal healthy subjects.

Materials and Methods

We studied twenty five paucibacillary, twenty five multibacillary leprosy patients and twenty five age matched healthy subjects. Non invasive bedside tests i.e. orthostatic test, Valsalva ratio, hand grip test, effect of deep breathing and standing were studied in all subjects.

Results

Both sympathetic and parasympathetic functions were altered in both the leprosy groups when compared to normal subjects. On intergroup comparison we observed that the paucibacillary group had higher values then the multibacillary leprosy group.

Conclusion

To comment regarding the alteration in cardiac autonomic function, this was a very small study group, we need larger study group to reach the proper conclusion.

Keywords: Paucibacillary; Multibacillary; Cardiac autonomic function; Sympathetic; Para-sympathetic.

INTRODUCTION

Leprosy is a chronic, infectious disease caused by Mycobacterium leprae. [1] More than 200,000 new cases are detected every year, most of them in developing countries such as India and Brazil. [2] The disease leads to several disabilities, including motor, sensory, and autonomic impairments. [3, 4] These complications affect the quality of life of the patients and are associated with high treatment and rehabilitation costs.

There is a significant amount of knowledge about the impairment of the motor, sensory, and autonomic functions caused by leprosy. [5, 6] The investigation of nervous functions has been important for identifying possible techniques that

monitor the neurological condition of patients, even when they have no clinical symptoms. Some studies have reported the association between peripheral neuropathy in leprosy and autonomic impairments such as cardiac autonomic neuropathy and the impairment of vasomotor reflexes. [7, 8, 9, 10] The altered coordination between sympathetic and parasympathetic actions of the autonomic system is prejudicial to patients suffering from leprosy due to decreased responsively of heart function to environment or internal changes. [7, 11]

As there are many indications of alteration of the autonomic nervous system caused by leprosy, we hypothesized that the autonomic balance in different postures could be altered in patients suffering with the disease compared to the healthy condition.

Who classifies leprosy, on the basis of findings from skin smears, as paucibacillary and multibacillary leprosy. In WHO classification , patients showing negative skin smears for acid fast bacilli (AFB) at all sites examined are grouped as paucibacillary leprosy where as patients having positive smear for AFB from any site are grouped as multibacillary leprosy. [1] Mycobacterium leprae not only affects somatic, motor and sensory nerves but also affects autonomic nerve fibres.

This study has been conducted to infer the autonomic function. [12, 13, 14, 15] However, there are very few studies in the literature comparing cardiac autonomic modulation in multibacillary and paucibacillary individuals at rest. This form of analysis could provide additional information about the impaired cardiac autonomic function involvement in leprosy. The relevance to evaluating the cardiac autonomic functions in leprosy patients is that this method is one more way to identify autonomic nerve functions that, together with other findings of autonomic, sensory, and motor functions, can assist in detecting nerve damage and the beginning of the treatment. Additionally, understanding sympathetic and parasympathetic heart functions can allow leprosy patients to help in the early prevention and treatment of heart diseases[16]. Therefore, the present study aimed to compare the cardiac autonomic functions in multibacillary and paucibacillary subjects.

AIMS AND OBJECTIVES

The aims of the study were

- To evaluate autonomic nervous system functions in leprosy patients.
- To compare the autonomic nervous system functions between paucibacillary, multibacillary leprosy patients and with the normal healthy subjects.

MATERIALS AND METHODS

A total of 50 cases (25 paucibacillary and 25 multibacillary) leprosy patients having symptoms related to, or as a consequence of, leprosy were enrolled for the study in the department of skin-VD and leprosy and referred to central research lab of BPS, GMC (W), Khanpur Kalan Sonipat for testing of cardiac autonomic neuropathy functions. All new cases were diagnosed on the basis of cardinal features of leprosy. Skin smears were taken from the eyebrows or earlobes and two active skin lesions for AFB. In doubtful cases, skin biopsy was done for histo-pathological confirmation. The cases were diagnosed as paucibacillary or multibacillary cases, based on clinical findings. Other investigations such as heamogram, urine examination, liver function tests, Kidney's function test and blood sugar levels were done. Cases were classified as paucibacillary or multibacillary on the basis of recent guidelines of the NLEP and treatment was given accordingly.

Classification

- Single lesion with negative smear – PB leprosy.
- Two to five lesions with negative smear-PB leprosy.
- Two to five lesions with positive smear-MB leprosy.
- More than five lesions with positive smear-MB leprosy.
- Twenty five normal healthy subjects were also tested as controls and results of the study were concluded. Subjects were selected by certain inclusion and exclusion criteria.

Inclusion criteria

- Age group 18-60 years.
- Any newly detected case of leprosy.

- Cases already on treatment, but those that have not completed the total duration of treatment.

Exclusion Criteria

- Mono-lesional cases were not included.
- Neuropathy because of diabetes, hypertension, chronic alcoholism, polio and other autoimmune disorders were excluded from the study.

Experimental procedures

The cardiac autonomic functions were conducted at the Central Research Laboratory at BPS, GMC (W), Khanpur Kalan, Sonepat. The room temperature was artificially controlled between 22°C and 24°C, and air humidity was kept between 40% and 60%. The autonomic functions were obtained using the CAN system which recorded the sympathetic and parasympathetic functions.

The volunteers lied down for 10 minutes and were not allowed to talk or perform movements to stabilize the cardiovascular parameter. Afterward, the heart rate capture was performed for 15 minutes in the supine position. Then, the subject moved from the supine position to the sitting position with a backrest with the knees flexed at 90° and the feet touching the floor. Again, the heart rate was recorded during 15 minutes. All the data were collected in the same time range (between 8:00 a.m. and 12:00 a.m.).

Following cardio vascular parasympathetic tests were carried out

Effect of deep inspiration & expiration on heart rate (E:I ratio). Beat to beat variation in heart rate with respiration depends on parasympathetic innervations. The patient lies quietly and breathe deeply at rate of 6 breaths per minutes (a rate that produces maximum variation in heart rate) while a heart monitor records the difference between the maximum and minimum heart rate.

Heart rate response to standing (30:15 ratios). This test evaluates the cardiovascular response elicited by a change from horizontal to a vertical position. The typical heart rate response to standing is largely attenuated by a parasympathetic blockage achieved with atropine. In healthy subjects, there is characteristic and rapid increase in heart rate in response to standing that is maximal at approximately the 15th beat after standing. This is followed by a relative bradycardia that is maximal at approximately 30th beat after standing. In patient with diabetes and autonomic neuropathy, there is only a gradual increase in heart rate. Because the maximum and minimum R-R intervals may not always occur at exactly 15-30 beat after standing.

Valsalva ratio: In healthy subjects, the reflex response to the Valsalva maneuver includes tachycardia and peripheral vasoconstriction during strain, followed by over shoot of blood pressure and bradycardia after release of strain. In patients with autonomic damage there is blunted heart rate response.

Following cardiovascular sympathetic tests were carried out

Change in blood pressure due to change of posture (Δ SBP):- the subject was asked to relax and lie down comfortably. Blood pressure was measured for the first time in supine position when green light glow on the screen, then when red light glow, the subject was asked to stand up quickly and the blood pressure was recorded immediately after standing for the second time. Then the blood pressure was recorded again after 1 minute of standing. At the end of test, the result was displayed.

Change (rise) in diastolic blood pressure during isometric grip exercise (sustained hand grip test-SHG) (Δ DBP). The blood pressure was recorded in sitting position. Then the subject was asked to hold a spring dynamometer in the dominant hand instructed to compress the dynamometer with full effort for a period of 5 minutes. The blood pressure was recorded thrice during these 5 minutes automatically. The alteration in blood pressure just before the release of spring dynamometer was taken as index of response to hand grip test.

All the data for the above tests was recorded and statistical analysis was carried out.

RESULTS

In the final analysis there were 25 paucibacillary leprosy patients (mean age 40.12±13.27) 25 multibacillary leprosy patients (mean age 36.12±11.60) and 25 normal healthy subjects (age range 18-60 years). There was male dominance in all the groups (64% male patient among leprosy patients and 70% among controls). The statical analysis for para sympathetic tests was

carried out separately in all three groups. After analysis all the three groups, the cardiac para sympathetic functions were compared within the three groups. Table 1 shows mean and standard deviation values for parasympathetic parameters (E:I ratio, 30:15 ratio and Valsalva) for all the three groups.

Table 2 shows parasympathetic parameters in (group 1) control and paucibacillary group (group 2). Control group shows higher values for all the parameters as compared to values for paucibacillary group, which has ϕ value 0.001 that is statistically significant.

Table 3 shows group wise comparison of mean ± SD between control (group 1) and multibacillary patients (group 2). Control (group 1) shows higher values for all the parasympathetic parameters as compared to values of multibacillary patients (group 3). P value is 0.001 for the parameters and which is statically significant.

Table 4 shows comparison between parasympathetic parameters of paucibacillary and multibacillary groups. Paucibacillary patients (group 2) have higher values for all the parasympathetic parameters as compared to values of multibacillary (group 3). P value is <0.05 for all the parameters and is statically significant.

Table 5 shows comparison of sympathetic function tests between control and leprosy patients. It shows control group has lower values for sympathetic parameters (orthostatic hypotension test, hand grip test) as compared to paucibacillary and multibacillary group. It also shows that the multibacillary leprosy patient has lower values of sympathetic parameters as compared to values of paucibacillary leprosy patients. P value is 0.001 in both sympathetic test and which is significant.

Table 1:- Group wise distribution of mean and SD values for parasympathetic test.

Test	Group I (control) Mean ±sd	Group II (PB) Mean ±sd	Group III (MB) Mean ±sd
E:I Ratio	69.12±13.56	47.24±17.38	6.68±2.19
30:15 Ratio	1.24±0.22	1.03±0.77	0.71±0.39
Valsalva	18.52±19.87	9.06±15.40	0.51±0.26

Table 2:- Group wise comparison of mean values (control and PB group)

Test	Group I (control) Mean ±sd	Group II (PB) Mean ±sd	p value
E:I Ratio	69.12±13.56	47.24±17.38	0.001
30:15 Ratio	1.24±0.22	1.03±0.77	0.001
Valsalva	18.52±19.87	9.06±15.40	0.001

Table 3:- Group wise comparison of mean values (control and MB group)

Test	Group I (control) Mean ±sd	Group III (MB) Mean ±sd	p value
E:I Ratio	69.12±13.56	6.68±2.19	0.001
30:15 Ratio	1.24±0.22	0.71±0.39	0.001
Valsalva	18.52±19.87	0.51±0.26	0.001

Table 4:- Comparison of Group II(PB) and Group III(MB).

Test	Group II (PB) Mean ±sd	Group III (MB) Mean ±sd	p value	Result
E:I Ratio	47.24±17.38	6.68±2.19	<0.05	significant
30:15 Ratio	1.03±0.77	0.71±0.39	<0.05	significant
Valsalva	9.06±15.40	0.51±0.26	<0.05	significant

Table 5:- Comparison of Sympathetic function tests (control Vs Cases)

Parameter BP (mmHg)	Control (n= 25)	Cases (n= 50) PB (n= 25)		MB (n=25)		P value
		mean	SD	Mean	SD	
Δ SBP (orthostatic hypotension test)	2.44 ± 2.08	7.84	4.723	6.2	5.212	0.001
Δ DBP (hand grip test)	2.28± 1.542	7.72	9.05	6.6	2.915	0.001

DISCUSSION

To measure and compare the effects of leprosy on cardiac autonomic functions, the analysis was done separately in all the three groups (group 1 control, group 2 paucibacillary, group 3 multibacillary). The results indicate that parasympathetic functions were decreased in both the leprosy groups.

No such study was conducted till now. Motor nerve conduction in leprosy patient was first study by Direkar in 1965. Out of 27 patients with leprosy, reduced motor verve velocities were observed. [17] Reduced motor nerve conduction velocity of the ulnar nerve at elbow was observed. R-R interval variation in leprosy patients was studied by Soysal A et al. [7] R-R intervals were found to be reduced in leprosy patients as compared to control and statistically significant. This showed parasympathetic innervations of the heart. Ulvi H et al studied R-R interval and sympathetic skin response in the assessment of the autonomic nervous system in leprosy patients. [11] The mean value of R-R interval variation was significantly lower when compared with the controls. The means Valsalva ratio in leprosy patients was smaller when compared to controls. The mean difference of systolic and diastolic blood pressure between supine rest and during standing in leprosy patients was higher compared to controls, but they did not reach statistical significance. These data indicates leprosy patients have the functional abnormalities of autonomous nervous system.

CONCLUSION

Parasympathetic functions were decreased in both the leprosy groups (multibacillary and paucibacillary) when compared to normal subjects .On intergroup comparison, we observed that the paucibacillary leprosy group had higher values (E:I ratio , 30:15 ratio, Valsalva ratio) than the multibacillary leprosy group ($p < 0.01$). We found that the leprosy group had higher sympathetic function tests values when compared to control subjects.

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