



EFFECT OF DISEASE DURATION ON CARDIAC AUTONOMIC FUNCTION TESTS IN PSORIATIC PATIENTS

Physiology

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ABSTRACT

Background: Psoriasis is a chronic, genetically determined and immune-mediated inflammatory disease of unknown etiology with a prevalence of 1-3% of human population worldwide and 0.44-2.8% in India. The literature reports an increased risk of cardiovascular diseases in Psoriatic patients. The present study was designed to explore the effect disease duration on autonomic functions in Psoriatic patients.

Aim and Objectives: The present study was aimed to assess the autonomic status in patients with Psoriasis in the early stage of the disease and in patients with chronic Psoriasis with an extended purpose to explore the effect of the duration of the disease on the autonomic nervous system in Psoriatic patients aged 30-40 years as compared to age and sex matched healthy controls.

Material and Methods: The present study was conducted in Department of Physiology of SMSMC on Psoriatic patients of both genders which were recruited from the Dermatology Department of SMS Hospital grouped in to new Psoriasis (n=40) (Less than one year) and old Psoriasis (n=40) patients group (more than one year). Age matched healthy subjects acted as controls (n=40). Parasympathetic function tests include E:I ratio, 30:15 ratio (lying to standing ratio) and Valsalva ratio; sympathetic function tests include blood pressure response to standing and blood pressure response to isometric hand grip.

Result: Change in diastolic blood pressure during IHG exercise was significantly lower in chronic/old Psoriatic patients. Change in systolic blood pressure on immediate standing was higher in chronic/old Psoriatic group ($p < 0.05$). E:I ratio, Valsalva ratio and 30:15 ratio were significantly decreased ($p < 0.05$) in chronic/old Psoriatic patients as compared to the new patients.

Conclusion: The deranged autonomic function tests in Psoriasis patients suggested definite autonomic dysfunction. Duration of disease seems to influence autonomic functions in patients with Psoriasis. Involvement of the parasympathetic system occurs in early phase of the disease and with increasing duration of the disease the sympathetic system also gets compromised. The cause of this progressive involvement could be due to the Psoriasis related alteration in the cardiovascular function due to the inflammatory mediators such as tumor necrosis factor-5 (TNF-5), IL-1, IL-12, IL-23, and IL-17. These inflammatory mediators act independently of conventional cardiovascular risk factor which promotes atherosclerosis. Therefore, routine autonomic function assessment of Psoriatic patients is necessary for a better prognosis.

KEYWORDS

Psoriasis, Sympathetic, Parasympathetic And Cardiovascular Risk.

INTRODUCTION

Psoriasis is one of the most prevalent T-cell-mediated chronic inflammatory diseases affecting around 1-3% of human population worldwide (1). Despite quite considerable advances in the last years, its pathogenesis is still not fully elucidated; however, inflammatory processes and oxidative stress are among those most frequently delineated (2). There is a clear genetic component with multifactorial inheritance and interactions between genetic predisposition and the environmental factors observed in the majority of patients (3,4). Several studies documented an increased prevalence of cardiovascular (CV) diseases and related mortality in patients affected by severe Psoriasis [Gelfand et al., 2006; Mehta et al., 2010]5. It has been shown in general population that the unbalance of the autonomic cardiovascular regulation system toward the sympathetic arm correlates with an increased CV risk [Sajadieh et al., 2004]6. Cardiac Autonomic Function Test has emerged as a simple, noninvasive method to evaluate the sympathovagal balance within the autonomic control of sinus node (7). There have been studies incriminating dysautonomia as one of the most important yet ignored causes of cardiovascular diseases in Psoriatic patients (8). The pathophysiology however remains unclear as the studies show contradictory results. There are some studies suggesting autonomic imbalance with a shift towards the sympathetic arm (9), there are others suggesting an involvement of only the parasympathetic system and a few suggesting that no such involvement of either of the systems occurs in Psoriasis (10). Due to the paucity of knowledge regarding the status of the autonomic function in the Psoriasis patients, we hypothesized that the contradictory results could be related to the effect of the course and duration of the disease on the autonomic nervous system. Hence in our study we made an attempt to assess the autonomic status in patients with Psoriasis in the early stage of the disease as recently diagnosed and in patients with chronic Psoriasis with a purpose to achieve an idea about the effect of the duration of the disease on the autonomic nervous system.

MATERIAL AND METHOD

The present study was a hospital based observational type of study

conducted in Department of Physiology of SMSMC on Psoriatic patients (Based on duration of the disease they were grouped in to new Psoriasis (n=40) Less than one year and old Psoriasis (n=40) patients group (more than one year), in the age group of 30-40 years and forty age and gender matched healthy controls. Psoriasis patients were recruited from Psoriasis clinic in Dermatology Department of SMS Hospital after a careful examination of the skin lesions by dermatologist. The age and gender matched healthy controls were selected from the accompanying attendants of the patients. Prior approval and consent was obtained by the institutional ethics committee and institutional research review board. A written informed consent was obtained from all the subjects before commencing any procedure. Patients having diabetes mellitus, thyroid disorders, vitamin B₁₂ deficiency, any form of anemia, patients on neuro protective and antihypertensive drugs, cardiac failure, cardiac arrhythmia, psychosomatic and neurological (Parkinsonism, ataxia etc.) disorders were excluded from the study.

ANS Function Assessment:

All the subjects were instructed to avoid caffeine for at least 4 hours and food for preceding 2 hours before the test. All the subjects were laid down in quiet room, with a room temperature of 25 °C. ANS function tests were carried out in the ANS function's laboratory. Cardiovascular autonomic function assessment was done according to Ewing's battery (7) using RMS CANWIN (cardiac autonomic neuropathy analyzer) machine between 9 -11 AM after a rest of 15 min. The autonomic function tests used were parasympathetic and sympathetic reactivity tests.

a) Parasympathetic Reactivity Tests.

1. Resting Heart Rate
2. Heart Rate Response to Deep Breathing (E:I Ratio)
3. 30:15 Ratio
4. Valsalva Maneuver

b) Sympathetic Reactivity Tests.

1. Blood Pressure (BP) Response to Standing
2. Blood Pressure response to Isometric hand grip (IHG) exercise

STATISTICAL ANALYSIS :

The data were statistically analysed using the SPSS software version 22. Mean and standard deviation of the variables determined for the three groups. One way ANOVA test was applied for statistical analysis. Difference of significance in inter and intra group of Psoriatic patient was assessed by Post hoc tukeys test. Statistical significance was assigned at p value 0.05.

RESULTS

Table-I shows the baseline characteristics of Psoriatic patients grouped as per duration newly diagnosed (less than one year) and old chronic patients (more than one year) and control groups. Age, height, weight and body mass index did not show any statistically significant difference between the three groups. Change in DBP during IHG exercise (Table II) that is a measure of sympathetic reactivity (9.60 ± 5.08 mm Hg) was significantly lower in chronic/old Psoriasis patients as compared to the new (12.47 ± 3.32 mm Hg) and controls (13.47 ± 2.28 mm Hg). Change in SBP on immediate

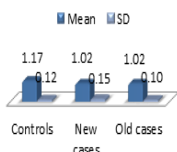
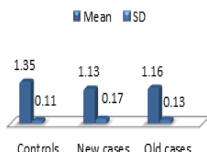
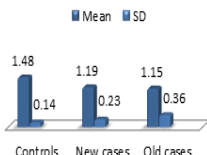
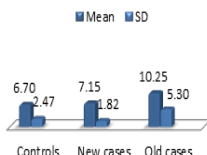
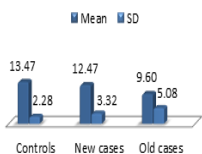
standing was higher in chronic/old Psoriasis group (10.25 ± 5.30 mm Hg) as compared to new (7.15 ± 1.82) and controls (6.70 ± 2.47 mm Hg) and the difference was statistically significant ($p < 0.05$). E:I ratio, Valsalva ratio and 30:15 ratio, that are indicators of parasympathetic reactivity showed significant ($p < 0.05$) fall in Psoriasis patients as compared to the healthy controls.

OBSERVATIONS**Table 1: Baseline Clinical Characteristics Of The Psoriasis (new And Old) And Control Groups**

Variables	Control(40)	New Patients(40)	Old Patient(40)	Pvalue
Age(years)	33.48 $\pm$ 3.40	33.15 $\pm$ 3.94	32.43 $\pm$ 2.37	NS
Weight(Kg)	55.45 $\pm$ 4.95	56.20 $\pm$ 5.25	56.10 $\pm$ 9.84	NS
Height(m)	1.61 $\pm$ 0.08	1.61 $\pm$ 0.09	1.60 $\pm$ 0.10	NS
BMI(Kg/m ²)	21.70 $\pm$ 3.35	21.80 $\pm$ 3.30	22.07 $\pm$ 3.89	NS
RestingHeartRate perminute	74.45 $\pm$ 6.74	73.30 $\pm$ 6.81	73.37 $\pm$ 4.92	NS

Table 2: Autonomic Function Test(aft) In Psoriasis(new And Old) And Control Groups.

AFTVariables	Controls(40)	New Patients(40) (less than one year)	Old Patients(40) (more than one year)	Control Vs New	Control Vs Old	New vs Old
30:15ratio	1.17 $\pm$ 0.12	1.02 $\pm$ 0.15	1.02 $\pm$ 0.10	S	S	NS
E:Iratio	1.35 $\pm$ 0.11	1.13 $\pm$ 0.17	1.16 $\pm$ 0.13	S	S	NS
ValsalvaRatio	1.48 $\pm$ 0.14	1.19 $\pm$ 0.23	1.15 $\pm$ 0.36	S	S	NS
BPreponseto standing(fall in systolic BP) MmofHg	6.70 $\pm$ 2.47	7.15 $\pm$ 1.82	10.25 $\pm$ 5.30	NS	S	S
BPreponseto IHG(Rise in Diastolic BP) MmofHg	13.47 $\pm$ 2.28	12.47 $\pm$ 3.32	9.60 $\pm$ 5.08	NS	S	S

Comparison of 30:15Ratio**Figure 1****Comparison of E:I Ratio****Figure 2****Comparison of Valsalva Ratio****Figure 3****Comparison of BP response to Standing****Figure 4****Comparison of BP response to IHG****Figure 5****DISCUSSION**

The present study demonstrated the extent of autonomic dysfunctions in Psoriatic patients with respect to the duration of the disease. In recently diagnosed (new) patients of Psoriasis there appears to be a compromise of only the parasympathetic activity and in patients of chronic (old) Psoriasis there is involvement of both the parasympathetic as well as the sympathetic system. Psoriasis patients who were diagnosed recently i.e. duration of the disease one

year or less without clinically overt features of autonomic dysfunction showed compromised parasympathetic activity as evidenced by 30:15 ratio (Figure 1), E:I ratio (Figure 2) and Valsalva ratio (Figure 3). Patients with history of Psoriasis of duration more than 1 year showed decreased parasympathetic activity as well as decreased sympathetic reactivity evidenced by BP response to standing (Figure 4) and IHG test (Figure 5). The cause has been attributed to the inflammatory mediators such as tumor necrosis factor-5 (TNF-5), IL-1, IL-12, IL-23, and IL-17. (11). These inflammatory mediators act independently of conventional cardiovascular risk factor which promotes atherosclerosis (12). Impairment in the autonomic function leads to increased cardiovascular disease risk in the Psoriasis patients (13,14). The status of the Autonomic function in Psoriasis have shown controversial results. Haligur et al., found derangement of sympathetic system in the Psoriasis by sympathetic skin response (SSR) and R-R interval variation (RRIV) (8). Pancar Yuksel E. et al., 2014 using heart rate recovery index (HRRI) had observed the impairment of parasympathetic system in Psoriatic patients (16). Biçer et al., 2010 denied involvement of the autonomic in the Psoriasis patients in 24 hrs Holter recording for heart rate variability (HRV) and turbulence analysis (10). The possible reason for the varied results might be due to the heterogeneity in the severity and duration of the disease among the patients. In our study, we have compared patients who were recently diagnosed as well as the ones with disease of longer duration with the normal subjects and found that the autonomic function was differently compromised in the two groups of patient. Recently diagnosed patients showed parasympathetic derangement, whereas chronic patients have both sympathetic and parasympathetic involvement. But in the above mentioned studies the disease duration was not taken into consideration and a heterogeneous group of Psoriasis patients were recruited as well as only one method was used to assess the autonomic function. The differing results in the newly diagnosed and the chronic patients could be attributed to the level of inflammatory markers and their association with the disease duration. When considered the limitations of this study, small number of the study patients is the major limitation. Larger studies are needed to support our results. This preliminary study opens up an opportunity to make further research in patients with Psoriasis to assess autonomic functions including the immune status and its contribution to autonomic dysfunction.

CONCLUSION

In conclusion, autonomic functions in Psoriatic patients seems to be effected by disease duration. Involvement of the parasympathetic system occurs in early phase of the disease and with increasing duration of the disease the sympathetic system also gets

compromised. Alteration in the cardiovascular function due to the inflammatory mediators such as tumor necrosis factor-5 (TNF-5), IL-1, IL-12, IL-23, and IL-17. These inflammatory mediators act independently of conventional cardio vascular risk factor which promotes atherosclerosis further contributes to the cause of this progressive involvement, however this requires further investigation.

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