Idiopathic Hyperhidrosis; Is response to Parasympathetic function test altered?

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ABSTRACT

Background:*Idiopathic Hyperhidrosis is characterized by excessive sweating, especially of palms and feet. It is said to be due to sympathetic over activity. However, autonomic nervous system as a whole, itself could be dysfunctional in this condition, rather than isolated sympathetic dysfunction. Thus, we have undertaken the present study to test and compare the autonomic function status in these patients with age and sex matched healthy individuals.*

Material and Methods: *Twenty, normal subjects with no known autonomic dysfunction as controls and twenty, known idiopathic Hyperhidrosis patients as subjects were taken for the present study. Autonomic function tests were performed in both these groups and were compared.*

Result:*Sympathetic function tests, which were performed, were within the normal range whereas parasympathetic tests were normal except for response to deep breathing test, which showed a significant increase ($P < 0.01$) in the Hyperhidrosis patients, compared to the controls.*

Conclusion:*Response to deep breathing, a parasympathetic test was significantly increased in patients with Hyperhidrosis compared to controls in the present study, which will conclude the study with the findings that the idiopathic Hyperhidrosis seems to be a complex dysfunction of autonomic nervous system, that involves autonomic pathways other than those related to excess sweating.*

Keywords:*Idiopathic Hyperhidrosis; Autonomic Function Test; Parasympathetic dysfunction; Sympathetic over activity.*

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INTRODUCTION

Idiopathic Hyperhidrosis, also called as Primary Hyperhidrosis is a syndrome which presents with excess sweating of the palms of the hands and soles of the feet. Hyperhidrosis is sweating beyond what is necessary to maintain thermal regulation or it is a condition characterized by excessive or profuse sweating in certain body regions. It can either be generalized or localized to specific parts of the body. This disorder affects 0.6-1.0% of the population. The etiology of this disorder is unclear though there may be genetic components, involving in this condition(1). Hyperhidrosis is believed to be due to sympathetic over activity and sympathectomy is one of the treatment procedures in these patients. Since etiopathogenesis of this disorder is unclear, sympathetic functions, being a part of autonomic nervous system is being performed in these patients to establish the possible involvement of this system in these patients.

Primary Hyperhidrosis is idiopathic in nature or is not associated with an underlying condition. Typical regions of excessive sweating include the underarms, palms, soles, groin and craniofacial areas. This disorder, also known as focal Hyperhidrosis is found to start during adolescence or even before. It is diagnosed by patients' report and by a physical examination. Focal Hyperhidrosis can have a significant impact on quality of life. Individuals can be affected from a social, psychological, emotional and professional perspective. Affected people are constantly aware of their condition and try to modify their lifestyle to accommodate this problem. This can be disabling in professional, academic and social life, causing embarrassments. Many routine tasks become impossible chores, which can psychologically drain these individuals.

As there are only few studies and literatures available regarding the evaluation of autonomic function tests in Hyperhidrosis patients and even less on primary Hyperhidrosis, this study was undertaken to assess the components of sympathetic and parasympathetic activity in these patients and to compare with age and sex matched healthy individuals.

MATERIALS AND METHODS

Source of data

The autonomic function test was assessed in control subjects and the Primary Hyperhidrosis patients, who are visiting the Dermatology department, KIMS, HUBLI.

Inclusion criteria

Twenty known cases of idiopathic Hyperhidrosis of 12-30 years of age of both sexes attending the Dermatology OPD of KIMS, Hubli and twenty age and sex matched healthy controls were included in the study. Informed consent was taken from each subject prior to the commencement of study.

Exclusion criteria

1. Individuals with age <10 years or >30 years.
2. Individuals with generalized hyperhydrosis, which may be due to infections like tuberculosis, malignancies like Hodgkin disease.
3. Patients with chronic diseases such as diabetes mellitus, renal failure, amyloidosis and other diseases, known to interfere with autonomic nervous system.
4. Patients with hypertention, ischemic heart diseases, congestive cardiac failure, valvular heart diseases, cardiomyopathy, cardiac arrhythmias.
5. Patients with neurological diseases such as multiple sclerosis, Guillain–Barré syndrome.
6. Patients with drug treatment, which are known to affect the autonomic nervous system including diuretics, antiarrhythmics, neuroleptics, antiepileptics and antihypertensive drugs.
7. Patients with signs and symptoms of anemia.
8. Pregnant patients.

STUDY DESIGN

Methods of collection of data

After considering the inclusion and exclusion criteria, the study groups were selected. The subjects were explained about the autonomic function tests, which have to be done and instructions were given to the subject before each parameter/component is done. The results were tabulated for analysis.

Tests, which were assessed in the present study

A) For Sympathetic functions

1. BP response to standing:

The test was performed by measuring the subject/patient's blood pressure with a sphygmomanometer while he/she is lying down quietly and again when he/she stands up. The postural fall in blood pressure was taken as the difference between the systolic blood pressure (lying) and the systolic blood pressure (standing) (2).

2. BP response to hand grip test:

The maximum voluntary contraction was determined first using a handgrip dynamometer. Handgrip was then maintained at 30% of that of maximum value as long as possible for the subject/patient up to five minutes. Blood pressure was measured three times before and at every one-minute interval during handgrip. The result was expressed as the difference between the highest diastolic blood pressure during handgrip exercise and the mean of the three diastolic blood pressure readings before the handgrip began (2).

3. Mental stress [Arithmetic] test:

This test is based on performing serial subtraction (usually 100 minus 7 or 1000 minus 13) which aims at activating sympathetic outflow. The subsequent increase in systolic blood pressure should exceed 10 mmHg (3).

B) For Parasympathetic functions

1. Resting heart rate:Resting heart rate was recorded in supine position on an electrocardiograph, in both the control and study subjects.

2. 30:15 pulse ratio [Immediate heart rate response to standing]: During the change from lying to standing, a characteristic immediate rapid increase in heart rate occurs, which is maximal at about the 15^{th} beat after standing. A relative overshoot bradycardia then occurs, maximal at about the 30^{th} beat.

This test was performed with the subject/patient lying quietly on a couch while the heart rate being recorded continuously on an electrocardiograph. The subject/patient was then asked to stand up unaided, and the point at started to stand was marked on the electrocardiogram. The shortest R-R interval at or around the 15^{th} beat and the longest R-R interval at around the 30^{th} beat after starting to stand was measured. The characteristic heart-rate response was expressed by the 30:15 ratios (2).

3. Expiration: Inspiration ratio:Subject was asked to breathe deeply at a rate of six breaths per minute. A standard ECG recording was taken during deep inspiration and expiration. Variation in heart rate was calculated as the rate of longest R-R interval during expiration to shortest R-R interval during inspiration. A value of 1.20 or higher was taken as normal (4).

4. Heart-rate (R-R interval) variation during deep breathing:Subject sits quietly and breathes deeply at six breaths a minute (5 seconds in and 5 seconds out) for 1 minute. ECG is recorded throughout the period of deep breathing. Onset of each inspiration and expiration is marked and the difference in R-R

interval (maximum R-R interval – minimum R-R interval) is calculated (2).

5. HR response to Valsalva maneuver:The test was performed by the subject/patient blowing into a mouth-piece connected to a modified sphygmom-anometer and holding it at a pressure of 40 mm Hg for 15 seconds while a continuous electrocardiogram is recorded. The manoeuvre was performed three times with one minute interval in between.The result was expressed as the Valsalva ratio, which is the ratio of the longest R-R interval after the manoeuvre (reflecting the overshoot bradycardia following release), to the shortest R-R interval during the manoeuvre (reflecting the tachycardia during strain). Ratio >1.21 is said to be normal (2).

STATISTICAL ANALYSIS

Student't' test was used to analyze the data. Sympathetic and parasympathetic tests were conducted and the data obtained for controls and cases were analyzed by 'SPSS software' to compare the different data. P value < 0.01 was considered as significant in this study.

RESULT

In the present study, we assessed the autonomic functions in patients with Idiopathic Hyperhidrosis and compared their autonomic status with that of age and sex matched healthy individuals.The main clinical characteristics related to autonomic functions in study and control groups are presented in this section. The results of sympathetic and parasympathetic function tests are summarized in Table 1 and Table 2 respectively.

Table 1: Sympathetic functions in control and study group individuals

Tests	Control	Hyperhidrosis Subjects
Blood pressure response to standing(mm Hg).	8.8 ± 0 .81	9.7 ± 0.36
Blood pressure response to sustained handgrip (mm Hg).	18 ± 1.01	17.9 ± 0.93
Mental Arithmetic Test (mm Hg)	16 ±2.62	16 ±2.70

*Data expressed as Mean ± SEM. (n=20)P< 0.01. *Significance.*

Table 2: Parasympathetic functions in control and study group individuals

Tests	Control	Hyperhidrosis Subjects
Resting Heart rate (Beats/ minute)	83.4 ± 3.47	87.4 ± 3.27
30:15 Pulse ratio (Immediate heart-rate response to standing)	1.94 ± 0.28	1.69 ± 0.19
Expiration: Inspiration ratio	0.61 ±0.01	0.60 ± 0.02
Heart rate (R-R interval) variation during deep breathing (Beats/minute)	38.1 ± 1.11	47.4 ± 2.60 *
Heart rate response to Valsalva manoeuvre (Valsalva Ratio)	1.889 ± 0.11	1.71 ± 0.11

*Data expressed as Mean ± SEM. (n=20), P< 0.01. *Significance.*

In the present study, all the sympathetic function tests were within the normal expected range where as all the parasympathetic tests were within the normal range except for the heart rate variation during deep breathing test, which showed a significant increase in the Hyperhidrosis patients, compared to the controls.

DISCUSSION

Cardiovascular autonomic function tests have been widely used to assess sympathetic and parasympathetic functions in different diseases.

Idiopathic Hyperhidrosis is a sweating disorder. The cause of this dysfunction is not well known. Hyperactivity of the sympathetic nervous system is widely believed to be responsible for the increased sweating in this disorder(5). Sweating centers, which are regulated at the level of neocortex and limbic systems, are hypothesized to be hyper-responsive to mental and emotional stimuli in patients with Hyperhidrosis(6). Nerve supply to the sweat glands in the body is sympathetic cholinergic except to the sweat glands on palms of hands, which is supplied by the parasympathetic nerve(7). As idiopathic Hyperhidrosis involves palms, sole and other areas of the skin, both sympathetic and parasympathetic dysfunction is expected in this condition. Parasympathetic hyperactivity is considered to be a predictor of high cardiovascular disease-related mortality in certain conditions.

In the present study, we conducted and compared the autonomic function tests in Idiopathic Hyperhidrosis patients with age and sex matched controls. Our study showed no significant differences in sympathetic function tests in these patients, compared to control. The parasympathetic tests like Resting heart rate, Expiration/Inspiration ratio, 30:15 pulse ratio and Heart-rate response to Valsalva maneuver did not show significant difference except for the Heart rate variation during deep breathing test,

which showed a significant increase ($p < 0.01$) in Hyperhidrosis patients.These observations may reveal that idiopathic Hyperhidrosis seems to be a complex dysfunction that involves autonomic pathways other than those related to sweating.

In the present study, cardiovascular autonomic function tests revealed that patients with Hyperhidrosis displayed a greater fall in systolic pressure values than controls in orthostatism though it was statistically non significant. Orthostatism and head-up tilt to 65° can be used to assess the presence of postural hypotension, defined as a fall of more than 20 mm Hg in systolic blood pressure on standing (8). The reason for such response in these patients is not clear. One explanation for this response may be excessive sweating and insufficient water intake. Indeed, dehydration is known to induce postural hypotension (9).

An increase in the diastolic blood pressure response to isometric hand grip and mental arithmetic test may be due to sympathetic nervous system activation. Sustained hand grip is a type of isometric exercise. With the start of an isometric muscle contraction, pulse rate is increased. This is largely due to a reduction in vagal tone, although increase discharge in cardiac sympathetic fibers also plays a role. Thereafter, the systolic and diastolic blood pressure also rises sharply. The rise in diastolic blood pressure will be abnormally small if there is extensive peripheral sympathetic abnormality. However, in the present study we were not able to appreciate such significant changes in Hyperhidrosis patients.

We performed four tests to assess parasympathetic function in Hyperhidrosis patients. The resting heart rate, 30:15 pulse ratio, the Expiration: Inspiration ratio, Heart rate variation during deep breathing and Heart rate response to Valsalva maneuver were assessed. In the present study, all the parasympathetic tests were within the normal range except for the heart rate variation during deep breathing test, which showed a significant increase in the Hyperhidrosis patients, compared to the controls. This result is in agreement with the previous study conducted by Marinis DM et al., (10) in which the heart rate response to deep breathing, Valsalva maneuver and hyperventilation revealed a marked parasympathetic hyperactivity in patients with idiopathic Hyperhidrosis. However, in our study, we could appreciate significant changes, only in heart rate variation to the deep breathing test and not in any other parasympathetic test in these patients.

Heart rate variation to the deep breathing test is a reliable and sensitive clinical test for early detection of cardiovagal dysfunction in a wide range of autonomic disorders(11). In most of the autonomic disorders, parasympathetic function is affected before sympathetic function. Therefore, this test provides a sensitive screening measure for parasympathetic dysfunction in many autonomic disorders. The relevance of our result, particularly the parasympathetic hyperactivity in our study subjects, may be considered based on such observations.

CONCLUSION

The present study concludes with the findings that, the heart rate response to deep breathing, a parasympathetic test is significantly changedin patients with Idiopathic Hyperhidrosis. Thus, idiopathic Hyperhidrosis seems to be a disorder with complex dysfunction of autonomic pathways, other than those related to sweating.

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