Research Article

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 of the hands and soles of the feet. It is said to be owing to sympathetic overactivity. However, autonomic nervous system as a whole could be dysfunctional in this condition, rather than isolated sympathetic dysfunction. **Aims and Objective:** We have undertaken this study to test and compare the autonomic function status in these patients with age- and sex-matched healthy individuals. **Materials and Methods:** Twenty, normal subjects with no known autonomic dysfunction as controls and 20, known idiopathic hyperhidrosis patients as subjects were taken for this study. Autonomic function tests were performed in both these groups and the results 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 with the controls. **Conclusion:** Response to deep breathing, a parasympathetic test, was significantly increased in the patients with hyperhidrosis compared with controls in this study; we will conclude this study with the findings that the idiopathic hyperhidrosis seems to be a complex dysfunction of autonomic nervous system, which involves autonomic pathways other than those related to excess sweating.

KEY WORDS: Idiopathic Hyperhidrosis; Parasympathetic Dysfunction; Sympathetic Overactivity

Introduction

Idiopathic hyperhidrosis, also called as primary hyperhidrosis is a syndrome that 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, involved in this condition.[1] Hyperhidrosis is believed to be owing to sympathetic overactivity and sympathectomy is one of the treatment procedures in these patients. As the etiopathogenesis of this disorder is unclear, sympathetic functions, being a part of autonomic nervous system, are 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,

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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 them with age- and sex-matched healthy individuals.

Materials and Methods

The autonomic function test was assessed in control subjects and the primary hyperhidrosis patients, who were visiting the Dermatology Department, KIMS, Hubli.

Inclusion Criteria

Twenty known cases of idiopathic hyperhidrosis in 12–30 years of age in both sexes attending the Dermatology Out-Patient Department of KIMS, Hubli and 20 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

Individuals with age <10 years or >30 years were excluded. Also individuals with generalized hyperhidrosis, which may be owing to infections such as tuberculosis; malignancies such as Hodgkin disease; and patients with chronic diseases such as diabetes mellitus, renal failure, amyloidosis, and other diseases, known to interfere with autonomic nervous system were screened and excluded. In addition, patients with hypertension, ischemic heart diseases, congestive cardiac failure, valvular heart diseases, cardiomyopathy, cardiac arrhythmias; patients with neurological diseases such as multiple sclerosis, Guillain–Barré syndrome; patients on drug treatments, which are known to affect the autonomic nervous system including diuretics, antiarrhythmics, neuroleptics, antiepileptics, and antihypertensive drugs were not included. Also patients with signs and symptoms of anemia or patients who were pregnant were excluded.

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 assessed and instructions were given to the subject before each parameter/component is assessed. The results were tabulated for analysis.

Tests assessed in this study were the following:

A. For sympathetic functions

1. Blood pressure (BP) response to standing: The test was performed by measuring the subject/patient's BP with a sphygmomanometer while he/she is lying down quietly and again when he/she stands up. The postural fall in BP was taken as the difference between the systolic BP (in lying and standing positions).[2]
2. BP response to handgrip 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 5 min. BP was measured three times before and at every 1-min interval during handgrip. The result was expressed as the difference between the highest diastolic BP during handgrip exercise and the mean of the three diastolic BP readings before the handgrip was maintained.[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 BP should exceed 10 mmHg.[3]

B. For parasympathetic functions

1. Resting heart rate: Resting heart rate was recorded in supine position on an electrocardiograph (ECG), 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 15th beat after standing. A relative overshoot bradycardia then occurs, maximal at about the 30th beat. This test was performed with the subject/patient lying quietly on a couch while the heart rate was being recorded continuously on an ECG. The subject/patient was then asked to stand up unaided, and the point at which the patient started to stand was marked on the ECG. The shortest R-R interval at or around the 15th beat and the longest R-R interval at around the 30th beat after starting to stand was measured. The characteristic heart rate response was expressed by the 30:15 ratios.[2]
3. Expiration/inspiration ratio: The 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: The subject was made to sit quietly and breathe deeply at six breaths a minute (5 s in and 5 s out) for 1 minute. ECG was recorded throughout the period of deep breathing. Onset of each inspiration and expiration was marked and the difference in R-R interval (maximum R-R interval – minimum R-R interval) was calculated.[2]
5. HR response to Valsalva maneuver: The test was performed by the subject/patient blowing into a mouthpiece connected to a modified sphygmomanometer and holding it at a pressure of 40 mmHg for 15 s while a continuous ECG was recorded. The maneuver was performed three times with 1-min interval in between. The result was expressed as the Valsalva ratio, which is the ratio of the longest R-R interval

after the maneuver (reflecting the overshoot bradycardia following release), to the shortest R-R interval during the maneuver (reflecting the tachycardia during strain). Ratio >1.21 is said to be normal.[2]

Statistical Analysis

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

Result

In this 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 the 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.

In this study, all the sympathetic function tests were within the normal expected range whereas 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 with the controls.

Discussion

Cardiovascular autonomic function tests have been widely used to assess the 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 hyperresponsive 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 the 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 this 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 with control. The parasympathetic tests such as 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 this 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 nonsignificant. Orthostatism and head-up tilt up to 65° can be used to assess the presence of postural hypotension, defined as a fall of more than 20 mmHg in systolic BP 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 BP response to isometric handgrip and mental arithmetic test may be owing to the sympathetic nervous system activation. Sustained handgrip is a type of isometric exercise. With the start of an isometric muscle contraction, pulse rate is increased. This is largely because of a reduction in vagal tone, although increased discharge in cardiac sympathetic fibers also plays a role. Thereafter, the systolic and diastolic BP also rises sharply. The rise in diastolic BP will be abnormally small if there is extensive peripheral sympathetic abnormality. However, in this 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 this 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 an earlier study conducted by De Marinis 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 those patients.

Table 1: Sympathetic functions in control and study group individuals

Tests	Control	Hyperhidrosis subjects
BP response to standing (mmHg)	8.8 ± 0 .81	9.7 ± 0.36
BP response to sustained handgrip (mmHg)	18 ± 1.01	17.9 ± 0.93
Mental arithmetic test (mmHg)	16 ± 2.62	16 ± 2.70

BP, blood pressure.
Data expressed as mean ± SEM, (n = 20).
$P < 0.01$.

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 maneuver (Valsalva ratio)	1.889 ± 0.11	1.71 ± 0.11

R-R interval is the interval between 2 consecutive R waves in ECG.
Data expressed as mean ± SEM, (n = 20).
*Significant.
$P < 0.01$.

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

This study concludes with the findings that the heart rate response to deep breathing, a parasympathetic test, is significantly changed in 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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