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Autonomic function in tension-type headache

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Abstract

The pathogenesis of tension-type headache (TTH) is poorly understood. TTH is mostly associated with the sympathetic nervous system. Reports considering autonomic nervous system functioning with regard to TTH are limited. Autonomic nervous system disorders could however play a role in the etiopathology of TTH. Compared with sympathetic nervous system functioning, techniques for evaluating parasympathetic nervous system activity are more limited. Therefore, the aim of the study was to measure heart rate recovery (HRR), an index of vagal activity, in TTH patients. Thirty-seven patients with TTH (15 with episodic and 22 with chronic TTH) and 37 control subjects underwent exercise tolerance testing according to modified Bruce protocol. Heart rate recovery (HRR) at 1 and 3 minutes (HRR1 and HRR3) were calculated. HRR 1 and 3 were found to be similar in patients and controls. However, the resting heart rate in patients with episodic TTH was found to be significantly lower than the resting heart rate in patients with chronic TTH and control subjects. These results suggest that parasympathetic nervous system function is not affected in TTH patients. However, sympathetic nervous system tonus, which is evaluated by resting heart rate, is low in patients with episodic TTH, suggesting sympathetic hypofunction.

Key words : Tension-type headache ; autonomic function.

Introduction

There are many unknown factors in the pathogenesis of headaches. Using different methods, the autonomic nervous system of headache patients has been investigated in several studies. Although the clinical features of some headache types clearly suggest that autonomic nervous system functions are involved, results of studies are contradictory concerning the involvement of sympathetic and parasympathetic nervous system functions in the pathophysiology of the different headache types.

Tension-type headache (TTH) is the most common type of headache with one year prevalence rates of 38.3% for the episodic form and 2.2% for the chronic form. It is a bilateral, pressure like headache of mild-to-moderate intensity that can last from 30 minutes to 7 days and has only one accompanying symptom (eg, nausea, vomiting, photophobia or phonophobia). In episodic TTH, there are less than 15 and in chronic TTH there are at least 15 attacks per month. The pathogenesis of TTH is poorly understood and autonomic nervous system disorders have been considered to play a role in the etiopathology of TTH (1). However, patients with TTH complain less frequently of autonomic symptoms such as nausea, vomiting or diarrhea, cutaneous vasoconstriction, vasodilation, piloerection, diaphoresis, photophobia and abnormal pupillary reactions than do migraine patients.

With regard to TTH, reports on the functioning of the autonomic nervous system are limited, as the condition is mostly associated with the sympathetic nervous system. Hypofunction of the sympathetic nervous system has been shown by pupillometry, cardiovascular reflex testing, the tilt test, and by measuring dopamine beta-hydroxylase activity and norepinephrine levels during the cold pressor test, and Mayer wave activity (2-7). Numerous methods are available to assess sympathetic nervous system function ; however, techniques for evaluating parasympathetic nervous system activity are limited. Heart rate recovery (HRR) following exercise has recently been promoted as a specific index of vagal activity with important clinical implications (8). An attenuated decrease in HRR is believed to reflect decreased parasympathetic nervous system activity (9). In this study, we aimed to evaluate autonomic nervous system function by measuring heart rate recovery in patients with TTH.

Material and methods

Thirty-seven pure TTH patients, 15 with episodic TTH (average age, 26.5 ± 8 years) and 22 with chronic TTH (average age, 27 ± 8.2), were studied. TTH had been diagnosed according to the criteria of the International Headache Society, and diagnosis was based upon patient history. Patients were excluded for possible organic causes for headache by history, neurologic and physical examinations and results of laboratory tests (1). To aviod a sex effect, we confined the study to women. The

presence of systemic disease (eg, diabetes mellitus) and disorders that could affect the autonomic nervous system (ANS) were exclusionary. Cardiovascular diseases were excluded by clinical history and results of physical examination and echocardiography. Except for mild analgesics, patients had not been taking any drug therapy for at least 1 year. No patients were using excessive analgesics and there were no differences in analgesic consumption between the groups. All patients were sudied during headache-free periods.

Thirty-seven age-matched women (mean age, 26 ± 5.6 years) who were free of migraine, TTH, other chronic pain syndromes, systemic diseases, or disorders that could affect the ANS were selected as control subjects from the outpatient population of our neurology clinic. These subjects were not on any medications. Medical history and physical and neurologic examinations were done by the same neurologist. The participants in patient and control groups didn't have a habit of caffeine intake. During the test, they were not anxious.

Informed consent was obtained from all patients before enrollment and the Ethics Committee of Baskent University approved the study protocol.

All patients and control subjects underwent electrocardiography (ECG) and transthoracic echocardiography (TTE). Only subjects with normal findings on ECG and TTE were included. Subsequently, they underwent exercise tolerance testing according to a modified Bruce protocol using a Quinton® treadmill system (Bothell, WA, USA). Exercise lasted in average 9.7 ± 1.9 minutes in both study groups. During each exercise stage and every minute for 3 minutes after recovery, blood pressure, heart rate, and cardiac rhythm were recorded. Following peak exercise, subjects walked a 2-min cool-down period at 1.5 mph at a 2.5% grade. HRR was calculated as the difference between heart rate at peak exercise and heart rate at the relevant minute of recovery. In an example, heart rate recovery at 1 min (HRR1) was calculated as the difference between heart rate at peak exercise and 1 min into the recovery cool-down period. We considered HRR1 and HRR3 in this study. Metabolic equivalents were calculated from the treadmill speed and the grade at peak exercise according to a standard nomo-gram (10). Workload of study subjects was estimated via metabolic equivalents (MET : 1 MET equals 3.5 ml of oxygen uptake per kilogram of body weight per minute).

Also, resting heart rate and peak heart rate during the exercise (beats/min) as well as systolic and diastolic blood pressure (mmHg) at rest and at peak values during exercise also were recorded and compared between groups.

The results of the following tests were normal in all subjects : serum fasting glucose, liver and renal function tests and thyroid function. We also compared total blood count, serum iron, lipid profile, vitamin B12 and folate between all groups.

Statistical analysis : Statistical analysis was performed with SPSS software 11.0 for Windows (SPSS, Inc., Chicago, Illinois). Continuous variables are presented as mean ± SD. The chi-square test was used for categorical variables. One-way analysis of variance (ANOVA) followed by a Bonferroni test was used to compare differences among the groups. Values for p were considered statistically significant at a level of < 0.05.

Results

Episodic TTH and chronic TTH durations were 3.4 ± 3.9, 3.1 ± 3.9 years, respectively. The frequencies of episodic TTH and chronic TTH attacks were 9 ± 3.9 and 20.9 ± 4 per month, respectively (Table 1).

In episodic TTH, chronic TTH, and control subjects, HRR1's were 27.7 ± 7.2, 28.8 ± 8.6, and 27.2 ± 10.4, respectively. In episodic TTH, chronic TTH, and control subjects, HRR3's were 66.3 ± 11.9, 65.8 ± 12.2, and 66.2 ± 14.1, respectively (Table 1). No significant differences were found between these 3 groups and between total TTH patients and control group regarding HRR1 and HRR3 ($p > 0.05$). Peak heart rate during exercise (beats/min) as well as peak systolic and diastolic blood pressures (mmHg) during exercise and at rest were also similar in these groups ($p > 0.05$). However, the resting heart rate in patients with episodic TTH was lower than that of patients with chronic TTH and control subjects ($p = 0.001$, 0.008 respectively). No significant difference between chronic TTH and control subjects regarding resting heart rate was found.

In episodic TTH, chronic TTH, and control subjects, METs were 12.3 ± 1.4, 12.3 ± 2.4, and 11.8 ± 1.7, respectively. No significant differences were found between these 3 groups regarding METs.

No statistically significant between group differences were found with regard to mean serum B12, folic acid, iron, total cholesterol, HDL, LDL, and triglyceride levels ($p > 0.05$).

Discussion

The pathogenesis of headaches is not well understood ; however, an autonomic nervous system disorder has been proposed as a responsible factor. Conflicting results exist regarding whether the sympathetic or the parasympathetic nervous system is involved in headaches.

Migraine has been investigated mostly with regard to autonomic nervous system functioning. The most common finding is that sympathetic hypofunction, but sympathetic hyperfunction and parasympathetic dysfunction also have been

Table 1

Demographic data of study subjects (all the subjects were women)

	ETTH (n = 15)	CTTH (n = 22)	Controls (n = 37)
Age (years)	29.5 ± 7.9	30.4 ± 7.4	30.5 ± 4.7
Disease duration (years)	3.4 ± 3.9	3.1 ± 3.9	-
Headache frequency (per month)	9 ± 3.9	20.9 ± 4	-
Resting HR (beats/m)	82.7 ± 17.1	102.7 ± 15.1	97.7 ± 15.5
Resting systolic BP (mmHg)	110 ± 11.3	115.2 ± 12.1	109.7 ± 9.3
Resting diastolic BP (mmHg)	74 ± 8.3	73.3 ± 9.1	69.7 ± 9.3
Peak HR (beats/m)	178.3 ± 9.5	182.9 ± 9.8	181.6 ± 11
Peak systolic BP (mmHg)	153.3 ± 21.9	158.2 ± 20.6	152.9 ± 14
Peak diastolic BP (mmHg)	83.3 ± 8.2	86.4 ± 8.5	82.7 ± 6.7
HRR1	27.7 ± 7.2	28.8 ± 8.6	27.2 ± 10.4
HRR3	66.3 ± 11.9	65.8 ± 12.2	66.2 ± 14
METs	12.3 ± 1.4	12.3 ± 2.4	11.8 ± 1.4

ETTH : episodic tension type headache, CTTH : chronic tension type headache, no :number of subjects, HR : heart rate, BP :blood pressure, HRR1 :heart rate recovery at the first minute after the exercise, HRR3 : heart rate recovery at the third minute after the exercise, METs : estimated workload in metabolic equivalents. Continuous variables are presented as mean ± SD.

reported. Concerning sympathetic nervous system function, pupillary sympathetic hypofunction, orthostatic hypotension, a decreased overshoot in the Valsalva maneuver, a low level of plasma norepinephrine, a poor response to the cold pressor test, and increased sympathovagal balance have been documented. Regarding parasympathetic nervous system functioning in migraineurs, some investigators have reported hyperfunction of cardiovascular parasympathetic activity, while others have reported hypofunction (2-5, 7, 11-17). However, intact parasympathetic nervous system function also has been shown in migraine patients (18-19).

In several studies in TTH patients, a sympathetic hypofunction has been suggested. Sliwka *et al.*, studied B waves and Mayer waves by using bilateral transcranial Doppler monitoring of the middle cerebral artery. Mayer wave activity of chronic TTH patients was found to be lower than control subjects, suggesting an impaired sympathetic activity (6). Takeshima *et al.*, investigated platelet factor 4, norepinephrine, and free fatty acids in a study of platelet activation under stress during a cold pressor test and found low norepinephrine levels which might indicate sympathetic hypofunction in TTH (3). By examining cardiovascular reflex responses during an orthostatic test and an isometric work test and by measuring pulse rate (R-R interval) variation, Mikamo *et al.*, demonstrated cardiovascular sympathetic hypofunction (2). Takeshima *et al.*, also reported pupillary sympathetic hypofunction in TTH (4). In the current study, resting heart rate was another variable that we measured during the exercise tolerance test to evaluate HRR. We found that it was lower in patients with episodic TTH than it was in patients with chronic TTH and control subjects, suggesting sympathetic hypofunction. By evaluating Valsalva manoeuvre, deep breathing, and sustained handgrip, and via an orthostatic test and spectral analsis of heart rate variability in the supine and standing positions, Pogacnik *et al.*, compared sympathetic nervous system activity between patients with episodic and those with chronic TTH and found no significant differences between groups. However, when compared with control subjects, total TTH patients showed cardiovascular sympathetic hypofunction (5).

There have been no reports on parasympathetic nervous system function in TTH patients. The rise in heart rate during exercise is thought to be due to the combination of parasymathetic nervous system withdrawal and sympathetic nervous system activation. The fall in heart rate immediately after exercise is thought to be a function of the reactivation of the parasympathetic nervous system. HRR following exercise recently has been promoted as a specific index of vagal activity with important clinical implications. An attenuated decrease in HRR is believed to reflect decreased parasympathetic nervous system activity (8, 9). Therefore, the rate of recovery of the heart rate immediately after exercise is expected to show us the parasympathetic nervous system functioning in patients with TTH.

We found HRR1 and HRR3 similar in the TTH and control groups. These results suggested that parasympathetic nervous system function is not affected in patients with TTH. Owing to the lack of research on parasympathetic nervous system functioning in this headache group, our results present novel knowledge regarding parasympathetic nervous system functioning in TTH patients.

In the other study, which included episodic TTH (number of subjects, n = 10), chronic TTH (n = 11), episodic migraine (n = 47) and control subjects (n = 25), we found that HRR1 and HRR3 were similar in all study groups. Resting heart rate was lower in patients with episodic TTH than it was in patients with chronic TTH and migraine, but

no significant differences were found between these 3 groups and control subjects. These results were interesting, but because of lack of difference from the control group, a sympathetic involvement couldn't be suggested for these headache types (20). However, in the current study, the resting heart rate in patients with episodic TTH was found to be significantly lower than that of patients with chronic TTH and control subjects. The increased number of the subjects in the present study may have been led to the significant difference between episodic TTH and control subjects. These results helped us to suggest a sympathetic dysfunction in episodic TTH. We think that further studies with larger goups are warrented to support our findings.

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