

## A Study to Evaluate the Involvement of Parasympathetic Nervous System in Tension Type Headache

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### Abstract

**Context:** Headache is one of the most common disorders of the nervous system seen in medical practice. Tension-type headache although most prevalent is yet understudied subtype of primary headache known to cause substantial disability and diminished quality of life in patients. The neurobiology of symptoms in tension-type headache is still speculated. A few studies done earlier have suggested sympathetic autonomic dysfunction associated with etiopathogenesis of tension-type headache. Altered stress reactivity of autonomic nervous system is now known to be associated with increased risk of cardiovascular mortality.

**Objectives:** There is a lack of data as regards involvement of parasympathetic limb of autonomic nervous system in tension type headache patients especially in the Indian population. The objective of the study is to evaluate the involvement of parasympathetic nervous system in tension type headache.

**Methods:** Various parasympathetic function tests were done to assess the parasympathetic activity in 50 tension-type headache patients. The evaluation was done by standard, bedside, non-invasive tests like deep breathing test, Valsalva manoeuvre and orthostatic test. The reference values of Ewing and Clark were used to interpret the results of the test.

**Results:** In the present study the basal heart rate was significantly decreased in tension type headache patients as compared to healthy controls. However parasympathetic function as evaluated by the different tests was found to be normal as compared to controls.

**Conclusion:** We conclude that the decrease in resting heart rate in tension type headache patients could be suggestive of sympathetic hypo function as reported by previous studies. However parasympathetic function is unaltered in tension type headache patients.

**Key words:** Parasympathetic nervous system, Deep breathing test, Valsalva manoeuvre, Orthostatic test, TTH

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### Introduction

“Tension type headache” (TTH) has historically been ascribed to persistent contraction of scalp, neck, and jaw musculature. Earlier known variously as psychomyogenic headache, muscle contraction headache, stress headache, its worldwide prevalence varies between 30 to 78%.<sup>1</sup> The International Headache Society has now actualized the diagnostic criteria for TTH. TTH is characterized by a bilateral, pressing, tightening pain of mild to moderate intensity, occurring in short episodes of variable duration (headaches lasting from 30 minutes to 7 days) and not attributed to other disorder.<sup>2</sup>

Different pathophysiological factors like myofascial pain, peripheral and central pain mechanisms and chemical mediators like serotonin, nitric oxide, substance P are postulated to play an

important role in TTH.<sup>3,4,5</sup> Epidemiological studies have also suggested an increased genetic predisposition in chronic TTH in general population.<sup>6</sup> Stress and mental tension are the most conspicuous precipitating factors in TTH.<sup>7</sup> Sympathetic nervous system involvement in TTH has been demonstrated by limited clinical and laboratory tests. Pupillary sympathetic hypofunction and subtle anisocoria was detected by physiologic pupillary tests evaluation in muscle contraction headache.<sup>8,9</sup> Serum dopamine-beta-hydroxylase activity which is an index of peripheral sympathetic activity was significantly lower in TTH patients as compared to controls.<sup>10</sup> Standard non-invasive orthostatic test was suggestive of sympathetic hypo function and co-related with Zerssen depression scale in TTH patients.<sup>11</sup>

Autonomic activity is fractionated and autonomic balance indicates ratio between levels of the sympathetic and parasympathetic activity.<sup>12</sup> However, sympathetic and parasympathetic activity does not always vary reciprocally and caution should be taken when interpreting measures of sympatho-vagal balance. There is insufficient data for parasympathetic nervous system involvement in TTH which necessitated its evaluation in present study.

## Materials and Methods

The study was conducted in a major Teaching Hospital and Medical College in Mumbai. All experimental procedures were approved by the ethics committee and subjects gave written informed consent prior to their participation. 50 consecutive diagnosed patients of TTH selected as per International Headache Society Diagnostic Criteria (age 20-50 years) and age and sex matched controls were evaluated in a quiet, temperature controlled room between 10 am to 12 pm to avoid diurnal variations in autonomic function. Subjects were non-smokers, had no history of taking alcohol or tobacco products and with no personal or parental history of cardiovascular, respiratory or any other known systemic disease. They did not regularly consume large amounts of caffeine (< 350 mg/ day).

**Basal Parameters:** After reporting subjects were asked to relax for 15 minutes in supine posture and resting blood pressure (BP) and heart rate were recorded. The blood pressure was recorded from the right arm using a standard mercury sphygmomanometer. ECG was recorded by INCO-Niviqure ECG & Data acquisition systems.

**Protocol of tests:** The parasympathetic reactivity was assessed by Maximum-Minimum heart rate during deep breathing test, Valsalva ratio during Valsalva maneuver, 30:15 ratio during lying to standing i.e. orthostatic test.<sup>13</sup>

**Deep breathing test:** A baseline recording of ECG was done for 30 sec. The patient was visually guided to breathe slowly and deeply at 6 cycles per minute. The maximum and minimum R-R intervals during each breathing cycle are measured. The result is expressed as the mean of difference between maximum and minimum heart rates for six measured cycles in beats per minute. Heart rate variation (maximum-minimum heart rate) of  $\geq 15$  beats/min was considered normal.

**Valsalva manoeuvre:** The baseline ECG was recorded. The subject was instructed to blow into a mouth piece attached to sphygmomanometer to raise the pressure to 40 mmHg for 15 sec. The Valsalva ratio was calculated from maximal RR interval during phase IV and smallest RR interval during phase II. VR ratio  $\geq 1.21$  was considered normal.

**Orthostatic test:** Subject was asked to stand up from the supine position and was instructed to remain

motionless for 2 minutes. Only the limb leads of the ECG machine were attached to the subject. The 30:15 ratio was calculated from maximum RR interval at around 30 sec and minimum RR interval at around 15 sec. A 30:15 ratio  $\geq 1.04$  was considered normal.

Each test was interpreted as normal/ borderline/ abnormal using criteria of Ewing and Clark (Table 1).<sup>14</sup>

**Statistical analysis:** Each parameter was tested for distribution of data. The data was entered into MS-Excel work sheet and Statistical analysis was done by using SPSS software version 20.0. Descriptive statistics i.e. mean and standard deviation was used for numerical data. Comparison of numerical variables among various groups was done by using unpaired t-test. The level of significance was set at 5%. All p-value < 0.05 was considered as statistically significant.

## Results

Sixty-five patients of TTH were referred from the neurology department for recruitment in the study over duration of 14 months (from April 2013 to May 2014). Only 50 patients were selected after exclusion and consent. The diagnosis of TTH was confirmed in the laboratory as per criteria laid by the International Headache Society.<sup>2</sup> Fifty age matched and sex matched healthy subjects were recruited for the study as controls.

**Basal Parameters:** Tests for normality of distribution found normal distribution for age and sex parameters between TTH patients and controls. The mean age of TTH patients was  $35.70 \pm 8.33$  while that of controls was  $35.96 \pm 8.12$ . The basal heart rate was significantly decreased in TTH patients ( $78.96 \pm 7.225$ ) as compared to healthy controls ( $82.02 \pm 7.731$ ). No statistically significant difference was found between mean systolic BP of TTH patients ( $113.16 \pm 6.41$ ) and controls ( $114.84 \pm 5.80$ ). Also mean diastolic BP of TTH cases ( $77.20 \pm 5.34$ ) was not significantly different from that in controls ( $78.20 \pm 5.27$ ). [Graph 1]

The results of all the tests in each subject were classified as normal, borderline or abnormal. All the three parasympathetic tests were found to be normal in 88 to 90% of cases. Tests were found to be abnormal only in 10-12% cases varying in severity from borderline to abnormal. (Table 2)

Also no significant difference was found between cases and controls for the various parasympathetic tests (Table 3).

**Table 1: Ewing and Clark criteria in tests of cardiovascular autonomic function**

Autonomic function tests	Normal	Borderline	Abnormal
Deep breathing test	$\geq 15$ beats /min	11-14 beats/min	$\leq 10$ beats/min
Valsalva ratio	$\geq 1.21$	1.11 -1.20	$\leq 1.00$
30 : 15 ratio on standing	$\geq 1.04$	1.01 -1.03	$\leq 1.00$

**Table 2: Comparison of basal parameters in cases and controls**

Basal Parameters	TTH	Controls
Heart Rate	78.96±7.22	82.02±7.73 *
Systolic BP	113.16±6.41	114.84±5.80
Diastolic BP	77.20±5.34	78.20±5.27

**Table 3: Comparison of percentage of autonomic function showing normal, borderline and abnormal results**

Test		Normal	Borderline	Abnormal
Deep breathing test	N	45	2	3
	%	90.0%	4.0%	6.0%
Valsalva Ratio	N	44	3	3
	%	88.0%	6.0%	6.0%
Orthostatic 30:15 ratio	N	45	1	4
	%	90.0%	2.0%	8.0%

Also no significant difference was found between cases and controls for the various parasympathetic tests (Table 4).

**Table 4. Comparison of parasympathetic function tests in cases and controls**

	Cases	Control	P value	Significance
Deep breathing test	19.620±5.409	18.620±3.528	0.276	Not significant
Valsalva ratio	1.294±0.168	1.269±0.052	0.323	Not significant
Orthostatic 30:15 ratio	1.142±0.105	1.161±0.080	0.302	Not significant

## Discussion

In the present study, a relatively large group of well-defined patients with TTH was investigated using the standard cardiovascular autonomic function tests for parasympathetic involvement. The basal heart rate was significantly decreased in TTH patients as compared to controls. Similar findings were reported by Deniz Yerdelen et al. who found that resting heart rate in patients with episodic TTH was significantly lower than that of controls.<sup>15</sup> Variations in heart rate at rest are mediated by the combined effects of cardiac vagal and sympathetic nerves acting on the sino-atrial node. Hence lower resting heart rate would be suggestive of sympathetic dysfunction in episodic TTH.

No clinical evidence of parasympathetic autonomic failure was noted. Heart rate variability by deep breathing test considered as sensitive index of parasympathetic function and orthostatic test was found to be abnormal in 10% of TTH patients. Abnormalities of heart rate variability by Valsalva manoeuvre were noted in 12% of TTH cases. We did not find evidence for dysfunction of the parasympathetic autonomic function in TTH patients as compared to controls. Mikamo et al. carried out deep breathing test in 15 muscle contraction headache patients and calculated variation coefficient of R-R intervals in electrocardiogram. They concluded that no significant difference was present in muscle contraction headache patients and controls.<sup>16</sup> Tomaz Pogacnik et al. studied 51 TTH patients using deep breathing test, orthostatic test and Valsalva manoeuvre. Deep breathing test was done at rate of 6 breaths/ minute for 90 seconds and repeated after 2 minutes. In spite of methodological

differences no evidence of parasympathetic involvement was found.<sup>17</sup>

Multiple and diverse factors are implicated in the etiopathogenesis of TTH. Traditionally TTH pain has been attributed to increased contraction and ischemia of head and neck muscles and increase in myofascial trigger points.<sup>3</sup> EMG activity has demonstrated increase activity in few motor units leading to sensitization of peripheral nociceptors.<sup>18</sup> Central sensitization of pain pathways resulting from prolonged nociceptive stimuli from pericranial myofascial tissues is postulated to be responsible for conversion of episodic to chronic TTH.<sup>19</sup> The temporal relation between TTH and sympathetic dysfunction has recently been investigated and concluded by varied battery of tests like orthostatic test, heart rate recovery and bilateral Doppler monitoring.<sup>11,15,20</sup>

The present study was initiated due to the apparent paucity of studies investigating parasympathetic limb of autonomic nervous system in TTH. Although sympathetic involvement is known in TTH our findings do not reveal any generalised parasympathetic component dysfunction. The autonomic involvement however needs to be evaluated and elucidated in a larger population database to further validate our findings.

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