CHRONIC TENSION-TYPE HEADACHE: MUSCLE OVERACTIVITY VERSUS DEFICIENT PAIN CONTROLS

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ABSTRACT

Objective: The oscillating school of thought between the peripheral and central mechanisms of pain origin hinders the selection of appropriate therapy for chronic tension-type headache (CTTH). The aim of this study was to assess the role of central and peripheral pain mechanisms together in CTTH.

Methods: In the present study, we compared surface electromyography (sEMG) amplitudes and nociceptive flexion thresholds in patients diagnosed with CTTH (n=30) with age-matched healthy controls (n=30). For central pain modulation with spinal and supraspinal influences on nociception, we recorded nociceptive flexion reflex (NFR) by stimulating the sural nerve and observing the biceps femoris muscle response. sEMG was done for the temporalis and trapezius muscles at rest, during mental activity and during maximum voluntary contraction to assess contribution from peripheral pain.

Results: We observed a decreased NFR threshold in CTTH patients as compared to healthy controls, suggesting a hyperalgesic state due to central factors. Electromyographic activity of trapezius muscle was increased at rest in CTTH while both temporalis and trapezius showed an overactivity in patients during mental task.

Conclusion: Central factors are important in the pathogenesis of CTTH while, peripheral factors, such as stress-related muscle spasm may also contribute to pain state.

Keywords: Central sensitization, Peripheral sensitization, Nociceptive flexion reflex, Electromyography.

INTRODUCTION

Tension-type headache despite being the most prevalent primary headache, has not received the attention it deserves due to an unclear etiopathogenesis. The controversial role of peripheral and central pain mechanism exists [1], making it difficult to target appropriate system (peripheral muscles or central pain pathway) for therapy [2], leading to unnecessary self-medication in patients [3]. Earlier, the tension-type headache was thought to be a purely muscular headache derived from overactivity of the pericranial muscles [4]. The muscles generally concerned were the pericranial and cervical muscles, with many reports suggesting the role of the trapezius muscle. However, these reports were inconsistent in terms of the muscle testing paradigms. We attempt to understand the role of two most frequently implicated muscles; trapezius and temporalis during rest, mental activity, and maximum voluntary contraction (MVC). Central sensitization could be the second side to this chronic debilitating headache, which is reflected by increased pain sensitivity reported with the disease. Nociceptive flexion reflex (NFR) which is an objective measure of pain and a reliable index of spinal pain modulation, may unmask the role of central pain modulation in chronic tension-type headache (CTTH) patients [5]. Therefore, both surface electromyography (sEMG) and NFR are reliable methods to look at peripheral and central pain modulation.

Our study is novel because it looks these parameters together in patients diagnosed with CTTH and compares with healthy controls, providing an insight into the pain mechanisms involved.

METHODS

This was a case–control study involving 3 30 patients with CTTH and30 healthy controls were recruited from from May 2015 to August 2016 after obtaining ethical clearance from the Institutional Ethical Committee. Both male and female CTTH patients, aged between 18 and 55 years, were enrolled from Neurology Outpatient Department. Headache diagnosis was based on the International Classification of Headache Disorders-3 beta [6]. Detailed history was taken, and patients asked to rate their pain on a scale of 1–10, ranging from no pain to worst imaginable pain (Numerical Rating Scale).

NFR recording

To measure the NFR threshold, the electro-cutaneous stimulation and sEMG recording sites were prepared and the electrodes placed. The recording was done 18th and 23rd day of menstrual cycle (mid-luteal phase) between 8 and 11 a.m. after an overnight fast. Patients were asked to lie comfortably in supine position for 15–20 min after which, their knee was flexed at 130°, and the ankle flexed at 90° on the couch. Two Ag-AgCl cup electrodes were used to stimulate the sural nerve at the retromalleolar area. The interelectrode distance was kept at 30 mm. Pre-gelled disposable Ag-AgCl disc electrodes (Nikomed, USA) were utilized to record sEMG from the short head of biceps femoris muscle. The ground was placed over the patella on the ipsilateral side. Electrical stimuli to the sural nerve were delivered in trains of five rectangular wave pulses of 1 ms duration at a frequency of 200 Hz with B.S.L. STMA, Biopac Systems, Inc. Santa Barbara, California [7,8]. To avoid stimulus habituation, the trains were delivered randomly every 5–15 s. The intensity of stimulation eliciting a response at a rate of 60–90% in a series of approximately 20 stimuli was considered the NFR threshold [5]. The stimulation was initiated from 10 V and increased in steps of 5 V until the response was recorded in the EMG tracing. The stimulus intensity was then reduced in steps of 1 V until the reflex disappeared. The NFR threshold was defined as the average of the voltage, which produced reflex during the ascending sequence and the

voltage below which the reflex could no longer be generated during the descending sequence.

EMG recording

Pairs of Ag-AgCl pre-gelled electrodes (Nikomed, USA) of diameter 1 cm were used to record sEMG from temporalis and upper trapezius muscle. The was cleaned and gently abraded. For temporalis, one electrode was placed 10 mm lateral to the external angle of the orbit and other directly above the first, the reference was placed over the the frontal bone. For the upper trapezius, electrodes were centered midway between the C7 and acromion [9]. EMG signals were recorded on Biopac Student Lab V 3.6.2 (B.S.L) system, bandpass filtered (30–250 Hz) and sampled at 1000 Hz. The recording was done at rest, during mental activity (subjects were asked to subtract 7 serially from 100) and with maximum voluntary contraction, where subjects were asked to clench their teeth or shrug their shoulders forcefully for the activation of temporalis and trapezius, respectively [10]. The EMG was analyzed offline using B.S.L® software. Alternate bins of 10 s analyzed excluding the first and the last 10 s, and peak to peak amplitude (in microvolts [µV]) was measured for the three conditions. For MVC, the area under the curve (AUC) (in µV-s) and time to fatigue onset (in seconds) was taken as a surrogate for fatigability.

Statistical analysis

Results are presented as median with quartiles for nonparametric and as mean ± standard deviation for parametric data. Statistical significance between control and CTTH group compared using unpaired t-test after checking for normality with D'Agostino and Pearson omnibus normality test. All analyses were done on GraphPad Prism v 5.0.

RESULTS

General characteristics of patients and controls are depicted Table 1. The NFR thresholds in CTTH (25.50±8.9) were significantly lower than controls (33.75±10.5), p=0.009. There was no significant difference in other NFR parameters such as latency, amplitude, and duration (Table 2).

sEMG amplitude at rest showed no significant difference in the amplitude (µV) of temporalis between CTTH patients and controls. While there was bilateral over activity at rest of the trapezius muscle in CTTH patients, which was statistically significant (p=0.001) in the right trapezius 62 (32, 148) compared to healthy controls 27 (20, 39) (Table 3).

sEMG during mental activity showed that there was significant (p=0.0013) overactivity of the right temporalis muscle (amplitude µV) in CTTH patients 47 (39, 77) compared with healthy controls 38 (26, 42). There was no such difference on the left side. The overactivity in trapezius was present bilaterally; the amplitude of EMG (inµV) of the left trapezius in CTTH patients 84 (44, 191) was significantly higher (p=0.042) than controls 38 (37, 86). Also, the EMG amplitude (in µV) of right trapezius in CTTH patients 95 (35, 207) was significantly higher (p=0.003) than controls 33 (20, 42) (Table 4).

For MVC, the area under curve (µV-s) (Table 5) and amplitude (µV) (Table 6) of temporalis and trapezius was not significantly different in CTTH patients when compared to healthy controls. While time to fatigue for MVC was significantly lower in temporalis (p=0.01) and trapezius (p=0.0007) muscles in the CTTH patients versus healthy controls.

DISCUSSION

Our findings showed an increase in the EMG activity of the trapezius at rest suggesting that muscle overactivity at rest in CTTH may be an important factor contributing to the pain experience although it was statistically significant on the right side. Previously, increased EMG activity was seen in 67% of CTTH patients with only slight changes during headache [4]. We found a significant difference in the EMG activity during mental activity; it is probable that such an activation is seen during active headache periods. The muscle spasm could both be

Table 1: General characteristics of patients and controls

Parameter	Healthy controls n=30	CTTH n=30
Age (years)	32.25±7.5	35.7±6.56
Duration of headache (years)	0	6.73±3.31
Average pain intensity (Numerical rating scale)	0	5.3±1.94

Data expressed as Mean±SD. SD: Standard deviation, CTTH: Chronic tension-type headache

Table 2: NFR parameters

Parameter	Healthy controls n=30	CTTH n=30	p
NFR threshold (volts)	33.75±10.5	25.50±8.9	0.009
Latency (ms)	108.2±21.6	107.4±21.3	0.7
Amplitude (µV)	272.5±120.5	288.4±166.4	0.9
Duration (ms)	44.41±5.06	44.35±7.20	0.9

Data expressed as Mean±SD. NFR: Nociceptive flexion reflex, SD: Standard deviation, CTTH: Chronic tension-type headache, µV: Microvolt

Table 3: EMG amplitude of temporalis and trapezius at rest

EMG at rest-amplitude (µV)	Healthy controls n=30	CTTH n=30	p
Temporalis			
Left	43 (35,48)	36 (22,44)	0.05
Right	34 (25,64)	35 (26,43)	0.8
Trapezius			
Left	48 (23,71)	65 (38,147)	0.07
Right	27 (20,39)	62 (32,148)	0.001

Data expressed as median with quartiles. CTTH: Chronic tension-type headache, EMG: Electromyography

Table 4: EMG amplitude of temporalis and trapezius during mental activity

EMG during mental activity-amplitude (µV)	Healthy controls n=30	CTTH n=30	p
Temporalis			
Left	64 (35,167)	63 (37,101)	0.07
Right	38 (26,42)	47 (39,77)	0.0013
Trapezius			
Left	38 (37,86)	84 (44,191)	0.042
Right	33 (20,42)	95 (35,207)	0.003

Data expressed as median with quartiles. CTTH: Chronic tension-type headache, EMG: Electromyography, µV: Microvolt

Table 5: EMG AUC of temporalis and trapezius during MVC

EMG during MVC -AUC (µV-s)	Healthy controls n=30	CTTH n=30	p
Temporalis			
Left	1214 (771,13776)	1709 (906,2726)	0.7
Right	1639 (870,2598)	1658 (811,2771)	0.9
Trapezius			
Left	3654 (1340,5444)	2658 (1432,5625)	0.9
Right	1745 (1048,4999)	3006 (1152,5952)	0.4

Data expressed as median with quartiles. MVC: Maximum voluntary contraction, AUC: Area under the curve, EMG: Electromyography, CTTH: Chronic tension-type headache, µV-s: Microvolt-second

a cause or effect of the condition and aberrant central pain modulating pathways are a likely cause of hyperalgesia and poor response to therapy. A 12-year-old longitudinal follow-up study demonstrated that the patients who develop CTTH had normal pericranial tenderness,

Table 6: EMG amplitude of temporalis and trapezius during MVC

EMG during MVC - amplitude (µV)	Healthy controls n=30	CTTH n=30	p
Temporalis			
Left	822 (592,1186)	797 (601,1395)	0.7
Right	647 (456,948)	867 (595,1499)	0.17
Trapezius			
Left	1946 (565,2557)	2012 (593,2709)	0.9
Right	1133 (476,2512)	1718 (921,3427)	0.3

Data expressed as median with quartiles. MVC: Maximum voluntary contraction, EMG: Electromyography, CTTH: Chronic tension-type headache, µV: Microvolt

Table 7: Time to fatigue of temporalis and trapezius during MVC

Time to fatigue (s)	Healthy controls n=30	CTTH n=30	p
Temporalis	30 (25,43)	21 (16,28)	0.01
Trapezius	45 (38,66)	29 (23,38)	0.0007

Data expressed as median with quartiles. CTTH: Chronic tension-type headache, MVC: Maximum voluntary contraction, s: Second

to begin with, suggesting that it is a consequence rather than cause [11]. There are many studies showing decreased pressure pain thresholds [12], while others have shown an inverse relation between pericranial tenderness and pain threshold [13]. The level of activity assessed by EMG in the pericranial muscles is on the higher side in patients with CTTH than in healthy controls. The absolute root means square frequency and relative percentage values at the initial and final period during sustained isometric contraction decreased significantly in the CTTH group. We are reporting an increased fatigability of the muscles during MVC. Some have studied this as outside of headache and found that muscle tenderness and EMG activity levels were significantly increased compared to values in controls subjects. It is concluded that one of the primary sources of pain in tension-type headache may be a local and reversible sensitization of nociceptors in the pericranial muscle, mechanical strain [14], and muscle ischemia [15]. Previous reports showed altered blood flow in muscle was caused by disturbed regulation of peripheral mechanisms because of central sensitization or generalized hyperalgesia [16]. Although the activity was not significantly different, it is probable that such an effect may be there during active headache episodes. A different muscle firing pattern or some muscle modifications in patients with CTTH may reflect the reorganization of the motor control strategy [17,18]. There are detectable distinct muscular responses in chronic headache sufferers. This finding could be due to adaptation to muscle underuse or sustained contraction, leading to impaired recruitment, and muscle fiber-type conversion with dominant type I fibers in CTTH [17].

The results of the present study indicate that in CTTH patients there is a decrease in the NFR thresholds with no significant change in the other characteristics such as latency, amplitude, and duration. NFR being a spinally mediated response subjected to supraspinal and limbic modulation and has been widely reported by pain researchers. NFR or RIII is a polysynaptic withdrawal reflex originally discovered by Sherrington in 1910 in decerebrate animals where he saw that electrical stimulation causes flexion of hip knee and ankle. It is different from the nocuous flexion reflex as the flexion phase is not maintained and flexion at knee and ankle ceases somewhat earlier than does the flexion at hip, whereas in the nociceptive reflex flexion at all three joints is maintained. Also, flexion is greater and is succeeded by extension only after the stimulus is withdrawn, whereas in the step-reflex it is succeeded by extension [19]. In humans, the afferents were carried by A delta and C fibers as demonstrated in paretic patients [20]. In 1960, when Kugelberg *et al.* electrically stimulated various areas in the foot and gluteal region and recorded response by needle EMG the threshold of the nociceptive reflexes varied considerably in different

regions according to its biological function although it could be elicited almost anywhere [21]. Stimulation of the sural nerve (through the skin) elicits two different reflex responses in the biceps femoris: The first RII is of short latency, low threshold and corresponds to tactile reflex Aβ fibers. The second (RIII) is of longer latency and a higher threshold and corresponds to a nociceptive reflex. The threshold of RIII was found to be the threshold of a pain sensation. Stimulation of the skin elicits only a late nociceptive (RIII) response in the biceps femoris. This was used as an index of efficacy of analgesic drugs, stress, mental activation, and homotopic noxious stimulation [22-25]. In an experimental situation, the nociceptive withdrawal reflex can be elicited by heat [26] or electrical stimulations. Electrical stimulation may either be of a pure sensory nerve, for example, the sural nerve [23], or cutaneous stimulation (stimulation of distal cutaneous afferents) on foot [27]. The NFR threshold correlates well with the subjective experience of pain in patients with sciatica [28], fibromyalgia [29], after functional neurosurgery [30]. and in demonstrating the efficacy of lidocaine in painful diabetic neuropathy [31]. The NFR has been investigated in patients with different types of chronic headaches [32]. A good correlation between the reflex and pain was demonstrated in patients with a migraine, but studies in patients with a tension-type headache and hemicrania continua have yielded conflicting data [33,34].

CONCLUSION

The results reflect a predominant role of central factors in the pathogenesis of CTTH and the peripheral muscle overactivity being a contributory factor. EMG activity of temporalis and trapezius muscle also shows an overactivity in our patients especially during the mental task and increased fatigability during MVC. However, some studies fail to show an increase in the EMG activity; this variation is largely due to different techniques and muscle groups. Therefore, we conclude that muscle overactivity could be a contributing factor toward the pain experience in CTTH. The spinally mediated NFR showed a significant difference in headache-free controls and pain patients. NFR is considered as a reliable and objective tool in pain assessment and is also affected by central pain modulating matrix. We observed a decreased NFR threshold as has been previously reported in CTTH suggesting a hyperalgesic state due to central factors.

AUTHOR'S CONTRIBUTION

Bhawna Mattoo: Design of the work; Data Acquisition and Analysis, interpretation of data, final approval. Suman Tanwar: Data acquisition and analysis, final approval. Rohit Bhatia: Patient recruitment, interpretation of data, final approval. Manjari Tripathi: Patient recruitment, interpretation of data, final approval. Renu Bhatia: Design of the work, interpretation, and final approval.

CONFLICTS OF INTEREST

The authors have no conflicts of interest concerning the work reported in this paper.

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