Contribution of Myofascial Trigger Points to Migraine Symptoms

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Abstract: This study evaluated the contribution of myofascial trigger points (TrPs) to migraine pain. Seventy-eight migraine patients with cervical active TrPs whose referred areas (RAs) coincided with migraine sites (frontal/temporal) underwent electrical pain threshold measurement in skin, subcutis, and muscle in TrPs and RAs at baseline and after 3, 10, 30, and 60 days; migraine pain assessment (number and intensity of attacks) for 60 days before and 60 days after study start. Fifty-four patients (group 1) underwent TrP anesthetic infiltration on the 3rd, 10th, 30th, and 60th day (after threshold measurement); 24 (group 2) received no treatment. Twenty normal subjects underwent threshold measurements in the same sites and time points as patients. At baseline, all patients showed lower than normal thresholds in TrPs and RAs in all tissues ($P < .001$). During treatment in group 1, all thresholds increased progressively in TrPs and RAs ($P < .0001$), with sensory normalization of skin/subcutis in RAs at the end of treatment; migraine pain decreased ($P < .001$). Threshold increase in RAs and migraine reduction correlated linearly ($.0001 < P < .006$). In group 2 and normal subjects, no changes occurred. Cervical TrPs with referred areas in migraine sites thus contribute substantially to migraine symptoms, the peripheral nociceptive input from TrPs probably enhancing the sensitization level of central sensory neurons.

Perspective: This article shows the beneficial effects of local therapy of active myofascial trigger points (TrPs) on migraine symptoms in patients in whom migraine sites coincide with the referred areas of the TrPs. These results suggest that migraine pain is often contributed to by myofascial inputs that enhance the level of central neuronal excitability.

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Keywords: Myofascial trigger points, migraine, pain thresholds, hyperalgesia.

A myofascial pain syndrome (MPS) is the complex of sensory (regional pain and hyperalgesia), motor, and autonomic symptoms caused by an active myofascial trigger point (TrP). In turn, a TrP is a spot of exquisite tenderness in a muscle or its fascia, localized in a taut, palpable band of fibers. It mediates a local twitch response under snapping palpation and gives rise to pain, tenderness, autonomic phenomena, and dysfunction in an area (referred zone) usually remote from its site but specific and characteristic for each muscle.3,8,9,27 Sensory testing (measurement of pain thresholds to electrical stimulation) reveals that TrPs are typical sites of superficial (skin/subcutis) and deep (muscle) hyperalgesia, whereas referred pain areas are sites of deep hyperalgesia, possibly also extended to superficial tissues when the triggers are particularly active.28-30

Trigger points are a frequent occurrence in every individual, due to a number of factors, among which microtraumatic events are particularly important.26 In the cervico-cranial district of headache patients, TrPs are more frequent than in the normal population, probably due to an increase in microtraumatic events in muscles of this district due to incorrect posture/antalgic attitudes that these patients may have as a consequence of their frequent headache attacks.27 Migraine patients in particular have been shown to present a significantly greater number of active myofascial trigger points in the cervical muscles, mostly ipsilateral to migraine headaches.6 When the referred area of these TrPs coincides with the

Received September 2, 2006; Revised May 27, 2007; Accepted June 1, 2007.

Supported by “G. D’Annunzio” University funds.

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doi:10.1016/j.jpain.2007.06.002
Materials and Methods

The study was divided into 2 phases.

Phase 1: Main Experiment

This was designed to assess the efficacy of TrP treatment with local anesthetic vs no treatment in patients [a true placebo treatment for TrP infiltration does not exist, as injection of saline or TrP penetration with a needle (dry needling) is a recognized effective therapy to TrP release] \(^26\) as compared with sensory assessment in normal subjects.

Patients and Subjects

Migraine patients without aura and normal subjects were considered for the study. Patients were all attending the Headache Center of the “G. D’Annunzio” University of Chieti. Normal subjects were chosen from the staff of the Department of Internal Medicine of the same University.

Inclusion criteria for patients to be subjected to active treatment (group 1) were an age range of 18 to 50 years and either sex, a history of migraine diagnosed by a specialist (according to 2004 IHS criteria) \(^{16}\) at least a year prior to examination, a number of migraine attacks equal to or greater than 6 per month in the preceding 2 months, a negative history for any condition known to affect general pain sensitivity, \(^7,14,23,28\) the presence of active myofascial trigger points in muscles of the cervical region whose referred pain areas coincided with the typical sites of migraine attacks, \(^{25}\) the existence of intolerance and/or scarce responsiveness to classic migraine treatments and intolerance and/or allergy to local anaesthetics, and written informed consent to participate in the study.

Inclusion criteria for normal subjects were an age range 18 to 50 years and either sex, a negative history for migraine and any cervico-cranial pain, a negative history for any condition known to affect general pain sensitivity, a negative clinical examination for the presence of myofascial trigger points in the cervico-cranial region, and written, informed consent to participate in the study.

Fifty-four patients (group 1) meeting the inclusion criteria for active treatment were selected (43 women, 11 men, ages 23 to 46 years, mean age: 31.4 ± 5.8 SD) out of 115 examined. They were affected with unilateral frontal or temporal migraine (with no alternation of side) and presented TrPs in the sternocleidomastoid (n = 19), semispinalis cervicis (n = 23) or splenius cervicis (n = 12) muscles (referred pain areas located in the same sites as the migraine attacks, that is, temporal and/or frontal regions) \(^{13,27}\) (Fig 1). Seven of them also had a diagnosis of tension type headache (TTH); however, the location of the TTH pain was different from that of the migraine attacks, that is, bilateral, mainly on head vertex and parieto-occipital areas, and had no relationship with the TrP stimulation; in fact, the TrP stimulation reproduced the migraine but not the TTH pain pattern. Patients with both migraine and TTH were able to clearly distinguish their migraine from their TTH pain.

Twenty-four patients meeting the inclusion criteria for control evaluation were selected (19 women and 5 men, ages 18 to 46 years, mean age: 33.3 ± 7) of 63 examined. They were affected with frontal or temporal migraine and showed TrPs in the sternocleidomastoid (n = 10), semispinalis cervicis (n = 8), or splenius cervicis (n = 6)

Figure 1. Referred pain areas in the examined patients. Left figure: Temporal area, referred from a trigger point either in the semispinalis cervicis (upper cross) or splenius cervicis (lower cross). Right figure: frontal area, referred from a trigger point in the sternocleidomastoid muscle. Modified from Simons et al. \(^{27}\)
(referred pain areas coinciding with migraine sites). Four patients also had TTH pain attacks, with characteristics similar to those of patients of the preceding group.

No patients had been under continuous treatment for their migraine for at least 3 months preceding the start of the study and all took only a rescue medication for their attacks if necessary (paracetamol, 1000 mg). Only 6 patients (4 patients in group 1, 2 patients in group 2) had suspended their classic migraine treatment (tryptans) for lack of efficacy; the remaining patients had interrupted previous tryptan treatment because of strong side effects, mostly a sense of chest/throat constriction, sudden weakness, tremors.

Twenty normal subjects (15 women and 5 men, aged 24 to 35 years, mean age: 29.3 ± 4) meeting the inclusion criteria were selected, of 37 examined.

There was no significant difference in mean age between the 3 groups of examined subjects (1-way ANOVA).

### Experimental Procedures

#### Palpation of Cervical Muscles for Trigger Point Assessment

Palpation of cervical muscles for TrP search was systematically performed in subjects of all groups by an experienced clinician (AF) who was blinded as to whether the examined subject was a patient or a normal individual. TrP assessment was performed by firstly identifying the taut band, by pincer or snapping palpation, then by firm digital pressure onto different points of the band itself. The TrP within the band was revealed by a jump sign reaction by the subject towards this pressure and by elicitation of a local twitch response (LTR) by snapping palpation (occurrence of LTR verified by a second investigator, GA). An active TrP was revealed by the occurrence of referred in addition to local pain.25,26 The patient was simply invited to report the kind of sensation felt upon TrP compression and its location. No solicitation regarding the referral of pain was made by the investigator.

#### Pain Thresholds and TrP Treatment

In the pain-free interval and in the absence of any pharmacologic treatment for at least the preceding 72 hours, all patients were submitted to pain threshold measurement to electrical stimulation in skin, subcutis and muscle in the trigger point and referred pain area (basal evaluation). Subsequent to threshold measurement, patients of group 1 (active treatment) were subjected to TrP infiltration with local anaesthetic (0.5 mL of bupivacaine (5 mg/mL)). The infiltration was repeated on the 3rd, 10th, 30th, and 60th day after the initial evaluation and pain threshold measurement was performed again on the same days, immediately before the new infiltration. Patients were told that the therapeutic approach to their headache involved a first 2-month preliminary phase in which the local “treatment” would probably be beneficial for the sensations of stiffness and local pain in the neck; to minimize the effect of expectation they were not told that the infiltration procedure was going to directly influence their migraine pain.

Normal subjects underwent measurement of pain thresholds in exactly the same locations as patients in basal conditions and on days 3, 10, 30, and 60.

Threshold evaluation was performed in a different room from that of the therapy and headache symptom assessment, by a different experimenter (AS) who was unaware of the group the subject belonged to.

### Migraine Parameters

For patients of both groups, the number and maximal intensity (Visual Analog Scale, VAS)2 of migraine attacks during the preceding 2 months were recorded, together with the number of times they had to take the rescue medication. The maximal intensity of the attack was defined as the highest level of pain they could bear before taking the rescue medication. The data were derived from the headache diary compiled routinely as part of their management protocol at the Headache Center of the “G. D’Annunzio” University. For the 60 days of treatment/study, all patients were asked to continue their migraine diary (number and intensity of attacks, number of times they had to take the rescue medication) and to avoid any other pain treatment on a continuous regimen (rescue medication allowed: 1000 mg paracetamol during pain attacks).

More in detail, the printed “headache diary” consists of a first section with indication of months, and days for each month where the patient is instructed to mark (in the relative day section) when a typical migraine attack is perceived and if any rescue medication is taken for that attack. The second section of the diary consists of a series of VAS, where the patient is invited to mark the maximal intensity of the attack on a specific day (and mark the date on it).

In the examined patients, at the end of the 2 months (both pretreatment and of treatment), the clinicians of the Headache Center counted the number of attacks relative to the 60-day period, then measured all VAS scales and calculated their mean: This was taken as the final value for that period and that patient.

#### Technique of Pain Threshold Measurement to Electrical Stimulation

A computerized constant current electrical stimulator was used (R.S.D. Stimulator, prototype, Florence 1997) to deliver 18-msec trains of 0.5-msec monophasic square wave pulses, frequency 310 Hz, repeated automatically every 2 seconds. The shape of the stimulating wave was constantly monitored via a double-trace oscilloscope connected to the stimulating device.10-12

To stimulate the skin, the current was passed through surface electrodes, consisting of a 10-mm-diameter circular plate in Ag/AgCl (reference electrode) and a cylinder in Ag/AgCl with a 0.3-mm-diameter base (stimulating electrode). They were connected to the skin via conductor paste, 1 cm apart. An adjustable spring device connected to the stimulating electrode maintained the
pressure exerted on the skin constant throughout measurement.

For stimulation of subcutis and muscle, 2 monopolar needle electrodes were used (0.3 mm in diameter, 25 mm in length, isolated with Teflon except for 1 mm at the tip). For subcutis measurement, the 2 needles were inserted vertically below the skin surface, 1.5 cm apart. For muscle measurement these same needle electrodes were used, their tips made to penetrate deep under the fascia (the intramuscular position was verified by observation of the movement of the electrodes under voluntary contraction and/or low-intensity electrical stimulation of the muscle).

The location of the electrodes to be placed for threshold evaluation (both surface and needle electrodes) was established by the clinicians of the Headache Center, based on the information provided by the experimenter responsible for palpation of cervical muscles. The sites to be tested were marked onto the skin surface and the patient was then sent to the room where threshold assessment was performed. For muscle threshold measurement at TrP level, the 2 needles were inserted 1.5 cm apart with the TrP situated in the middle between the 2 tips, so as to avoid penetration of the TrP with the needle as this procedure may result in release of the TrP itself.27 Insertion of these thin electrodes was not reported as painful by the subjects. In the referred pain areas, the 2 electrodes were placed horizontally in the middle of 1 frontal area (left or right, according to the referred pain pattern) or the temporal area (about 1 cm above the upper edge of the ear).

Stimulation began at very low current values (0.01 mA) and the intensity was automatically increased by the device with each stimulus repetition in increments of 0.03 mA, until the subject reported a first, nonpainful sensation (of touch in skin, paresthetic in subcutis, of slight twitch in muscle) and subsequently in increments of 0.1 mA, until the subjects reported a clear painful sensation. With the stimulation parameters and electrodes used, the sensation has distinct characteristics in the 3 tissues: Pricking pain for skin, linearly radiating prickling pain for subcutis and cramp-like pain for muscle. Pain thresholds were always measured by the method of the limits, that is, the value when pain was first perceived was stored by the computer device and the stimulus was then decreased, always at the same rate (0.1 mA), with storing of the value when pain disappeared. It was increased again until pain reappeared and the corresponding value was stored. The mean of the 3 readings was automatically calculated by the computer stimulator and displayed as final pain threshold for each tissue.

The subjects were instructed to signal the appearance/disappearance of the sensation by pressing a button connected to the computer stimulator. They were informed that the assessments were not intended to be tests of pain endurance, that no suprathreshold stimuli were supposed to be given, and that they should therefore not try to bear any pain before reporting it. They were also informed that they were free to stop the stimulus any moment for any reason and refuse continued participa-

tion at any time, without penalty of any sort (see Reference 11 for a more detailed description of the technique).

Before starting measurement of pain thresholds in the selected areas, a test measurement was performed in a control area (deltoid region of 1 side: Skin, subcutis and muscle) to familiarize the subjects with the procedure. Threshold values recorded on that occasion were discarded.

All measurements were performed in the pain-free interval, that is, outside the period of headache attacks in patients. When possible, they were all performed at the same time of day (between 10:00 and 12:00 AM); if the patient presented a crisis during that time frame, it was performed at least 6 hours after the pain disappeared. In fertile women of all groups, care was taken to measure thresholds in basal conditions always in the same relative phase of their cycle (follicular phase).11

Cutaneous Thresholds in Migraine Sites of Patients Without Active Cervical Trigger Points

A number of migraine patients have been reported to present cutaneous allodynia in the typical migraine sites for several days after an attack, though not evidenced by electrical stimuli.4,17,31 To rule out the possibility that any change in cutaneous pain thresholds in the referred area in our patients was due to the effect of the preceding migraine attack rather than to the TrP action, we needed to verify that no significant change in cutaneous thresholds was present, in the interval between attacks, in migraine patients without active cervical TrPs. We therefore examined migraine patients responding to the same inclusion criteria as patients of group 1, except that they had to be negative for the presence of active trigger points in muscles of the cervical region. Ten patients were selected (8 women, 2 men, aged 25 to 45 years, mean age: 30.4 ± 8.07). In the interval between attacks, cutaneous pain thresholds to electrical stimulation were evaluated in their typical migraine sites (frontal/temporal regions) with exactly the same procedure as for the other experimental groups.

TrP Infiltration Technique

The infiltration was performed deeply at muscle level. The needle tip was made to penetrate deep under the fascia and then a small amount of anesthetic was injected first into the point. Then the needle was withdrawn slightly, its inclination changed fractionally and again a small quantity of anesthetic was injected. The procedure was repeated 6 times so as to perform micro-injections all around the TrP in a circular area of approximately 2 mm in diameter.27 Just 1 trigger point was injected in each patient so as to avoid different procedures in different patients. When more than 1 TrP was present in the same patient, the most active 1 was chosen for the injection.
Infiltration was performed by the clinicians of the staff of the Headache Center, who were not blinded to the patient's group.

Phase 2: Secondary Experiment

Although a true placebo treatment is not possible for TrP infiltration, a secondary experiment was designed to verify the possible influence of a “placebo-like” procedure in migraine patients, for a more limited period of time (30 days). This consisted of penetration of a needle not in the TrP site, but in a nearby area, in a position similar to that used for insertion of one of the needles for threshold evaluation. These patients were given the same information as those subjected to TrP infiltration, that is, that the procedure would probably be beneficial for the sensations of stiffness and local pain in the neck. Selection criteria for patients of this experiment were the same as those for patients undergoing no treatment (see Main Experiment).

Twelve patients meeting these criteria were selected (9 women and 3 men, aged 24 to 44 years, mean age: 32.33 ± 6.44 years) of 38 examined. Their mean age did not differ from that of patients and normal subjects examined in the first phase. They were affected with fronto-temporal or temporal migraine and showed TrPs in the sternocleidomastoid (n = 7), semispinalis cervicis (n = 3), or splenius cervicis (n = 2) (referred areas coinciding with migraine sites). Two patients also had TTH pain attacks, with characteristics similar to those of the patients’ groups of the main experiment.

All 12 patients underwent threshold measurement in the TrPs and referred areas in basal conditions. Threshold measurements were repeated on the 3rd, 10th, and 30th day after the initial evaluation, immediately before the “placebo-like” treatment.

For 30 days before start of treatment and 30 days of treatment, all patients compiled the migraine diary with notation of number of pain attacks and their peak intensity, with the same procedure adopted for patients of the main experiment.

The protocol adhered to the guidelines established by the Declaration of Helsinki for human studies and was approved by the local Ethics Committee of the “G. D’Annunzio” University of Chieti (main experiment plus amendment for secondary experiment).

Statistical Analysis

Mean ± SEM values were calculated of thresholds for each tissue and evaluation time, of number of migraine attacks, of maximal pain intensity of attacks and of number of rescue medications taken (relative to periods of 60 days before therapy and 60 days of therapy for the main experiment and 30 days before therapy and 30 days of therapy for patients of the minor experiment). The comparison between threshold values in the groups of patients and normal subjects (in basal conditions and at the end of treatment) was performed via 1-way ANOVA, followed by Bonferroni test for multiple comparisons. The temporal trend of thresholds during therapy was evaluated via 1-way ANOVA for repeated measures, with the Bonferroni test for multiple comparisons. The comparison between migraine parameters (number and intensity of attacks, number of rescue medications taken) of the periods preceding and after therapy was performed via Student’s t test for paired samples.

To examine the relationship between the change in pain thresholds in migraine sites and the change in migraine pain due to treatment in group 1: Pain thresholds for each tissue in the target at the end of treatment (60th day) were expressed as a percentage of thresholds recorded in basal conditions for each patient; number and intensity of migraine attacks in the 60 days of treatment were expressed as a percentage of number and intensity of attacks recorded in the 60 days preceding treatment for each patient; the linear regression analysis was applied between the percentage threshold at the 60th day (independent variable) and the percentage number or intensity of migraine attacks in the 60 days of treatment (dependent variable).

Significance level was established at \( P < .05 \).

Results

Phase 1: Main Experiment

Pain Thresholds

In basal conditions, pain thresholds to electrical stimulation of skin, subcutis and muscle in patients of group 1 (active treatment) and group 2 (no treatment) were significantly lower than normal in both the TrP and the referred pain area (site of migraine pain), testifying hy-
peralgesia (1-way ANOVA: significant trend: \( P < .0001 \)) (Fig 2).

In patients of group 1, during treatment, thresholds increased progressively and significantly in skin, subcutis, and muscle not only in the TrP but also in the referred area (ANOVA for repeated measures: \( P < .0001 \)) (Fig 3). At the end of treatment as compared to baseline, the threshold increase in the TrP and referred area was, respectively: 127.8% and 33.3% in skin, 123% and 20.5% in subcutis, 62%, and 39.9% in muscle.

In patients of group 2 (no treatment), thresholds did not change significantly over the 60 days of study either in the trigger and referred area (Fig 4). At the end of treatment as compared to baseline: Skin threshold decreased by 2% and 3% in the TrP and referred area, respectively; subcutis thresholds increased by 8.5% in the TrP and decreased by 3.3% in the referred area; muscle thresholds increased by 3.4% in the TrP and decreased by 0.6% in the referred area.

In normal subjects, there was no significant trend for variation of thresholds over a period of 60 days on repeated measurements (Fig 5).

At the 60th day after treatment, the comparison between treated patients, untreated patients and normal subjects revealed a significant trend for variation of thresholds for all tissues in both the TrP and the referred area (1-way ANOVA: \( P < .0001 \)). Internal comparisons revealed that: in treated patients, all thresholds were still significantly lower than normal (.001 < \( P < .05 \)), except for the skin and subcutis in the referred area, in untreated patients, all thresholds were significantly lower than in untreated patients (.001 < \( P < .01 \)) (Bonferroni test for multiple comparisons).

**Cutaneous Thresholds in Migraine Sites of Patients Without Active Cervical Trigger Points**

Pain thresholds to electrical stimulation in migraine patients not presenting active cervical TrPs, measured at frontal/temporal sites in between attacks, were: 1.82 ± 0.11 mA (mean ± SEM). They did not differ significantly from thresholds measured at the same level in normal subjects (1.95 ± 0.12 mA, Student’s \( t \) test for unpaired samples). In these patients, the mean number of migraine attacks and their intensity in the preceding 6 months were: 18.1 ± 1.11 and 80.8 ± 3.16 mm, respectively; they did not differ significantly from migraine parameters in patients of groups 1 and 2 (see paragraph below).

**Migraine Parameters**

In group 1 patients, number and maximal intensity of migraine attacks during treatment decreased by 46.8% and 17.6%, respectively, compared with pretreatment; the difference was highly significant (\( P < .001 \)), whereas in group 2 patients, both number and intensity of attacks decreased very slightly (by 3.1% and 4.9%, respectively) and not significantly (Fig 6).

The mean number of rescue medications taken was 15.44 ± 0.38 (SEM) before treatment (60 days preceding start of treatment) and 7.3 ± 0.32 in the 60 days during treatment (reduction of 52.7%). The difference was statistically significant (\( P < .006 \)).
In patients of group 2, the mean number of rescue medications taken in the 60 days preceding and following admission to the study was 16.16 ± 0.54 (SEM) and 15.79 ± 0.61, respectively (reduction of 2.3%); the difference was not statistically significant.

Pain Thresholds Versus Migraine Parameters in Treated Patients

In group 1, the threshold increase at the end of treatment was inversely and linearly correlated to the decrease in the number of migraine attacks in skin \( Y = -0.21X + 79.145 \) (r: −0.3711; \( P < .006 \)) and muscle \( Y = 0.07X + 63.28 \) (r: −0.5947) \( P < .0001 \).

Phase 2: Secondary Experiment

Pain Thresholds

In basal conditions, pain thresholds to electrical stimulation of skin, subcutis, and muscle in these patients did not differ significantly from those of patients of group 1 (active treatment) and group 2 (no treatment) of the first phase, but were significantly lower than those of normal subjects at both TrP and referred site level (site of migraine pain), testifying hyperalgesia (1-way ANOVA: \( P < .0001 \); Bonferroni test for internal comparisons with normal subjects: \( P < .05 \)).

During treatment, thresholds increased slightly (5% to 18%) but not significantly in all tissues at both TrP and referred site level (ANOVA for repeated measures: no significant trend). At the end of treatment, all values were still significantly lower than normal \( P < .0001 \) \( P < .05 \) (Fig 7). This result was different from that recorded in patients undergoing active treatment during the first phase, in whom the number of rescue medications taken in the first 30 days of treatment decreased significantly with respect to the 30 days immediately preceding treatment \( \text{from} 7.75 \pm 0.21 \text{ to} 3.66 \pm 0.17 \text{ (decrease: 52.8%),} \) \( P < .0001 \).

Migraine Parameters

Number and maximal intensity of migraine attacks during treatment decreased slightly compared to pretreatment, but the difference was not significant \( 10.08 \pm 0.62 \text{ vs} 9.33 \pm 0.70 \) (SEM) for number (decrease: 7.4%); \( 78.16 \pm 3.62 \text{ vs} 71.83 \pm 3.8 \) mm for intensity (decrease: 8.1%)\). This was different from the results in treated patients of the first phase, where the comparison between number and mean intensity of attacks in the month preceding therapy and the first month of therapy showed a significant decrease \( 9.22 \pm 0.25 \text{ vs} 4.92 \pm 0.16 \) (decrease: 46.6%), \( P < .0001 \) for number; \( 80.70 \pm 1.69 \text{ vs} 66.52 \pm 1.57 \) mm (decrease: 17.6%), \( P < .0001 \) for intensity.

The mean number of rescue medications taken by patients of the secondary experiment was 7.30 ± 0.44 (SEM) in the 30 days preceding start of treatment and 7 ± 0.50 in the 30 days of treatment (decrease: 4.1%). The difference was not statistically significant. This result was different from that obtained in patients undergoing active treatment during the first phase, in whom the number of rescue medications taken in the first 30 days of treatment decreased significantly with respect to the 30 days immediately preceding treatment \( \text{from} 7.75 \pm 0.21 \text{ to} 3.66 \pm 0.17 \text{ (decrease: 52.8%),} \) \( P < .0001 \).

Discussion

Migraine patients with cervical active myofascial trigger points whose referred areas coincide with the site of

Figure 5. Pain thresholds to electrical stimulation of skin, subcutis, and muscle in normal subjects (n = 20, mean ± SEM) evaluated in sites corresponding to patients’ trigger and referred areas during the study period.

Figure 6. Migraine parameters (number and intensity of attacks) relative to the 60 days immediately preceding treatment (−60) and the 60 days of treatment (study) (+60) in patients of group 1 (n = 54) and group 2 (n = 24) (mean ± SEM). Asterisks above SEM bars refer to comparison between values of the period −60 and the period +60. ** ** ** ** ** ** P < .001.

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migraine present skin, subcutis and muscle hyperalgesia in both the TrP and the referred area in the pain-free period, confirming previous results in patients affected with myofascial pain syndromes from trigger points located in other body districts.\textsuperscript{28-30} The decreased cutaneous pain thresholds in migraine sites in basal conditions could theoretically be attributed to a different factor other than the presence of the TrP since it has been shown that migraine patients may present cutaneous allodynia for several days after the last painful attack.\textsuperscript{4,17} However, previous studies on assessment of thresholds in the intercritical phase suggest that this allodynia is modality-specific, being mostly present at mechanical but not electrical stimulation.\textsuperscript{20,31} Furthermore, our evaluation in migraine patients without active cervical trigger points reveal no decrease in skin threshold at migraine sites with respect to normal values in the interval between attacks: This provides further support for the notion that the electrical stimulation modality is not influenced by a possible allodynic state due to migraine. In our experimental conditions it is thus reasonable to interpret the cutaneous threshold decrease in migraine sites of patients with cervical myofascial pain syndromes as a reflection of the trigger point activity rather than of the migraine state.\textsuperscript{30}

Local infiltration of the TrP results in a progressive reduction of tissue hyperalgesia not only at trigger level but also in the referred areas, testifying a de-sensitization of the migraine zones. This desensitization process mostly involves the superficial (skin, subcutis) rather than deep (muscle) tissues. This is in line with the “general law” of the desensitization process that is normally seen in areas of secondary hyperalgesia of somatic tissues of the body wall, a process that typically proceeds from the surface to the deep tissues. This phenomenon, for instance, is classically observed in areas of referred pain/hyperalgesia from viscera and has previously been extensively documented.\textsuperscript{10,12}

Our patients also show a reduction of the specific migraine symptomatology, particularly in terms of number of attacks. Though the intensity of the attacks decreases less dramatically (<2 cm of VAS, slightly below the point of clinical relevance, according to several studies),\textsuperscript{22} the global spontaneous “pain burden” appears notably reduced, as also testified by a considerable decrease in assumption of rescue medication.\textsuperscript{22} This reduction of pain symptoms in the patients runs parallel to the threshold increase in superficial tissues at the referred (migraine) sites. In contrast, patients in whom no specific TrP therapy is performed show no changes in the profiles of either pain sensitivity in parietal tissues in the TrP and referred area or spontaneous migraine symptoms over comparable periods of time. Also normal subjects evaluated over similar periods of time do not show significant changes in the profile of their sensory thresholds in the evaluated areas, testifying a stable pattern of the threshold parameter utilized in this study over repeated measurements. In migraine trials, the placebo response is high, in terms of both efficacy and side effects.\textsuperscript{7} Thus, a proper control group to assess the placebo effect in our study would have been appropriate, consisting of patients with placebo treatment for their trigger points. Unfortunately, as already mentioned, a true placebo treatment for TrP infiltration does not exist, since dry needling, or injection of saline, is per se an effective therapeutic approach for TrP release.\textsuperscript{26} A “placebo-like” procedure, however, was attempted in our study, where the effect of a pseudo-TrP treatment with dry needle penetration in an area near the TrP was assessed. This procedure produced a slight increase in sensory thresholds and a very slight improvement in migraine pain, but the results were not significant and were markedly different from those reported by patients subjected to active (local infiltration) treatment. Though the lack of a true placebo group represents a limitation in the present study, we believe that the strong difference in the results obtained in the treated vs the non-treated and “placebo-like”-treated groups of migraine patients here evaluated provides sufficient support for the hypothesis that TrPs with these characteristics may contribute substantially to subjective and objective migraine symptoms, by increasing the susceptibility to the triggering of the attacks. The pathophysiology of this phenomenon remains to be elucidated; it is possible that an increased nociceptive input from the neck areas, due to the TrP presence, further enhances the level of sensitization of sensory neurons in the central nervous system and thus the transmission of migraine pain.\textsuperscript{5,15} A central nervous system hyperexcitability has, in fact, been demonstrated in neurophysiological research in migraine\textsuperscript{19} and a number of studies using quantitative sensory testing, including pressure algometry, have indeed shown an enhanced general sensitivity to painful stimuli in both adult and young migraineurs during as well as between attacks, a condition particularly pronounced at neck level.\textsuperscript{18,32}

Figure 7. Pain thresholds to electrical stimulation of skin, subcutis, and muscle in patients subjected to “placebo-like” therapy (n = 12, mean ± SEM) in the trigger and referred area during the study period.
Trigger points are strong sources of peripheral nociceptive input that can powerfully potentiate this mechanism. Microdialysis data in active TrP areas have, in fact, shown significantly higher levels of pronociceptive substances such as bradykinin, substance P, protons, calcitonin gene-related peptide, tumor necrosis factor-α, interleukin-1β, serotonin, and norepinephrine, with respect to areas of normal muscle and also areas of latent trigger points. If these points are formed in muscles whose projection coincides with the site of the migraine attacks, then a summation process may occur at central level that increases the migraine pain, in other terms, the peripheral input from the trigger enhances the level of excitability of the same neurons that are involved in the processing of the migraine pain, thus lowering the threshold for their activation by the classic migraine triggers. As a consequence of treatment, the peripheral input from the trigger is lowered, so the level of excitability of migraine neurons is reduced, together with their susceptibility towards migraine triggers.

Regardless of possible mechanisms, however, the results here obtained suggest that in the case of myofascial trigger points whose referred areas coincide with sites of migraine, systematic local TrP treatment is an important therapeutic approach, as it can eventually allow a substantial reduction of doses of specific migraine drugs, which is particularly important for patients with problems of intolerance/allergy to these compounds.

Acknowledgments

The authors are grateful to the staff of CIRS (Center for Informatics and Statistics of the “G. D’Annunzio” University of Chieti) for their help with the statistical analysis of the results.

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