A randomized controlled study on the effect of two different treatments (FREMS and TENS) in myofascial pain syndrome

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Aim. Myofascial pain syndrome (MPS) is a frequent cause of chronic musculoskeletal pain. Transcutaneous electrical nerve stimulation (TENS) is one of the most frequently employed treatments in MPS. The aim of this study is to compare the short and medium-term effects of frequency modulated neural stimulation (FREMS) to those of TENS in MPS.

Methods. Forty subjects with upper trapezius MPS were randomly allocated to 1 of 2 groups, treated with either FREMS (n=19) or TENS (n=21). Each treatment consisted in 10 sessions lasting 20 min each. Patients were evaluated before treatment, at 1 week, and at 1 and 3 months after the end of treatment. Clinical evaluation included parameters for measurement of pain levels using the neck pain and disability visual analogue scale (NPDVAS) and algometry, evaluation of myofascial trigger point characteristics and measurement of the range of cervical movement (range of motion, ROM).

Results. The FREMS group showed a significant improvement in the NPDVAS, algometry, in myofascial trigger point characteristics, and in the ROM (homolateral rotation, controlateral rotation, bending and extension) after the end of treatment and at 1 and 3 months follow-up evaluation. The TENS group showed significant improvement in the same outcome measures except for algometry and cervical extension, but these improvements were maintained only at the 1 month follow-up evaluation. However, were not observed statistically significant differences between FREMS of TENS in many of outcome measures.

Conclusion. Both FREMS and TENS have positive short-term effects on MPS. But, medium-term effects were achieved only with FREMS.

Key words: Myofascial pain syndrome - Musculoskeletal system - Pain - Rehabilitation.
The superior trapezius muscle is one of the most frequently affected muscles. Myofascial pain has a high prevalence among individuals with regional pain complaints. The prevalence varies from 21% of patients seen in a general orthopedic clinic, to 30% of general medical patients with regional pain, to as high as 85% to 93% of patients presenting to specialty pain management centers. The pathophysiology of MPS remains largely unknown. Recently, electrodiagnostic evidence has demonstrated the pathologic increase in release of acetylcholine (ACh) by the nerve terminal of an abnormal motor endplate under resting condition. This would suggest a primary dysfunction, according to the integrated hypothesis proposed by Simons et al., which postulates a positive feedback loop. It is hypothesized that the increase in release of Ach at the level of the motor endplate due to mechanical trauma or chemical stimulation of the nerve terminal results in sustained depolarization of the postjunctional membrane of the muscle fiber and produces sustained sarcomere shortening and contracture. This occurrence results in localized ischemia, which in turn results in the release of substances that sensitize nociceptors, produce pain, and induce release of neurovasoreactive chemicals. These chemicals lead to increases in the release of Ach, which sustains the cycle.

Numerous therapeutic approaches have been used with varying success rates to treat MPS and can be divided into pharmacologic and nonpharmacologic treatments. The first group includes injection of local anesthetics or saline, dry needling, botulinum toxin, systemic pharmacological therapy with non-steroidal anti-inflammatory drugs, antidepressants, benzodiazepine, tramadol, α2-adrenergic agonistics and anticonvulsives. The second group comprises physiotherapy rehabilitative treatments: ultrasound therapy, transcutaneous electrical nerve stimulation (TENS), relaxation techniques, acupuncture, stretching exercise, mesotherapy, massage therapy, and repetitive magnetic stimulation (rMS). Among physical therapies, TENS is one of the most frequently employed treatments. Also if the effects are controversial, many randomized controlled trials showed the efficacy of TENS on musculoskeletal pain. In particular, a controlled study on chronic low back pain, showed that intensity of pain was significantly reduced more by TENS than placebo, 1 week after the end of treatment. Frequency modulated neural stimulation (FREMS) is a new type of transcutaneous electrical stimulation and this is the first time that FREMS is used in the treatment of musculoskeletal pain. The possible advantage of FREMS over conventional electrical stimulation is that the electrical impulses vary in frequency, intensity and duration, according to a predetermined sequence, which probably permit a modulation on the peripheral and central systems.

The aim of the present study was to compare the short (1 week and 1 month), and medium (3 months) term efficacy of FREMS to TENS in patients with MPS.

Materials and methods

Patients

We enrolled 40 patients (10 male and 30 female; mean age 44.2±15.0 years) suffering from MPS of the upper trapezius muscle in a randomized, controlled trial among those undergoing treatment at the Centro di Rieducazione Funzionale of the Policlinico G. B. Rossi in Verona between September 2003 and April 2004. Demographic and clinical characteristics are detailed in Table I. Thirty of the 40 patients had more than one trigger point in the superior trapezius muscle; in this case, only the most painful trigger point was treated. No patient had trigger points in other muscles. Diagnosis of MPS was based on the following criteria, as suggested by Esenyel et al.: presence of a tender spot characterized by spontaneous pain or associated with movement of the right or left superior trapezius muscle; reproduction or enhancement of the clinical symptoms by compression of the active trigger point; presence of a palpable taut band peripherally to the trigger point. Non-essential criteria considered in diagnosis were: presence of spontaneous pain in areas of the body different from the superior trapezius muscle; elicitation of referred pain by compression of the active trigger point; weakness of the trapezius muscle; restricted ROM of the cervical spine; palpable or local twitch response upon snapping palpation of the most sensitive spot in the taut band.

The following patients were excluded from the study: 1) patients with clinical signs and symptoms of fibromyalgia; 2) patients aged below 18 or above 80 years; 3) patients with mental retardation; 4) patients with neurological deficits involving the upper limbs.
Furthermore, we also excluded patients presenting contraindications for the administered therapies, which comprised those suffering from cardiovascular disease, hypertension, coagulopathies, ulcer, recent severe hemorrhage, renal insufficiency, severe hepatic disease, neoplasia, epilepsy, cutaneous pathology or pain of central origin; patients with metallic implants (clips, cardiac valves, pacemakers) and pregnant women were also excluded. All patients were informed on the experimental nature of the study and gave their consent for participation. The study was approved by the Ethics Committee of the University of Verona Hospital.

Patients were divided into 2 groups according to a simple randomization scheme. The first group (3 men and 16 women; mean age 48.9±13.9 years) was treated with FREMS and the second group (7 men and 14 women; mean age 39.9±14.8 years) was treated with TENS.

Patients were informed that they would be submitted to 1 of 2 possible different treatment procedures in order to evaluate which was more effective against pain. At the third month follow-up period, each patient was informed whether treatment actually had been administered.

Patients were evaluated by the same examiner who was blinded regarding the treatment. The treatments were performed by another examiner who was blinded about the clinical status of the patients.

Multiple comparisons using the Indipendent-Samples T-Test showed that age, sex, education, duration of pain crises, number of trigger points, history of cervical trauma, previous intake of analgesic and previous physical treatment were not statistically different between the 2 groups.

Prior to participation in the study, patients were instructed to avoid any physical therapy for 2 months and to refrain from taking any analgesic medication for 15 days. During the study period, none of the patients underwent any form of therapy excepted for the experimental treatment.

### Treatment procedures

Patients in each group received 10 treatment sessions (5 days a week for 2 consecutive weeks) lasting 20 min each.

### FREMS

FREMS is a new type of transcutaneous electrical stimulation (Lorenz Therapy®) that is characterized by sequences of electrical impulses, which vary in frequency, intensity and duration according to a predetermined sequence (Figure 1).

The FREMS device was administered using the electrical stimulator ETS 501-PhysioFlog® (Lorenz Biotech SpA, Medolla, Modena, Italy). Every electrical stimulus emitted is a negative monophasic impulse, characterized by high voltage (<300 V), low intensity (<10 μA) and short duration (10-40 μs), with a spike of short duration (7 ns).
The stimuli were arranged in specific protocols obtained from empirical studies; the sequences were recorded on a computer that controlled the Lorenz Therapy™ device during treatment. The program used is characterized by an increase of duration in the early phase (from 10 to 40 µs) and an increase in frequency in the late phase (from 1 to 40 Hz). We used 2 electrodes applied on the affected superior trapezius muscle: the positive electrode (red electrode) was placed on the most painful trigger point and the negative electrode (black electrode) at 8-10 cm to the outside of trigger point.

Stimulation intensity was adjusted from each patient based on the subjective pain threshold; the goal is to perceive significant local sensation without excessive discomfort.

TENS

TENS treatment was performed according to parameters recommended by Graff-Radford et al.\textsuperscript{22} using a Phyaction 787 instrument (Uniphy, Ekkersrijt, Netherlands). The negative electrode was placed on the most painful trigger point of the superior trapezius muscle and the positive one was placed on the acromial tendon insertional site. The current frequency was set at 100 Hz, pulse width was set at 250 µs, and was delivered in an asymmetrical rectangular biphasic wave form, with zero net DC current, and the intensity was set to the patients comfort, below the threshold of muscular contraction (<39 mA). To define the stimulation intensity, we increased the intensity until significant local sensation was perceived without excessive discomfort. If there was a reduction in the sensation perceived after several minutes of stimulation, the stimulation intensity was increased until significant local sensation was again perceived.

Testing procedure

Patients were clinically evaluated before treatment (T0), after 1 week (T1), 1 month (T2) and 3 months (T3) following the end of treatment. Evaluation parameters included the following: i) measurement of the subjective intensity of pain through the neck pain and disability visual analogue scale (NPDVAS) and the algometry; ii) evaluation of the myofascial trigger point characteristics through manual palpation; iii) evaluation of the ROM of the cervical spine.

NPDVAS

Disability related to pain in everyday life activities and to functional limitation of the cervical spine was evaluated with the NPDVAS.\textsuperscript{14, 32} Patients were asked 20 questions about subjective pain intensity and problems in performing everyday life activities. Answers to each question were scored on an analogical continuum, where 0 represents absence of disability and 10 intolerable disability. The total score ranges from 0 to 200, and consists of the sum of scores for the single answers.

Algometry

Pain threshold at the trigger point was measured with a pressure algometer (Effegi, Alfonlins, Italy), according to the technique recommended by Fischer.\textsuperscript{33} The principal myofascial trigger point of the superior trapezius muscle was identified and marked, so that successive measurements would be performed over the same area. After having explained the pain threshold measuring technique, the patient was invited to maintain a relaxed position, since muscular tension prevents transmission of pressure to the trigger point and results in falsely high threshold indications. The algometer was applied to the trigger point with the metal rod perpendicular to the surface of the skin. Compression pressure was gradually increased at the rate of approximately 1 kg/s. The patient was asked to signal when he began to feel pain or any discomfort, at which point compression was stopped. Four consecutive measurements were performed during an interval of 2 min. The average of these evalua-
EVALUATION OF MYOFASCIAL TRIGGER POINT CHARACTERISTICS

Each patient was asked to point with his finger the most painful zone in the affected trapezius muscle. Subsequently, the myofascial trigger point characteristics were evaluated by the examiner through palpation of the zone pointed out by the patient. Zero points were assigned when the examiner noticed an increased consistency of the trigger point in absence of pain; 1 point when the consistency was increased but the patient reported pain only after an explicit question from the doctor; 2 points when the consistency was increased and the patient spontaneously reported pain at the manual pression; 3 points when the consistency was increased and the patient manifested withdrawal from palpation.

ROM

ROM of the cervical spine was evaluated by means of a tape measure, according to the technique proposed by Clarkson et al. Bending and extension were evaluated by measuring the distance between the point of the chin and the suprasternal sulcus in the positions of maximum bending and extension of cervical spine. Lateral bending was evaluated measuring the distance between mastoid process and homolateral acromion in the positions of maximum bending at both sides of the cervical spine. Rotation was evaluated by having the patient rotate his head up to the limit of movement and measuring the distance between the point of the chin and the acromion at both sides of the cervical spine.

Statistical analysis

The 2 analysis of variances (ANOVAs) with repeated measures were used for comparing data recorded before and 1 week after treatment (T0-T1), before and 1 month (T0-T2) and before and 3 months after treatment (T0-T3), and for comparing the effect of treatment among the FREMS and TENS groups. For this purpose, we evaluated the differences in performances before and 1 week after treatment (T1–T0), and before and after 1 (T2–T0) and 3 months after treatment (T3–T0) in all outcome measures between the 2 groups.

The statistical analysis considered a time factor at 4 levels (T0, T1, T2, T3) and a group factor between subjects at 2 levels (FREMS and TENS).

Post-hoc comparisons were performed with paired- and independent-samples t-tests.

The a level chosen for all analyses was 0.05.

Results

WITHIN-GROUP TREATMENT EFFECT

The ANOVA statistical analysis showed that the time factor is significant at NPDVAS, algometry, evaluation of trigger point characteristics, homolateral rotation, controlateral rotation, bending and extension and isn’t significant at homolateral bending and at controlateral bending.

FREMS GROUP

The FREMS group showed a significant improvements of performance in all pain testing procedures (NPDVAS, algometry) and in the evaluation of myofascial trigger point characteristics. The ROM evaluation showed a significant increase in the range of homolateral rotation, controlateral rotation, homolateral bending, bending and extension of the head. These improvements persisted both at 1 and 3 months post-treatment. The results of statistical analysis are summarized in Table II.

TENS GROUP

The TENS group showed significant improvements in performance in NPDVAS, in the evaluation of myofascial trigger point characteristics and, in ROM evaluation, in homolateral rotation, controlateral rotation and bending of the head. At the 1 month follow-up visit, this improvement had returned non-significant levels in all outcome measures, except for NPDVAS and evaluation of myofascial trigger point characteristics. No significant effects of TENS were seen at the 3-month follow-up visit. For the results of statistical analysis see Table II.

Between-groups treatment effect

The ANOVA statistical analysis showed that the time x group factor is significant at algometry, evaluation of TP characteristics and extension and isn't significant at NPDVAS, homolateral bending, controlateral bend-
The effects of FREMS did not differ significantly from those of the TENS group in T1–T0, T2–T0 and T3–T0 differences in all outcome measures, except for algometry, extension, homolateral bending and evaluation of trigger point characteristics. The results of statistical analysis are summarized in Table III.
Discussion and conclusions

The results of the present study show the possible short and medium-term therapeutic effects of FREMS in the treatment of MPS as measured by both subjective and objective indices and through myofascial TP characteristics. Overall, the positive benefits of FREMS treatment lasted from a week to 3 months after the end of therapy. In the TENS group, significant improvement was observed at 1 week and 1 month following the end of treatment in some outcome measures (NPDVAS, homolateral rotation and evaluation of trigger point characteristics), but at 3 months follow-up did not show any significant improvements.

Another interesting point of our study is that the effects of FREMS showed a tendency towards progressive improvement over time. Indeed, the positive effects of treatment at NPDVAS, algometry and evaluation of trigger point characteristics still show significant benefits following the end of treatment. However, the statistical analysis of the differences (T1–T0, T2–T0, T3–T0) of all outcome measures between the 2 groups showed significant differences only at algometry, extension, homolateral bending and at evaluation of trigger point characteristics.

The use of TENS is recommended as clinical therapy for chronic MPS. However, only a limited number of studies have reported that TENS can actually relief pain in MPS in the immediate post-treatment period and the possible medium and long-term effects of TENS have never been addressed.

It has been proposed that pain relief resulting from TENS could be explained by an action at the level of peripheral and/or central nervous system. The peripheral effect could be due to a slowing of conduction in both small and large afferent nerve fibers. As to the central effect, the activation of large afferent fibers induced by TENS may stimulate inhibitory neurons in the spinal dorsal horns, thus suppressing the neurons in laminae I, II, and V, which ordinarily fire in response to noxious stimuli and also may activate supraspinal inhibitory systems acting on nociceptive spinal neurons.

The use of FREMS in the treatment of musculoskeletal pain is new. There have been no studies investigating its mechanism of action. Even if the characteristics of electrical stimulus modulation provided by FREMS are different with respect to TENS, it can be hypothesized that both methodologies provide similar interferences on the peripheral and central nervous systems. Indeed, the evidence of this mechanism is provided by the short and medium term efficacy of FREMS.

The most immediate and challenging questions regard the mechanism by which FREMS induces relief of chronic musculoskeletal pain and why these effects

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**Table III.** — Main results of the study: between groups comparisons.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Between group comparison</th>
<th>1 week-before difference</th>
<th>1 month-before difference</th>
<th>5 months-before difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPDVAS</td>
<td>F=1.617 p=0.189</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Algometry</td>
<td>F=3.227 p=0.025</td>
<td>t=2.621 p=0.013</td>
<td>t=0.7135 p=0.176</td>
<td>t=2.548 p=0.130</td>
</tr>
<tr>
<td>Cervical ROM</td>
<td></td>
<td></td>
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<tr>
<td>Homolateral bending</td>
<td>F=2.391 p=0.072</td>
<td>t=2.063 p=0.046</td>
<td>t=3.110 p=0.004</td>
<td>t=2.649 p=0.012</td>
</tr>
<tr>
<td>Controlateral bending</td>
<td>F=1.251 p=0.295</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homolateral rotation</td>
<td>F=1.843 p=0.143</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controlateral rotation</td>
<td>F=1.175 p=0.522</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bending</td>
<td>F=0.243 p=0.866</td>
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<tr>
<td>Extension</td>
<td>F=4.20 p=0.007</td>
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<tr>
<td>Trigger point</td>
<td></td>
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<tr>
<td>Evaluation of TP characteristics</td>
<td>F=12.752 p&lt;0.001</td>
<td>t=0.552 p=0.584</td>
<td>t=2.848 p=0.007</td>
<td>t=5.323 p&lt;0.001</td>
</tr>
</tbody>
</table>

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last longer after FREMS than after TENS stimulation. It is possible that the reduction of pain of MPS resulting from FREMS stimulation could be explained by interfering with 2 neuromuscular mechanisms responsible of sustained pain. First we can hypothesize that the reduction of pain itself could possibly lead to the interruption of a pathological vicious circle accounting for the chronic nature of MPS that Simons calls a “feed-back positive circle”. In this vicious circle, pain could sustain tissue anomalies typical of MPS and tissue anomalies themselves lead to a reinforcement of pain. These results could be responsible, as suggested by Simons, of resumption in performing, daily activities during the 2 weeks of treatment that stretched the upper trapezius muscle inhibitory neurons in the spinal dorsal horns, and also may activate supraspinal inhibitory systems acting on nociceptive spinal neurons. Moreover, Barrella et al. (Barrella M, Toscano R, Zanella A, Valdes V, Bevilacqua M. Predictable modulation of H-reflex amplitude in normal volunteers: electrical trans-cutaneous stimulation characterized by incremental changes in frequency and duration. Submitted) showed that FREMS, in 10 normal subjects, causes a reversible modulation of H-reflex.

This suggests that the 2 type of electrical stimulation may have a similar, but not identical mechanism of action at neuromuscular level. Indeed, FREMS therapy is based on changes in frequency, intensity and duration of electrical impulses emitted by an electrical stimulator. This peripheral electrical modulation, might be responsible for medium-term cortical inhibition.

Well, it is possible to conclude that, if TENS is more efficacy than placebo on the treatment of musculoskeletal pain, also FREMS therapy can carry out the same effects.

These results should encourage further research aimed at establishing the long-term cortical and peripheral modifications and clinical improvements in the treatment of MPS. In particular, it would be interesting to investigate the effect of FREMS on the spinal and cortical sensory and motor systems. Although no statistically significant differences were observed between FREMS of TENS, it can nonetheless be asserted that FREMS appears to be a valid alternative to TENS and more to placebo, showing high efficacy in treatment of MPS.


