Efficacy of dietary supplement with nutraceutical composed combined with extremely-low-frequency electromagnetic fields in carpal tunnel syndrome

Teresa Paolucci1, Giulia Piccinini2, Sveva Maria Nusca2*, Gabriella Marsilli2, Alice Mannocci3, Giuseppe La Torre3, Vincenzo Maria Saraceni1, Maria Chiara Vulpiani2, Ciro Villani4

1) Complex Unit of Physical Medicine and Rehabilitation, Policlinico Umberto I Hospital, “Sapienza” University of Rome, Italy
2) Unit of Physical Medicine and Rehabilitation, Sant’Andrea Hospital, “Sapienza” University of Rome: Via di Grottarossa 1035/1039, 00189, Rome, Italy
3) Department of Public Health and Infectious Diseases, Policlinico Umberto I Hospital, “Sapienza” University of Rome, Italy
4) University Department of Anatomic, Histologic, Forensic and Locomotor Apparatus Sciences, Section of Locomotor Apparatus Sciences, Policlinico Umberto I Hospital, “Sapienza” University of Rome, Italy

Abstract. [Purpose] The aim of this study was to investigate the clinical effects of a nutraceutical composed (Xinepa®) combined with extremely-low-frequency electromagnetic fields in the carpal tunnel syndrome. [Subjects and Methods] Thirty-one patients with carpal tunnel syndrome were randomized into group 1-A (N=16) (nutraceutical + extremely-low-frequency electromagnetic fields) and group 2-C (n=15) (placebo + extremely-low-frequency electromagnetic fields). The dietary supplement with nutraceutical was twice daily for one month in the 1-A group and both groups received extremely-low-frequency electromagnetic fields at the level of the carpal tunnel 3 times per week for 12 sessions. The Visual Analogue Scale for pain, the Symptoms Severity Scale and Functional Severity Scale of the Boston Carpal Tunnel Questionnaire were used at pre-treatment (T0), after the end of treatment (T1) and at 3 months post-treatment (T2). [Results] At T1 and T2 were not significant differences in outcome measures between the two groups. In group 1-A a significant improvement in the scales were observed at T1 and T2. In group 2-C it was observed only at T1. [Conclusion] Significant clinical effects from pre-treatment to the end of treatment were shown in both groups. Only in group 1-A they were maintained at 3 months post-treatment.

Key words: Carpal tunnel syndrome, Nutraceuticals, Magnetic fields

INTRODUCTION

One of the main causes of hand dysfunction is carpal tunnel syndrome (CTS), which is the most common peripheral neuropathy. CTS is characterized by compression of the median nerve in the carpal tunnel. Due to its high prevalence, early diagnosis of CTS is critical and can reduce the disability that is caused by this condition. The lifetime risk of developing CTS is approximately 10%.

The primary symptoms of classical CTS are numbness and tingling with or without pain in at least 2 of the median nerve-innervated fingers. These symptoms are often aggravated during sleep and in the daytime due to static or repetitive hand function. Most causes of CTS are idiopathic or spontaneous, in which bilateral symptoms develop in...
over 60% of patients. Common conditions that are related to secondary CTS include high-energy wrist traumas, endocrine disorders (as diabetes mellitus and hypothyroidism), pregnancy, rheumatoid arthritis, anomalous carpal tunnel structures, and occupational factors, such as repetitive motion and exposure to vibrating tools\(^3\)\(^,\)\(^5\). Large patient numbers, long outpatient waiting times, and traditional referral pathways in public health systems create delays in accessing treatments for this condition, necessitating alternative care pathways for the management of patients with CTS\(^6\)\(^,\)\(^7\). Severe cases of carpal tunnel syndrome are usually treated surgically, whereas conservative treatment is recommended for mild to moderate cases. Although it is not described in the literature the ideal technique or combination of approaches due to the limitations of the studies\(^8\)\(^–\)\(^10\), several conservative treatments relieve symptoms and improve functional ability such as splinting, oral drugs, injections, specific manual techniques, neural gliding exercises, physical therapies and nutraceuticals. Among physical therapies, a combination of static and dynamic magnetic fields (PEMFs) is shown efficacious in CTS, significantly reducing short- and long-term pain and improving objective neuronal functions\(^11\)\(^,\)\(^12\). Furthermore, there is evidence of the effect of extremely-low-frequency electromagnetic fields (ELF-EMFs) on several aspects of physiology; in particular, they have analgesic effects and elicit antinociceptive responses\(^13\)\(^,\)\(^14\). Percutaneous magnetic stimulation relieves palliative pain, presumably through modulation of unmyelinated C-fibers. Studies have suggested that it influences the excitability of inward rectifying K\(^+\) channels\(^15\). These observations implicate magnetized wrist wraps as a novel therapeutic device. Crow RS\(^7\) has shown that spontaneous remission can occur in CTS patients, which can persist. Nevertheless, the underlying neuropathology tends to progress. Also, oral supplementation to patients with mild to severe CTS is a common clinical practice and it is proved to be effective in nerve compression syndromes\(^16\)\(^–\)\(^18\). Nutraceuticals that contains alpha-lipoic OR/AND curcumin, B-group vitamins and Acetyl-L-carnitine (ALCAR) have significant anti-inflammatory, antioxidant, and neuroprotective effects on peripheral nerves\(^19\)\(^–\)\(^21\). Some studies\(^22\)\(^–\)\(^24\) show an antioxidant capacity of the alpha-lipoic acid, its ability to decrease neuronal sensitivity to pain by inhibiting neuronal T-type calcium channels, its ability to improve distal sensory and motor nerve conduction. Curcumin appears to have an antinociceptive property\(^25\) but also an anti-inflammatory action\(^26\) because it inhibits the production of several inflammatory mediators. In a recent Cochrane review\(^27\) it’s shown a moderate evidence that B-group vitamins at high doses may determine a significant short-term reduction in pain, numbness, and paresthesia. In a study of Curran MW\(^28\), Acetyl-L-carnitine (ALCAR) has been shown to be effective to increase peripheral nerve regeneration. Oral supplementation with a combination product that contains alpha-lipoic acid to patients with mild to severe CTS is a common clinical practice combined with physiotherapy or alone but there are few efficacy studies on the matter. It could be hypothesized that the use of nutraceutical stabilizes or could to strengthen the benefit of physical therapy by ELF-EMFs in CTS. The aim of this study was to investigate the efficacy of nutraceutical composed of alpha lipoic acid, N-acetyl-L-carnitine, curcumin, vitamins B, E, and C in patients treated with ELF-EMFs in carpal tunnel syndrome (CTS).

**SUBJECTS AND METHODS**

This study took place from July 2015 to January 2016. Thirty-one patients with an average age of 58.5 (± 10.9) years were diagnosed with CTS and were recruited at the Physical Medicine and Rehabilitation Unit of Policlinico Umberto I Hospital, Sapienza University of Rome (Italy). Clinical diagnosis of CTS was made on the basis of the American Academy of Neurology (AAN)\(^29\) by a physiatrist. Electrophysiologic diagnosis of CTS was made on the basis of the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM), the American Association of Neuromuscular and Electrodiagnostic Medicine, American Academy of Neurology and the American Academy of Physical Medicine and Rehabilitation guidelines\(^30\) by a neurophysiologist: if the results of the sensory and motor nerve conduction study (NCS) are abnormal (sensory distal latency: SDL>3.5 ms; motor distal latency: MDL>4.20 ms and nerve conduction velocity: NCV<49 m/s) in comparison to the result of the sensory and motor NCS of one another adjacent nerve in the symptomatic limb, the diagnosis of CTS is confirmed. Per these guidelines, unilateral CTS patients were included in the study, with a duration of symptoms of over 3 months, no other physical or medical therapy, no history of trauma of the wrist or hand, and no general metabolic disease. Patients were excluded if they had cervical radiculopathy, polyneuropathy, osteoarthritis or inflammation of joints in the hand, such as rheumatoid arthritis; had undergone CTS surgical release; were pregnant; aged under 18 years; or had a pacemaker or a history of cancer or epilepsy. The patients were informed in detail through an oral presentation on the scope and procedures per the Declaration of Helsinki by a researcher. Then, they were asked to participate in this clinical study, in which they were randomly allocated to a group 1-A (nutraceutical + ELF-EMFs) and group 2-C (placebo + ELF-EMFs), according to a computer-generated simple randomization list at a 1:1 ratio (software MATLAB R2007b\(^5\), The Matworks Inc., USA). With regard to concealment of the allocation, a physiatrist had identified the patients to confirm the inclusion and exclusion criteria, had obtained signed informed consent forms for participation in this study, had administered the evaluation scales, had performed the treatment with ELF and had administrated the nutraceutical or placebo. Thirty-one patients were divided in the group 1-A (n=16) with an average age of 58.7 (± 11.0) years and the group 2-C (n=15) with an average age of 58.3 (± 11.2) years. We collected data on age, gender, body mass index (BMI), dominant hand, professional activity. The patients, the physiatrist and the neurophysiologist were blinded with respect to the nutraceutical and placebo groups. The drug vials were identical and had a numerical identification code, which was made public to the researcher, by an external collaborator, only after the data collection and statistical analysis. Sealed envelopes were prepared for each group. Participants received their randomization letter after the first visit had been completed. This study protocol was
developed in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The study protocol (clinicaltrials.gov registration number: NCT02891512) was approved by the Ethics and Experimental Research Committee of Sapienza University of Rome (N=2,545/15) and was carried out per National Health Council Resolution No. 196/96. In addition to ELF EMFs, Group 1-A (N=16) was treated with a dietary supplement that was composed of alpha-lipoic acid (300 mg), N-acetyl-L-carnitine (400 mg), standardized turmeric extract (root) curcumin (150 mg [95%]), vitamin B1 (6.25 mg), vitamin B2 (6.25 mg), vitamin B6 (2.38 mg), vitamin B12 (6.25 mcg), vitamin E (9 mg), and vitamin C (125 mg) (Xinepa®, Kolinpharma Srl-Italy, number of registration 934388568). The dosage was twice daily, after breakfast and dinner for 1 month, beginning from the evening of the first ELF EMFs session. The registration number for Xinepa® at the Italian Ministry of Health is 69794. Group 2-C (N=15) was treated with a placebo dietary supplement twice daily, after breakfast and dinner for 1 month, starting from the evening of the first ELF EMFs session. Groups 1-A and 2-C received ELF EMFs at the level of the carpal tunnel 3 times per week for 12 sessions using an electromedical appliance (Limfa® Technologies—Registration Number. DD 60095484, Report N 2810660001 medical devices 1210963/R-Italy). All patients were seated with the upper limb resting on the table and the carpus positioned on the emitter. Each session lasted 47 minutes and entailed two consecutively run programs: (1) anti-edema (21 minutes) and (2) anti-inflammatory (26 minutes). The LIMFA® device is equipped with a touch screen display that allows the operator to select the programs. Its technology emits predetermined sequences of weak ELF fields, variable in shape, intensity and frequency. The results are obtained using the sequences and not the simple and fixed ELF fields (one frequency, one intensity, one shape). The frequencies varies from 1 to 80 Hz (multifrequency magnetic field), and the intensity sets to 100 μT. These sequences are registered at SIAE for the patent. To limit the bias, the same clinical investigator who was blinded to the treatment group allocation performed all assessments. The visual analog scale (VAS)32 and the Boston Carpal Tunnel Questionnaire (BCTQ)33, 34 were administered pretreatment (T0), after the end of treatment (T1) and 3 months post-treatment (T2). The VAS for self-assessment of pain was performed by the patient to quantify painful sensations before treatment and during follow-up. This scale is a 10-cm horizontal axis in which 0 means no pain and 10 indicates the worst pain possible. The BCTQ evaluates the severity of symptoms (symptoms severity scale [SSS], 11 questions) and functional severity scale (FSS, 8 questions). For each question, the patient’s responses were scored from 1–5 arranged in an increasing order of symptoms severity and the degree of difficulty felt in each activity described. This calculation is the sum of answers divided by the number of questions. At T0 and T1 (within the first week after the end of treatment) electrodiagnostic parameters were analyzed: median sensory distal latency (SDL), median motor distal latency (MDL), sensory nerve action potential amplitude (S-AMP), motor nerve action potential amplitude (M-AMP), median sensory nerve conduction velocity (SCV), median motor nerve conduction velocity (MCV). Splinting, other medications and physical therapies were not allowed during the study or follow-up.

The calculation of the sample size was performed using online sample size calculator software developed by DSS Research (https://www.dssresearch.com/). The clinically important difference of 0.70 points in the SSS score of the BCTQ, before and after the treatment with a standard deviation of 0.6 were used to compute the sample size according to the research by Peters-Veluthamanagil C35. The level of significance is set at alpha=0.05 and the power of the study at beta=0.80. The sample size required is 13 subjects per group.

The descriptive statistics included median with interquartile range (IQR, 25th and 75th percentiles) for quantitative variables and percentage and tables of frequencies for qualitative variables. A nonparametric approach was considered, based on the low number of patients. To compare treatment groups versus the control at the 3 times (T0, T1, and T2), nonparametric Mann-Whitney test was performed. The significance of the change in median in each group (T0 vs. T1 and T0 vs. T2) was determined by nonparametric Wilcoxon signed-rank test. The association between qualitative variables was evaluated by Fisher’s exact test. An analysis was planned according the intention-to-treat principle. IBM SPSS Statistics ver. 20.0 (Chicago, IL, USA) was used for the statistical analyses. All tests were two-tailed with a level of significance of p<0.05.

RESULTS

Thirty-one patients with diagnosis of CTS were included in the study and divided randomly into two groups homogeneous for gender (p=0.220), dominant hand (p=0.886) but not for professional activity (p=0.015) (Table 1). No statistically significant differences (p>0.05) were found in the two groups at baseline for BMI, Age, VAS, BCTQ-SSS and FSS and Electrodiagnostic parameters (Table 2). No patient was dropped out during treatment (Fig. 1). At the evaluation times between groups for the Mann-Whitney U test it wasn’t found a statistically significant difference (p>0.05) (Table 3). At Wilcoxon signed-rank test in the group 1-A we observed a significant reduction of VAS, BCTQ- SSS and BCTQ-FSS both at T1 and at T2 vs T0 (median T0=3.0, median T1=0.0, median T2=0.0 for VAS; median T0=2.4, median T1=1.4 and T2=1.3 for BCTQ-SSS; median T0=1.5, median T1=1.2 and T2=0.8 for BCTQ-FSS; p<0.05) and a significant improvement in median sensory distal latency (SDL) at T1 (respectively T0=3.3 ms and T1=3.1 ms; p<0.05) (Table 4).

The Group 2-C confirmed the same statistically significant results of the Group 1-A at T1. Instead the results at follow-up (T2) were not significant (p>0.05) (Table 5).
DISCUSSION

Compared to our starting hypothesis that the use of nutraceutical stabilizes or could to strengthen the benefit of physical therapy by ELF-EMFs in CTS our results didn’t show significant clinical effects compared to placebo in patients treated with ELF-EMFs. However in group 1-A (nutraceutical group+ ELF-EMFs) we observed significant clinical improvement (VAS, BCTQ-SSS and BCTQ-FSS) at T1 and it was also maintained at T2 while in group 2-C (only ELF-EMFs) these results were observed only at T1. Although with a no statistical significance difference between the two groups, the one with dietary supplementation with the nutraceutical keeps the results even after both treatments have been suspended at follow-up (T2). Both groups had shown significant clinical effects from pre-treatment to the end of treatment. Both groups had also shown a significant improvement in median sensory distal latency (SDL) from pre-treatment to the end of treatment. In the literature, nutraceuticals that contains alpha-lipoic OR/AND curcumin, B-group vitamins and Acetyl-L-carnitine (ALCAR) have shown various properties on carpal tunnel syndrome and neurological pain disorders\textsuperscript{19–21}. Alpha-lipoic acid has shown antioxidant and neuroprotective activities and it may lead to a significant improvement of clinical outcomes and electromyographic findings\textsuperscript{18}. Notarnicola A\textsuperscript{16} verified the trend toward better pain regression in the nutraceutical group (nutraceutical composed of Echinacea angustifolia, alpha lipoic acid, conjugated linoleic acid and quercetin) versus shock wave therapy in CTS. Also, a significant clinical impairment was reported in 112 subjects with moderately severe CTS after a 90-day treatment with a fixed association of alpha-lipoic acid and gamma-linolenic acid\textsuperscript{19}. The efficacy of alpha-lipoic acid may be increased by curcumin with regard to its neuroprotective, antioxidative and antinociceptive effects\textsuperscript{25, 36}. B-group vitamins are also used as a conservative and adjunct therapy in the treatment of CTS with vitamin C, for its antioxidant and protective effects on tendons\textsuperscript{27}. There are significant relationships between plasma vitamin levels and specific symptomatic components of CTS with regard to slowing of the median nerve\textsuperscript{25}. Other studies showed that patients with antiretroviral toxic neuropathy\textsuperscript{38}, diabetic neuropathy\textsuperscript{39} and chemotherapy-induced neuropathy\textsuperscript{40} have less pain and better motor and sensory function if treated with Acetyl-L-carnitine (ALCAR). We also know that in the literature there are studies of feasibility, safety and efficacy of testing static magnetic field therapy for CTS\textsuperscript{41}. Although the precise mechanism of ELF-MFs

### Table 1. Demographic and clinical data of participants at baseline

| Variables | Total group (n=31) | Group 1-A (n=16) | Group 2-C (n=15) |
|-----------|--------------------|------------------|------------------|
| Hand affected | Dominant hand (n, %) | 10 (62.5) | 9 (60.0) |
| | Non dominant hand (n, %) | 6 (37.5) | 6 (40.0) |
| Professional activity | Hand work (n, %) | 8 (50.0) | 14 (93.3)* |
| | No hand work (n, %) | 8 (50.0) | 1 (6.7) |
| Gender | Male (n, %) | 2 (12.5) | 5 (33.3) |
| | Female (n, %) | 14 (87.5) | 10 (66.7) |

*Significant difference between groups (p<0.05).

### Table 2. Clinical and electrodiagnostic variables in the two groups at baseline

| Variables | Total group (n=31) | Group 1-A (n=16) | Group 2-C (n=15) |
|-----------|--------------------|------------------|------------------|
| BMI (kg/m²) | 28.7 (25.4–33.2) | 26.0 (22.4–32.1) | 30.6 (26.9–33.6) |
| Age (years) | 56.0 (50.0–69.0) | 55.0 (52.0–71.3) | 59.0 (50.0–68.0) |
| VAS (cm) | 5.0 (0.0–6.0) | 3.0 (0.0–6.0) | 5.0 (0.0–7.0) |
| BCTQ-SSS | 2.5 (1.8–3.4) | 2.4 (1.6–2.9) | 2.5 (1.8–3.4) |
| BCTQ-FSS | 1.7 (1.0–2.2) | 1.5 (1.0–2.1) | 1.8 (1.1–2.5) |
| SCV (m/s) | 38.2 (27.6–43.9) | 38.9 (29.5–45.3) | 36.4 (33.3–43.6) |
| SDL (ms) | 3.3 (2.1–3.8) | 3.3 (2.9–3.8) | 3.0 (3.0–3.9) |
| MCV (m/s) | 52.9 (50.0–55.8) | 51.4 (49.2–55.2) | 53.7 (50.0–64.5) |
| MDL (ms) | 4.9 (4.1–6.2) | 4.6 (4.1–5.5) | 5.3 (4.1–6.3) |
| S-AMP (µV) | 4.6 (3.1–7.9) | 5.5 (2.2–8.3) | 3.8 (3.3–7.5) |
| M-AMP (mV) | 9.2 (5.3–12.1) | 10.0 (5.2–12.1) | 7.3 (5.3–12.4) |

VAS: visual analogue scale; BCTQ-SSS: Boston carpal syndrome-symptoms severity scale; BCTQ-FSS: Boston carpal syndrome-functional severity scale; SCV: sensory nerve conduction velocity; SDL: sensory distal latency; MCV: motor nerve conduction velocity; MDL: motor distal latency; S-AMP: sensory nerve action potential amplitude; M-AMP: motor nerve action potential amplitude.
Table 3. Between group analysis after the end of treatment (T1) and after 3 months post treatment (T2)

| Variables       | T1 Group 2-C (median, 25th–75th) | T1 Group 1-A (median, 25th–75th) | T2 Group 2-C (median, 25th–75th) | T2 Group 1-A (median, 25th–75th) |
|-----------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| VAS (cm)        | 3.0 (0.0–4.0)                    | 0.0 (0.0–3.0)*                   | 0.0 (0.0–4.0)                    | 0.0 (0.0–2.0)                    |
| BCTQ-SSS        | 1.5 (1.2–2.1)                    | 1.4 (1.2–2.5)*                   | 1.4 (1.2–1.9)                    | 1.3 (1.0–2.2)                    |
| BCTQ-FSS        | 1.0 (1.0–1.6)                    | 1.2 (1.0–1.9)                    | 1.3 (1.0–2.2)                    | 0.8 (0.8–1.9)                    |
| SCV (m/s)       | 38.9 (29.5–45.3)                 | 40.5 (0.0–48.4)                  | -                                | -                                |
| SDL (ms)        | 3.3 (2.9–3.8)                    | 3.1 (0.0–3.3)*                   | -                                | -                                |
| MCV (m/s)       | 51.4 (49.2–55.2)                 | 52.5 (47.3–56.6)                 | -                                | -                                |
| MDL (ms)        | 4.6 (4.1–5.5)                    | 4.2 (3.6–5.7)                    | -                                | -                                |
| S-AMP (µV)      | 5.50 (2.20–8.28)                 | 7.40 (0.00–11.00)                | -                                | -                                |
| M-AMP (mV)      | 10.0 (5.2–12.1)                  | 8.1 (5.5–12.0)                   | -                                | -                                |

*Significant difference between pre-treatment (T0) and post treatment (T1 and T2) (p<0.05).

VAS: visual analogue scale; BCTQ-SSS: Boston carpal syndrome-symptoms severity scale; BCTQ-FSS: Boston carpal syndrome-functional severity scale; SCV: sensory nerve conduction velocity; SDL: sensory distal latency; MCV: motor nerve conduction velocity; MDL: motor distal latency; S-AMP: sensory nerve action potential amplitude; M-AMP: motor nerve action potential amplitude.

Table 4. Group 1-A before (T0) and after (T1 and T2) treatment

| Group 1-A (n=16) | T0 (median, 25th–75th) | T1 (median, 25th–75th) | T2 (median, 25th–75th) |
|------------------|------------------------|------------------------|------------------------|
| VAS (cm)         | 3.0 (0.0–6.0)          | 0.0 (0.0–3.0)*         | 0.0 (0.0–2.0)*         |
| BCTQ-SSS         | 2.4 (1.6–2.9)          | 1.4 (1.2–2.5)*         | 1.3 (1.0–2.2)*         |
| BCTQ-FSS         | 1.5 (1.0–2.1)          | 1.2 (1.0–1.9)*         | 0.8 (0.8–1.9)*         |
| SCV (m/s)        | 38.9 (29.5–45.3)       | 40.5 (0.0–48.4)        | -                      |
| SDL (ms)         | 3.3 (2.9–3.8)          | 3.1 (0.0–3.3)*         | -                      |
| MCV (m/s)        | 51.4 (49.2–55.2)       | 52.5 (47.3–56.6)       | -                      |
| MDL (ms)         | 4.6 (4.1–5.5)          | 4.2 (3.6–5.7)          | -                      |
| S-AMP (µV)       | 5.50 (2.20–8.28)       | 7.40 (0.00–11.00)      | -                      |
| M-AMP (mV)       | 10.0 (5.2–12.1)        | 8.1 (5.5–12.0)         | -                      |

*Significant difference between pre-treatment (T0) and post treatment (T1 and T2) (p<0.05).

VAS: visual analogue scale; BCTQ-SSS: Boston carpal syndrome-symptoms severity scale; BCTQ-FSS: Boston carpal syndrome-functional severity scale; SCV: sensory nerve conduction velocity; SDL: sensory distal latency; MCV: motor nerve conduction velocity; MDL: motor distal latency; S-AMP: sensory nerve action potential amplitude; M-AMP: motor nerve action potential amplitude.

- Not collected.
remains unknown, they have unexpected short-term analgesic effects in neuropathic pain: a low-frequency pulsed magnetic field has analgesic, vaso-active, neuron-stimulating, and trophic effects in patients with diabetic polyneuropathy. Some groups have hypothesized that ELF-MFs in the picotesla and millitesla ranges improve neurotransmission and correct local immune pathology and that a physics-based combination of simultaneous static and time-varying dynamic magnetic field stimulation in CTS can influence the neuromodulation of nociceptive C and large A-fiber functions, likely through ion/ligand binding. This study has some limitations: the lack of a biochemical assessment of nutraceutical (thus, we were unable to determine the biochemical correlates of this result); the lack of nerve conduction study in all follow-ups (unfortunately, due to our unfunded research, it was not possible to ask patients an additional NCS at follow up); a brief duration of nutraceutical treatment. To obtain clearer results, our protocol should be amended to include increases in dosage of the integrator. The clinical value of oral supplementation with alpha-lipoic acid, curcumin phytosome and B-group vitamin before and after surgery in CTS patients could be recommended but for a minimum of 3 to 6 months. In our research, we maintained a label supplementation dosage to ensure the safety of the patients-up based on ethical considerations and cost. It might be desirable, in the light of these results, to plan a well designed randomized clinical trial, enlarging the sample size, lengthening the observation times (up to 1 year) and increasing in dosage of the integrator.

In conclusion, the nutraceutical composed of alpha lipoic acid, N-acetyl-L-carnitine, curcumin, vitamins B, E, and C has showed significant clinical effects for CTS in maintaining the result to follow up, demonstrating a positive association with the use of physical therapy as ELF-EMFs.

ACKNOWLEDGEMENT

We thank the Electromyography service of S. Pietro Hospital, Rome, Italy.

Conflict of interest
The authors declare no conflicts of interest.

REFERENCES

1) Kuo TT, Lee MR, Liao YY, et al.: Assessment of median nerve mobility by ultrasound dynamic imaging for diagnosing carpal tunnel syndrome. PLoS One, 2016, 11: e0147051. [Medline] [CrossRef]
2) Jabelecki CK, Andary MT, So YT, et al.: AAEM Quality Assurance Committee: Literature review of the usefulness of nerve conduction studies and electromyography for the evaluation of patients with carpal tunnel syndrome. Muscle Nerve, 1993, 16: 1392–1414. [Medline] [CrossRef]
3) Newington L, Harris EC, Walken-Bone K; Carpal tunnel syndrome and work. Best Pract Res Clin Rheumatol, 2015, 29: 440 –453. [Medline] [CrossRef]
4) Aboonq MS: Pathophysiology of carpal tunnel syndrome. Neuroscis Riyadh, 2015, 20: 4 –9. [Medline]
5) Sonohata M, Tsuruta T, Mine H, et al.: Clinical characteristics of neuropathic pain in patients with carpal tunnel syndrome. Hand Surg, 2014, 19: 43–48. [Medline] [CrossRef]
6) Lewis KJ, Ross L, Coppeters MW, et al.: Education, night splinting and exercise versus usual care on recovery and conversion to surgery for people awaiting...
41) Colbert AP, Markov MS, Carlson N, et al.: Static magnetic field therapy for carpal tunnel syndrome: a feasibility study. Arch Phys Med Rehabil, 2010, 91: 1098–1104. [Medline] [CrossRef]

42) Musaev AV, Guseinova SG, Imamverdieva SS: The use of pulsed electromagnetic fields with complex modulation in the treatment of patients with diabetic polyneuropathy. Neurosci Behav Physiol, 2003, 33: 745–752. [Medline] [CrossRef]

43) Bistolfi F: Extremely low-frequency pulsed magnetic fields and multiple sclerosis: effects on neurotransmission alone or also on immunomodulation? Building a working hypothesis. Neuroradiol J, 2007, 20: 676–693. [Medline] [CrossRef]