A new road to improve vitamin D and balance through Taopatch® and proprioceptive protocol in Multiple Sclerosis patients

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Abstract

In multiple sclerosis patients (MS), symptoms such as fatigue, lack of physical energy, spasticity, motor coordination disorders, tremors, dizziness and postural instability are most common. Cattaneo et al. (2007) studied the effects of stability training on MS patients, describing its efficacy in reducing all risks, by improving stability, and strength. The present study aimed to confirm our 2021 results on MS patients, combining the Taopatch® device with a proprioceptive rehabilitation protocol (PRP) targeting strength, balance, and biochemical parameters including vitamin D levels. Twenty MS patients, 8 males and 12 females, volunteered in the study. A KERN MAP Version 1.2 08/2012, Hand Grip Dynamometer was used to determine handgrip strength, whilst baropodometric and stabilometric measurements were assessed using the Sensor Medica® systems. The proprioceptive rehabilitation protocol included: 10 minutes of Motomed; 10 minutes of Human Tecar proprioceptive path; 15 minutes of physical exercises; and 15 minutes of massage therapy of whole spine. All patients wore the Taopatch photo emission devices (Tao Technologies), applied with the protocol of Carbonari B, et al. (2021) Testing procedures and blood sampling were carried out before and after the rehabilitation protocol. The paired sample t-test revealed statistically significant improvements for the baropodometric measures ($p<0.05$). In addition, the intervention induced a statistically significant improvement in the right ($p = 0.023$) and left ($p = 0.021$) handgrip strength. We didn't highlighted any statistically significant variation in hemathological parameters, but an increasing trend of vitamin D levels was detected. Combination of an adequate and specific rehabilitation protocol with application of Taopatch®, a photon emission device, improved handgrip strength of the upper limbs, rebalanced body structure decompensated in MS patients and also acting on vitamin D levels. In conclusion, Taopatch® is a supportive therapy for home-based PRP intervention, inducing an improvement in the quality of life and reducing spasticity associated with the disease.

Key Words: Proprioceptive rehabilitation protocol; biochemical parameters; vitamin D; balance; nanotechnology- based device; handgrip test; Taopatch®.

Eur J Transl Myol 32 (4): 10774, 2022 doi: 10.4081/ejtm.2022.10774

Multiple sclerosis (MS) is the most prevalent chronic inflammatory disease of the central nervous system (CNS), affecting more than 2 million people worldwide.[1] Etiopathogenesis is controversial and, to date, there is no effective treatment that stops neuroaxonal damage or promotes its remyelination.[2] In general, the therapies administered cause an alteration of the hematochemical parameters. Increasingly, a lack of vitamin D has been found in subjects suffering of MS; this turns out to be a very critical point, given that it seems to be able to modulate the activity and progression of the disease.[3] Inflammation affecting the CNS causes focal lesions, of variable and unpredictable extent, in the white and gray

matter of the brain and spinal cord, resulting in demyelination of axons.[4] The damage, resulting from the multifocal lesion, arises several symptoms of which, those most commonly experienced in MS patients, are paresis, sensory or balance disorders, fatigue and motor disability, upsetting the quality of life.[5] In fact, it is a disabling condition that also affects the musculoskeletal system by modifying its anatomical characteristics.[6] In this MS, context of a recent review, is defined as an impairment of walking, expressed as a reduction in speed, resistance and/or postural stability during or in an upright position. There is evidence to support the benefits of physical activity on the function of walking as indicators of motor disability, as it could act on centralized mechanisms increasing grey and white matter volumes in the context of different brain structures, including the basal ganglia, and leading to improved mobility of MS patients.[7] In a pilot study conducted from Proia et. (2019)[8] there were interesting results in terms of improvements in some impaired skills, such as balance, following a period of proprioceptive training. Pilates training, in MS patients, is also proven to improve functional balance by reducing the risk factors for falls.[9] Other results come from classical rehabilitation protocols (neuromotor rehabilitation and rhythmic auditory stimulation) and/or from the latest innovative technologies such as gait robot training and exergaming. Among these, exercise has shown a positive effect on fatigue management while other rehabilitation approaches or non-invasive brain stimulation have been shown to reduce spasticity. The rehabilitation protocols, as documented by neuroimaging tools, have had beneficial effects on pyramidal system (o tracts) and fatigue. They have increased the neuroplasticity and have had neuroprotective effects.[10] Other analyzed parameters come from the observation that the MS patients have high concentrations of blood lactate, under resting conditions; that evidence could be used as biomarker of the onset and progression of MS.[11] However, as suggested by Proia et al. (2016)[12] the recent discovery of a lactate receptor, at the encephalic level, has made possible to reconsider its role as an hormonelike involved in complex processes, such as the memory and neuroprotection. Recently, Amato et al.,[13] confirmed its neuroprotective role in a cohort of MS patients following a 12-week lactic acid training program. Indeed it could have a positive influence in the levels of brain-derived neurotrophic factor (BDNF), and of dehydroepiandrosterone sulphate (DHEAS), the most abundant neuroprotective steroid hormone in the human body that may improve myelination, beside other important biological functions.[13]

Supporting the effects of physical exercise, biomechanical devices may improve management of disabling symptoms in MS.[14-15] A study of Carbonari et al. (2021)[16] is one of the few that used Occlusal Splints and Taopatch® in athletes, showing positive effects on muscle performance, balance and posture.

Taopatch® is a new nanotechnology used in healthcare made up of nanocrystals, or quantum dots, that that when excited by body infrared and sunlight, it converts into multiple wavelength between 200 nm e 600 nm; in humans will act as specific light therapy with benefits on the whole organism, without releasing any chemical substance. Is already known that phototherapy enhance vitamin D production's; this could be really useful since is well documented the deficiency in MS patients.[1] Taopatch® has a small circular size, (16 mm in diameter) and is 1 mm thick. It is comfortable, non-invasive and practical to apply on the skin by adhesive tape. The materials are hypoallergenic and the mixture of quantum dots, the upconverting nanoparticles, are located inside the device.

In a study by Lomeo et al. (2019)[15] it has been shown that Taopatch® in MS subjects was been able to improve and prolong the effects on proprioception, balance and affected limbs constituting a valid therapeutic approach in this pathology.[16]

Therefore, the aim of this study was to highlight the effects of a proprioceptive rehabilitation protocol (PRP) combined with the application of the Taopatch® device to improve balance, strength and vitamin D levels in MS patients.

Materials and Methods

The MS patients enrolled in our study was evaluated before and after ten weeks of training. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Palermo 1, Decree N 7/2016 Policlinico Giaccone Hospital, Palermo, Italy. Informed written consent was obtained from all enrolled MS patients. Before study, an anamnestic examination was carried out by specialized medical personnel.

Twenty subjects (age: 44.88 ± 4.45; height: 168.25 ± 8.66; weight: 72.31 ± 17.28), diagnosed with a score in the Extended Disability Status Scale (EDSS) between 5.5 and 6.5, voluntarily enrolled in this study, at the "Vitality" Physical Medicine and Rehabilitation Center of Vita, Sicily, Italy.

From the 20 subjects enrolled, only 13 completed the study (five males and eight females), i.e., >50% of those recruited according the below inclusion criteria:

- Age between 35 and 45 years
- Absence of clinical relapses, in the 12 months preceding the study;
- Total score not less than 5.5 and not more than 6.5 in the EDSS;
- Absence of other diseases (tumors, epilepsy, severe cardiovascular diseases, osteoporosis, etc.)
- Presence of spasticity in arms and legs

Subjects performed a proprioceptive rehabilitation protocol at home with the Taopatch® device worn all the time. The device was applied on the group and it was positioned on two different points: below the vertebrae C7 posteriorly and on the xiphoid process anteriorly. The

devices were applied before starting the training period (ten weeks, 24 hours a day).

Standardized blood testing was performed at the Center of Neurology Unit at the "Paolo Giaccone" University Hospital in the morning after overnight fasting for routine blood parameters and also for vitamin D in order to monitor systemic homeostasis. The serum was used to measure the biochemical markers using automated procedures according to standard commercial assays.

Blood samples were collected in specific tubes containing any anticoagulant and were centrifuged immediately at 1509× g for 10 min at 4 ◦C. The hematochemical parameters analyzed included: red blood cells, hemoglobin, hematocrit, white blood cells, platelets and vitamin D.

Participants in both groups performed at baseline (T0) and post training period (T1) a hand grip test (Handgrip test) with a MAP Hand Dynamometer (KERN MAP Version 1.2 08/2012) to assess the strength of the flexor muscles, with the maximum isometric grip (MIG), recognized as an important health indicator for determining musculoskeletal function, as well as weakness and disability.

The evaluations of the postural structure were assessed through the Sensor Medica® devices, combined with the Freestep® by Sensor Medica® program. This method allowed to perform stabilometric measurements, with detection of postural oscillations and strategies for maintaining balance in a neutral orthostatic position, and baropodomentric, such as analysis of the pressure points of the foot on the ground in static conditions and of the gait during walking. The device consists in a pressure platform with resistive sensors with conductive rubber. The PRP lasted 10 weeks, with a biweekly frequency, with the time of intervention of 60 minutes. The protocol consisted in a proprioceptive circuit based on the use of equipment to train the upper and lower limbs, for rehabilitation and postural re-education, physical exercise and therapeutic massage of the entire spine.

Specifically, it was divided into:

- 10 minutes of Motomed, a latest generation of cycle ergometer for the training of both the lower and upper limbs. The instrument allows to change the pre-

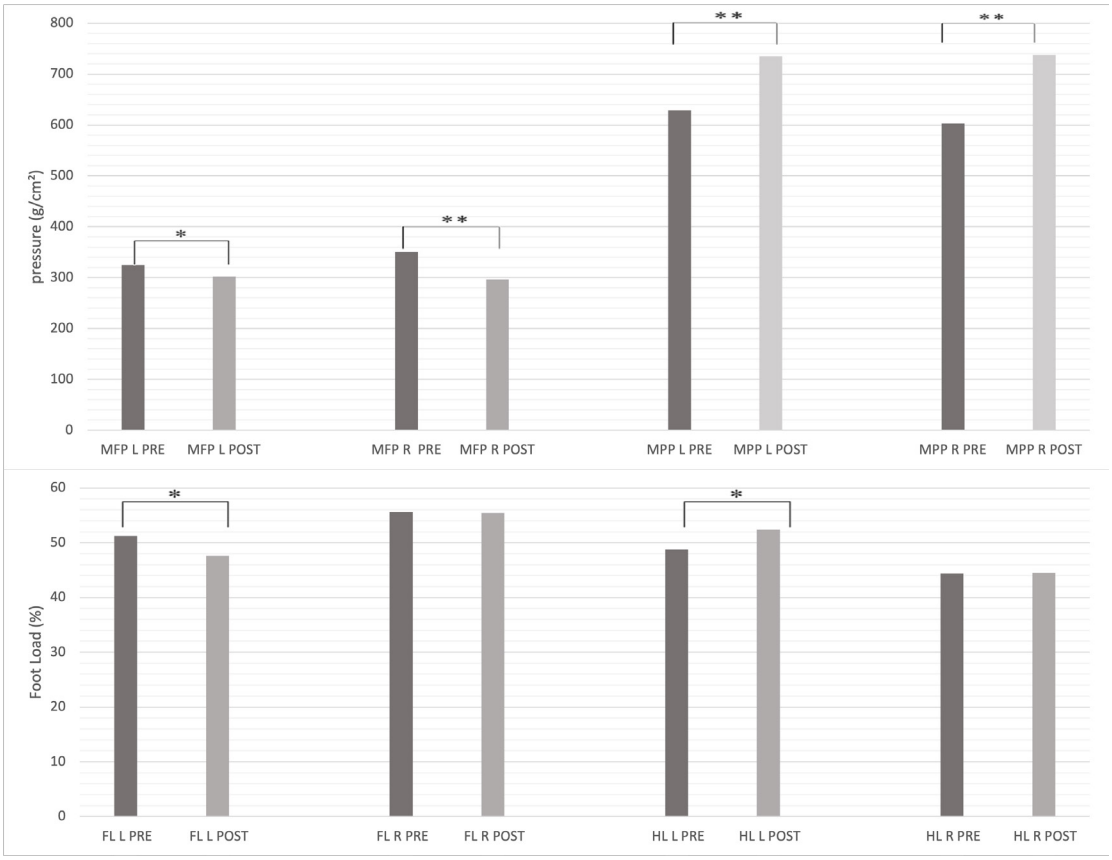

Fig 1. *A, upper panel and B, lower pane.: Some of the baropodometric parameters considered in the study and their changes from pre to post intervention. Notes: *: p<0.05; **:p<0.01; fig.A: MFP: mean foot pressure; MPP: maximum pressure point; L: left foot; R: right foot. ; fig.B: FL: forefoot load; HL: hindfoot load; L: left foot; R: right foot.*

selected training during the use in complete autonomy. Furthermore, it is possible to download the data of each training session and vice versa to download new programs to implement the activity;

- 10 minutes of Human Tecar Mat, besides having proprioceptive surfaces of different sizes, this sophisticated mechanism is designed to be adapted even to confined spaces, reproducing a path with different levels of instability, in order to simulate the conditions of a natural soil, forcing the body to readapt continuously. In this way the patients during the proprioceptive exercise received a positive stress when searching of a new balance, resulting in a good stimulus on the muscle tone and strength of the lower extremities. The exercise, carried out barefoot on various surfaces, aimed to sensitized the proprioceptive response by the CNS to the external stimulus (foot-ground);
- 15 minutes total of exercise, as described from Amato et al. (2021) ;[15]
- 15 minutes of massage therapy of the entire spine, with the treatment of self-myofascial release (SMFR) applied individually, following the protocol of Amato et al. (2021).[17]

The Kolgomorov–Smirnov test was used to check for normal distribution. Student t-tests were used to compare the baseline characteristics of the two groups. Changes between baseline and T1 of the group were analyzed by paired t-test. Within the group changes were calculated as percentage changes. Unpaired t-test were used to compare these differences in the two groups. All tests were two-tailed, and a 5% probability level was considered significant. We used SPSS (IBM SPSS Statistics 23) for statistical analysis.

Results

The paired sample t-test revealed statistically significant improvements for the baropodometric measures ($p<0.05$) associated with the intervention. In particular, in regards the mean foot pressure (MFP) we detected a reduction from T0 and T1 both for the left feet (324 ± 63 to 302 ± 58) and for the right feet (350 ± 65 to 296 ± 54) (Figure 1a). As to concern the maximal foot pressures (MPP), we found a change statistically significant in increase; in fact, we started with a value of 628 ± 124 to 735 ± 144 for the left feet and 602 ± 114 to 737 ± 140 for the right feet (Figure 1a). Analyzing both the forefoot and the hindfoot load, we found a difference statistically significant only on the left foot, a decrease for the forefoot load (51± 7 to 47 ± 8) and an increase for hindfoot load (48 ± 7 to 52 ± 8) (Figure 1b). In addition, the strength was detected, by using the handgrip test and we highlighted a statistically significant improvement in the right ($p = 0.023$) and left ($p = 0.021$) hand. In fact, it has gone from a value of 24 ± 8 to 26 ± 10 for the right hand and from 22 ± 9 to 24 ± 8 for the left hand (Figure 2). As regard the hemathochemical parameters analyzed,

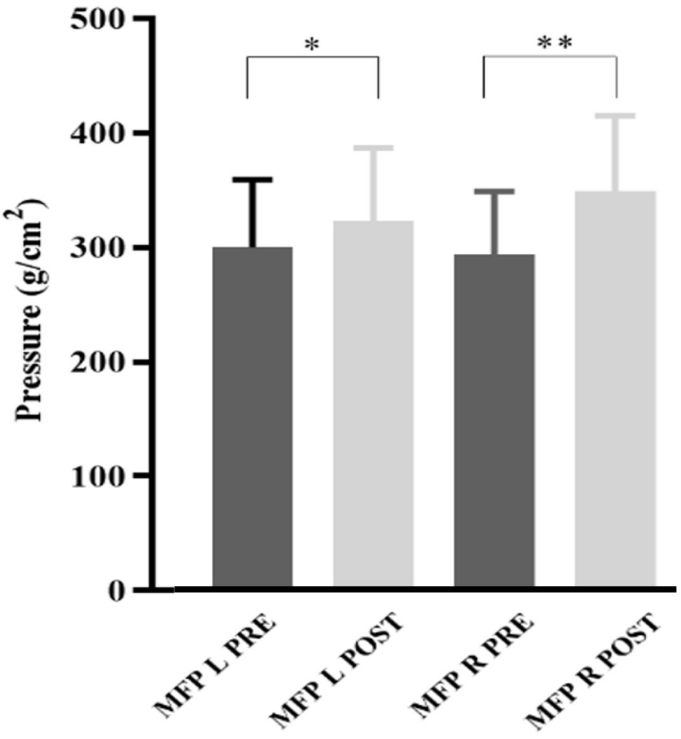

Fig 2. *Strength improvements in both hands are statistically significant.*

we didn't highlighted any statistically significant variation; however, it is necessary to underline an increasing trend as regards the levels of vitamin D. In fact, on average, an increase in the level was obtained from 25 ng/mL, an insufficient value, to 32 ng/mL which appears to pass from an insufficient levels to a sufficient concentration (data not shown).

Discussion

Multiple sclerosis (MS) is the most prevalent chronic inflammatory disease of the central nervous system of which the etiopathogenesis is still controversial. It is still known that physical activity can improve the symptoms correlated to this pathology. Based on the encouraging results of our previous study,[17] we decided to investigate the effect of the protocol which combined the photon emission device (Taopatch®) with a specific proprioceptive rehabilitation protocol (PRP) for balance, i.e., for functional parameters correlated with reducing known risk factors of falls.

The results here reported showed statistically significant improvements for the baropodometric measures ($p<0.05$) associated with the intervention in particular of maximal and mean foot pressures (Figure 1a) and the forefoot and hindfoot loads (Figure 1b). By analyzing the change, it appears to have been a worsening since there was a reduction of the foot pressure as well as of mean foot pressure. Instead, attention must be paid to another factor; before and after the treatment, there was a rebalance between the right and the left foot. As a matter of fact, rather than a big difference at the beginning of the protocol between the two feet, we detected a balance which led at similar values: MFP left foot 302 vs right foot 296 and MPP 735 left foot vs 737 right foot. This result shows that the PRP exerts a positive effect improving the balance in both feet, as the result of the improvement of the expression of ground pressure. To support this evidence, there are the results of the assessment on the forefoot and hindfoot load; we detected a decrease on forefoot on left after the PRP offset of the increase of the load on the hindfoot. Hence, there is a reduction of the load on the forefoot and an increase on the hindfoot for the left foot, while the right foot remains unchanged.

This is a demonstration that the PRP induces a new balance in the MS patients. In addition, as far as strength is concerned, the intervention induced a statistically significant improvement in both hands, with a p Value of 0.023 for the right and 0.021 for the left hand (Figure 2). According to other study already published a change in handgrip score reliably indicates a true change in functional abilities that are the actual or potential capacities of an individual to perform the activities and tasks that can be normally expected. Furthermore, this type of approach has been shown to have great potential to influence vitamin D levels, a parameter that shows a deficiency in MS patients.

In conclusion, if we put all our results together, we can say that the proprioceptive rehabilitation protocol setup by our team is a valid protocol to improve handgrip strength of the upper limbs and the expression of the body weight on the ground in contrast with the force of gravity, by improving the quality of life. Such improvements could be seen in a cluster of MS patients severely affected by this disease. We can consider the PRP a support home-based therapy in which the most important role is played by Taopatch® device, as previously described in our study,[17] that amplifies the effect of the proprioceptive training protocol by improving the quality of life.

Further studies are need to better understand other potential effects of the Taopatch® device on MS patients and how it could help them to decrease their symptoms.

List of acronyms

BDNF - brain-derived neurotrophic factor
CNS - central nervous system
DHEAS - dehydroepiandrosterone sulphate
EDSS - extended disability status scale
FL - forefoot load
HL - hindfoot load
MFP - mean foot pressure
MFS- mean foot pressure
MIG - maximum isometric grip
MPP - maximal foot pressures
MS - Multiple sclerosis
PRP - proprioceptive rehabilitation protocol
PRP - Proprioceptive Training Protocol
RR-MS - relapsing remitting MS
T0 - Baseline
T1 - After Training period

Contributions of Authors

AA and PP conceptualization, writing, original draft preparation; PP, GM, AI, PR, DG, AA, RS review and editing; FR,VF, DG, FF data collection.

All authors have read and approved the final edited typescript.

Acknowledgments

The authors thank the patients who volunteered for the study and also physical medicine and rehabilitation center "Vitality" from Vita, Sicily, Italy.

Funding

This research was conducted with PosturaLab Italia funding.

Conflict of Interest

The authors declare no conflicts of interests.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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References

1. Díaz C, Zarco LA, Rivera DM. Highly active multiple sclerosis: An update. Mult Scler Relat Disord. 2019 May;30:215-224. doi: 10.1016/j.msard.2019.01. 039. Epub 2019 Jan 24.
2. Lemus HN, Warrington AE, Rodriguez M. Multiple Sclerosis: Mechanisms of Disease and Strategies for Myelin and Axonal Repair. Neurol Clin. 2018 Feb;36(1):1-11. doi: 10.1016/j.ncl.2017.08.002.
3. Feige J, Moser T, Bieler L, Schwenker K, Hauer L, Sellner J. Vitamin D Supplementation in Multiple Sclerosis: A Critical Analysis of Potentials and Threats. Nutrients. 2020 Mar 16;12(3):783. doi: 10.3390/nu 12030783.
4. Lassmann H. Multiple Sclerosis Pathology. Cold Spring Harb Perspect Med. 2018 Mar 1;8(3):a028936. doi: 10.1101/cshperspect.a 028936.
5. Ślusarz R, Olkiewicz J, Bonek R, Filipska K, Biercewicz M, Wiśniewski A. The Impact of Motor Disability and the Level of Fatigue on Adherence to Therapeutic Recommendations in Patients with Multiple Sclerosis Treated with Immunomodulation. Int J Med Sci. 2021 Aug 27;18(15):3609-3614. doi: 10.7150/ijms.61964..
6. Owens B. Multiple sclerosis. Nature. 2016 Nov 30;540(7631):S1. doi: 10.1038/540S1a..
7. Baird JF, Sandroff BM, Motl RW. Therapies for mobility disability in persons with multiple sclerosis. Expert Rev Neurother. 2018 Jun;18(6):493-502. doi: 10.1080/14737175.2018. 1478289. Epub 2018 May 30.
8. Proia P, Amato A, Puleo R, Arnetta F, Rizzo F, Di Grigoli L, Zangla D, Schirò G, Ragonese P, Messina G. Efficacy of 12 weeks of proprioceptive training in patients with multiple sclerosis. Journal of Human Sport and Exercise, 2019;14(5proc), S1986-S1992. doi.org/10.14198/ jhse.2019.14.Proc5.19
9. Gheitasi M, Bayattork M, Andersen LL, Imani S, Daneshfar A. Effect of twelve weeks pilates training on functional balance of male patients with multiple sclerosis: Randomized controlled trial. J Bodyw Mov Ther. 2021 Jan;25:41-45. doi: 10.1016/j.jbmt.2020.11.003. Epub 2020 Nov 7.
10. Donzé C, Massot C. Rehabilitation in multiple sclerosis in 2021. Presse Med. 2021 Jun;50(2):104066. doi: 10.1016/j.lpm.2021. 104066. Epub 2021 May 11.
11. Cerexhe L, Easton C, Macdonald E, Renfrew L, Sculthorpe N. Blood lactate concentrations during rest and exercise in people with Multiple Sclerosis: A systematic review and meta-analysis. Mult Scler Relat Disord. 2022 Jan;57:103454. doi: 10.1016/j.msard.2021.103454. Epub 2021 Dec 5.
12. Proia P, Di Liegro CM, Schiera G, Fricano A, Di Liegro I. Lactate as a Metabolite and a Regulator in the Central Nervous System. Int J Mol Sci. 2016 Sep 1;17(9):1450. doi: 10.3390/ijms 17091450.
13. Amato A, Ragonese P, Ingoglia S, Schiera G, Schirò G, Di Liegro CM, Salemi G, Di Liegro I, Proia P. Lactate Threshold Training Program on Patients with Multiple Sclerosis: A Multidisciplinary Approach. Nutrients. 2021 Nov 27;13(12):4284. doi: 10.3390/nu13124284.
14. Juzeniene A, Grigalavicius M, Juraleviciute M, Grant WB. Phototherapy and vitamin D. Clin Dermatol. 2016 Sep-Oct;34(5):548-55. doi: 10.1016/j.clin dermatol.2016.05.004. Epub 2016 May 20.
15. Lomeo A, Cacciaguerra G, Garsia D, Scolaro A. Utilisation des dispositifs nanotechnologiques dans les pathologies dégénératives cérébrales. Étude prospective sur 28 patients atteints de sclérose en plaques. Hegel. 2019; 2, 114-121. https://doi.org/10.3917/heg. 092.0114
16. Carbonari B, Balducci F, Cesaretti G, Cesanelli L, Botticelli D, Messina G. Performance, balance and posture variations with Occlusal Splint and Taopatch® devices: a retrospettive cross-over study. J Sports Med Phys Fitness. 2021 Feb;61(2):317-323. doi: 10.23736/S0022-4707.20.11053-3. Epub 2020 Jul 30.

17. Amato A, Messina G, Feka K, Genua D, Ragonese P, Kostrzewa-Nowak D, Fischetti F, Iovane A, Proia P. Taopatch® combined with home-based training protocol to prevent sedentary lifestyle and biochemical changes in MS patients during COVID-19 pandemic. Eur J Transl Myol. 2021 Aug 31;31(3):9877. doi: 10.4081/ejtm.2021.9877.

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Submission: August 4, 2022
Accepted for publication: August 5, 2022