

REVIEW

BY PROF. DR. VESSELINKA NESTOROVA, M.D.

CHAIRMAN OF THE SCIENTIFIC COMMITTEE

CHOSEN BY ORDER No. R – 109-357 / 19.09.2022

OF THE RECTOR OF VARNA MEDICAL UNIVERSITY

TOPIC: The dissertation paper of Dr. Lili Yordanova Yosifova, for awarding the academic research degree of Doctor of Medicine (M.D.) in the field of higher education - 7. Health Care and Sports, Professional Field 7.1. Medicine, Scientific Specialty of Physiotherapy, Thalassotherapy and Rehabilitation at the Medical University of Prof. Dr. Paraskev Stoyanov in the city of Varna, on the following topic - "Study of the effect of high-energy laser in diabetic sensorimotor neuropathy" with Dissertation/Doctoral advisors Assoc. Prof. Dr. Evgenia Vladeva-Dimova, M.D. and Assoc.Prof. Dr. Mira Siderova, M.D.

Brief Resume of the Candidate

Dr. Lili Yordanova Yosifova was born in the city of Ruse, where she completed her secondary education in 1995. In 2001, she finished her studies at the Pleven Medical University with a Master's degree in medicine. In 2010, she received a diploma for the specialty of "Physical medicine and rehabilitation". In 2011, she finished her individual training in Social Medicine and Health Management at the Varna Medical University. Her professional career began in 2002, at the Ruse General Hospital as a resident physician in the Department of CARIL (Cardiology, Anesthesiology, Resuscitation/Emergency Medicine and Intensive Care). Since 2004, she has been working as a doctor in Physical medicine and rehabilitation in a number of medical facilities for outpatient and inpatient care. In 2017, Dr. Lili Yordanova Yosifova was appointed as a physician in Physical medicine and rehabilitation at UMHAT St. Marina in the city of Varna. In the same year, she was appointed an assistant at the Section of "Thalassotherapy, Physiotherapy and Rehabilitation" with the Department of "Physiotherapy, Rehabilitation, Thalassotherapy and Occupational Diseases" of the Varna Medical University.

Dr. Lili Yordanova Yosifova has finished a number of qualification courses and post-graduate studies: Laser therapy, Electrodiagnostics and Electrostimulation, Postisometric relaxation,

Acupuncture. She has passed the following qualification courses: "Pedagogical competence", "Legal framework, regulating the training of doctoral students", "Methodology of scientific research work", "Ethics of scientific research", "Statistical methods for data processing and presentation", "Communication and presentation techniques and skills", etc. Her main professional and scientific interests are in the field of acupuncture, laser acupuncture and laser therapy.

Dr. Lili Yordanova Yosifova is fluent in Russian and English, both written and spoken.

Dr. Lili Yordanova Yosifova is a member of the Bulgarian Medical Union, the Association of Physical medicine and rehabilitation and of the Programme board of the Master's degree programme "Rehabilitation, Thalassotherapy, Wellness and Spa", she is also the Director of studies for said Master's degree programme.

Diabetic neuropathy is one of the most common complications of diabetes, affecting about 50 % of patients with type 2 diabetes.

Diabetes mostly changes the sensory fibers of the peripheral nervous system expressed by changes in sensation and paresthesias and also disrupts the trophic function of the vegetative fibers of the nerves which causes the development of skin changes - ulcers and of diabetic neuro-osteoarthropathy (Charcot foot). These late complications of Diabetic sensorimotor neuropathy, in addition to increasing the economic costs of treatment and disability, also carry a risk of severe disability for sick.

Diabetes takes the fifth place as cause of health loss in Bulgaria, mainly due to premature death. Compared to the other countries of the European Union, Bulgaria ranks third in terms of age-standardized frequency of years of life lost due to diabetes in women and fourth in terms of health loss in men.

The neuropathic pain that often accompanies diabetic polyneuropathy is still a challenge for conventional pharmacological therapy. Given the limited response to pharmacotherapeutics, medical professionals are increasingly considering other forms of treatment, including photobiomodulation, involving laser treatment.

There are data that high-energy laser therapy combining two wavelengths (MLS-laser) is a physical factor with highly pronounced anti-oedematous, anti-inflammatory, regenerative and pain-relieving effects. Further it is also noted that compared to traditional laser therapy, MLS laser therapy is distinguished by a shorter course of treatment and longer-lasting therapeutic effects.

Dr. Yossifova's dissertation paper makes a comparative analysis and evaluation of the effects of treatment with high-energy laser radiation and the application of placebo procedures in patients with diabetic neuropathy. It studies the influence of high-energy laser radiation (MLS-laser) on superficial and deep sensory and electroneurographic parameters of the peripheral sensory and motor nerves of the lower limbs in diabetic neuropathy. The effect of the MLS-laser on neuropathic pain was monitored and a therapeutic algorithm of administering was configured, with the selection of optimal laser parameters and a course of treatment in diabetic neuropathy, as well as the duration of the therapeutic effect with analysis of short-term and long-term results.

Features of the dissertation paper presented for review

The dissertation paper of Dr. Lili Yordanova Yosifova is presented in 99 standard pages, in eleven sections of adequate ratio, illustrated with 25 Figures, 11 Tables and 3 Appendices. The structure is according to the requirements, specified in the Regulations for the development of the academic staff of the Varna Medical University.

The scientific work has the following structure: "Introduction" - 3 pages, "Reference Literature" - 28 pages, "Objectives and tasks of the research" - 1 page, "Materials and methods" - 12 pages, "Results" - 21 pages, "Discussion" - 12 pages, "Final Part" - 1 page, "Conclusions" - 1 page, "Contributions of the scientific work" - 1 page, "Scientific publications, related to the dissertation paper" - 1 page.

The Referenced Literature consists of 129 sources, 11 of which are in Cyrillic and 118 - in Latin. Around 40 % of the citations are from the last ten years, 16 % of which from the last five years.

Three full-text publications in periodical scientific publications, presented by Dr. Lili Yordanova Yosifova, are related to the topic of the dissertation paper.

A major focus in the Referenced Literature review is a detailed consideration of the epidemiology, pathogenesis, and clinical presentation of diabetic neuropathy. The means of pathogenetic and symptomatic treatment of the disease are described, as well as the challenges of pharmacological therapy. The structure and mode of operation of lasers, as well as the specifications, parameters and interaction with the biological targets of laser radiation are comprehensively presented. Historically are presented the application and clinical experience with low-intensity laser therapy and high-energy laser (MLS laser) in diabetic sensorimotor neuropathy.

The basis of the dissertation is a clearly formulated objective - To study the effect of high-energy laser (MLS - laser) in diabetic sensorimotor polyneuropathy and to create its own work protocol.

In realizing the set objective, the author has identified the following tasks:

To investigate the effect of high-energy laser radiation on superficial and deep sensation of the lower extremities in diabetic neuropathy.

To trace the influence of high-energy laser radiation on the electroneurographic parameters of the peripheral sensory and motor nerves of the lower limbs in diabetic neuropathy.

To conduct a comparative analysis and evaluation of the effects of treatment with high-energy laser radiation and the application of placebo-procedures in diabetic neuropathy.

To investigate the effect of high-energy laser therapy on neuropathic pain and to determine the presence or absence of side effects and adverse local or general reactions.

To prepare a therapeutic algorithm for working with a source of high-energy laser radiation, with the selection of optimal parameters of the laser and a course of treatment for diabetic neuropathy.

Materials and methods

For the purposes of the study, 69 patients were examined, they met the precisely defined criteria. For objectification of pain, the short form of the McGill Pain Questionnaire, version SF-MPQ-2, was used. For the objectification of the function of the myelinated nerve fibers of the peripheral nerves were used a study of the vibration sense of the lower limbs with a 128 Hz Rydel-Seiffer tuning fork, a study of the sense of touch with a 10 g Semmes-Weinstein monofilament and a study of temperature sensitivity with a temperature discriminator. The

electro-neurographic parameters (distal latency, action potential amplitude and conduction velocity) of sensory and motor fibers of peripheral nerves of the lower limbs were analysed.

Patients were assessed at three time points: at baseline, before starting the treatment, upon completion of therapy (on the 21st day) and on the 90th day of treatment.

The selected statistical methods provide a complete and reliable assessment of data, in accordance with the purpose of the presented study.

Following the research and analysis of available data on the treatment of diabetic neuropathy using photobiomodulation, Dr. Lili Yordanova Yosifova applied two treatment methods in both groups of patients. One group was treated with Multiwave Locked System (MLS) laser therapy - the experimental group, while the other received an "imitating" laser therapy, with the robotic device and the light guide directed without releasing the beam - Sham-laser - the control group.

Results and discussion

The results correspond to the set tasks. The doctoral student has synthesized and illustrated well, with tables and figures the distribution of patients in the two groups and the obtained results.

Before the therapy, there was no statistically significant difference between the monitored and compared groups in terms of duration of diabetes and neuropathy, demographic and anthropometric parameters and subjective complaints. The analysis of initial values of the monitored indicators, suggests that there is no difference between the two groups, which leads to their homogeneity with respect to each other.

A statistically significant effect was achieved in the experimental group after the therapy, and the positive effect was maintained until the end of the observed period. Pain reduction, improvement of superficial and deep sensation, as well as electroneurographic data of n. suralis, n. tibialis and n. peroneus, give Dr. Lili Yosifova reason to recommend deep tissue laser therapy as a non-pharmacological adjunct to standard therapy in patients with painful diabetic peripheral neuropathy.

The discussion of obtained results highlights their significance by comparing them with other studies in global reference sources.

Finally, the most important results of the study were summarized.

Five clearly formulated conclusions have been synthesized, which briefly and precisely provide a summary of the results of the conducted research and fully meet the set goals and objectives. The doctoral student has clearly indicated the contributions of the dissertation paper to Bulgaria - three of a scientific and theoretical nature and two of scientific and practical nature.

The abstract is structured in accordance with the requirements, and its content corresponds to the dissertation paper. Ten tables and nineteen figures are presented to illustrate the results obtained from the scientific research.

Conclusions

The dissertation paper of doctoral student Lili Yordanova Yosifova on the topic "Study of the effect of a high-energy laser in diabetic sensorimotor neuropathy" presents results and conclusions with an ingenious contribution to science. It meets all the requirements of the Academic Staff Development Act of the Republic of Bulgaria, (ASDA), the Implementing Regulations of ASDA and the Regulations of the Varna Medical University.

The dissertation paper shows that the doctoral student, Dr. Lili Yordanova Yosifova, has acquired in-depth theoretical knowledge and demonstrates that she has qualities and skills for independent conduct of scientific research.

Based on the above, I confidently give my positive assessment of the dissertation paper.

I recommend to the highly respected Scientific Committee to award Dr. Lili Yordanova Yosifova the academic research degree " DOCTOR"



Date: 20th October 2022

Prof. Dr. Vesselinka Nestorova, MD, PhD

City of Varna