

Dissertation for ARD (academic research degree) „Doctor“ to **DR LILI YORDANOVA YOSIFOVA**

THESIS STATEMENT

by Assoc. Prof. Maya Krastanova, M.D., PhD

Member of the scientific committee

Chosen by order № 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.

TIMELINESS OF THE PROBLEM:

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

Diabetes mainly changes sensory function, causing impaired sensitivity and progressive numbness, which facilitates the development of ulcers and is a prerequisite for the development of diabetic neuro-osteoarthropathy (Charcot foot). These late complications of DSPN, in addition to increasing the economic costs of treatment and disability, carry the risk of amputation, even death. Loss of sensation, temperature discrimination and pain lead to instability and an increased risk of falling, with subsequent fractures.

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

The neuropathic pain that often accompanies diabetic polyneuropathy is still a challenge for conventional pharmacological therapy. Given the unsatisfactory pharmacotherapy, non-pharmacological forms of treatment are increasingly being considered, including photobiomodulation, involving lasers.

There are many studies in the available literature on the effects of low-intensity laser therapy (LILT) in diabetic neuropathy (DPN). A large part of them are on cell cultures in vitro or on experimental animals and a limited number are

clinical studies. All of them demonstrate that LILT is beneficial in the treatment of patients with DPN, both in terms of pain and superficial and deep sensation and nerve conduction. The indicated parameters for laser treatment in this contingent of patients are too varied, as are the methods of application.

There are data that high-energy laser therapy combining two wavelengths (MLS-laser) is a physical factor with highly pronounced anti-edematous, anti-inflammatory, regenerative and pain-relieving effects. In addition, it is noted that compared to traditional laser therapy, it is distinguished by a shorter course of treatment and longer-lasting therapeutic effects. In the available literature, there are two clinical studies on the effect of the MLS-laser in diabetic neuropathy, which were conducted with a very limited number of participants.

Dr. Yosifova'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 parameters of the laser and a course of treatment in diabetic neuropathy.

CHARACTERISTICS OF THE DISSERTATION SUBMITTED FOR THESIS STATEMENT

The dissertation paper of Dr. Lili Yordanova Yosifova is presented in 99 standard pages, in eleven sections with an 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 MU-Varna.

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 work" - 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 the lasers, as well as characteristics, parameters and interaction with the biological targets of the 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 a high-energy laser (MLS - laser) in diabetic sensorimotor polyneuropathy and to create its own work protocol.

In realizing the set objective, the author 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 analyzed.

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 of treatment.

The selected statistical methods provide a complete and reliable assessment of the 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 treatment, 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.

CONCLUSION

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 and 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 doctoral student introduces an innovative method for treating the pathology in question, which is non-invasive, therefore it has no negative side effects. With its painlessness, it is very well received by patients. Last but not least, the advantage of the method is the shortening of treatment times and the smaller number of procedures that need to be carried out within one treatment course.

Unfortunately, conducting the study in an epidemic setting, significantly narrowed the number of covered patients, but the results show the positive effect of one such type of therapy. I believe that Dr. Yosifova will continue to apply and expand the method in the future and will be able to compare it with the effect of applying other physiotherapeutic treatment methods. Also, this factor can be combined with other suitable natural and reshaped physical factors for a longer lasting effect. 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.

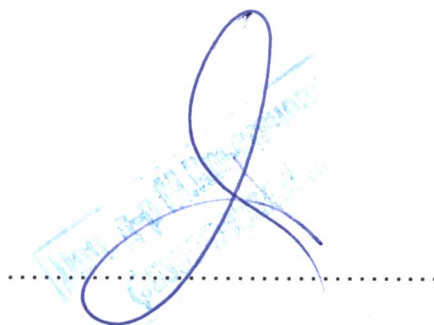
I believe that the development of a protocol for the treatment of diabetic neuropathy patients with high-energy laser radiation is of great practical importance and can support the work of doctors in Physical medicine and rehabilitation who have a similar device and deal with the relevant contingent of patients.

I propose to the respected members of the scientific committee to award the doctoral student Dr Lili Yordanova Yosifova the academic research degree "

Doctor" in the scientific specialty "Physiotherapy, Thalassotherapy and Rehabilitation".

Date: 1st November 2022

City of Pleven

A handwritten signature in blue ink is written over a blue rectangular stamp. The signature is a stylized, cursive name. The stamp contains text that is partially obscured by the signature but appears to be an official seal or stamp of the institution.

*Assoc. Prof. Maya Krastanova, M.D., PhD
Head of Physiotherapy and Rehabilitation Clinic
of UMHAT „dr G. Stranski“ - Pleven*