

THESIS STATEMENT

BY ASSOC. PROF. KOSTA DIMITROV KOSTOV, M.D., PhD

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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.

Dr. Lili Yordanova Yosifova graduated from higher education in medicine in 2001 at the Pleven Medical University. 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. 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. 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. She is fluent in Russian and English, both written and spoken.

She 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.

The dissertation paper presented to me for thesis statement is in accordance with all the requirements of the Academic Staff Development Act of the Republic of Bulgaria, (ASDA), the Implementing Regulations of ASDA and the relevant Regulations of the Varna Medical University. The dissertation paper of Dr. Lili Yordanova Yosifova is presented in 99 standard pages, in eleven sections - "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, 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 topic of the dissertation paper is extremely relevant, as it is related to a socially significant disease - diabetes mellitus, and more specifically to its most common neurological complication - diabetic polyneuropathy, which affects about 50 % of patients with type 2 diabetes. Diabetic neuropathy in addition to increasing economic costs of treatment and disability, leads to the development of severe trophic changes in the limbs with the risk of amputation, even death. Loss of sensation, temperature discrimination and pain lead to instability and increased risk of falls with subsequent fractures. 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 considered, including photobiomodulation, using lasers. In the presented dissertation paper, Dr. Yossifova 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.

The Referenced Literature is presented in detail and informative, based on 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. 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.

On the basis of the in-depth and comprehensive analysis of the literary data, the doctoral student adequately formulates the objective of the dissertation - 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 doctoral student has set herself 5 tasks, which are clearly formulated and correspond to the purpose of the study.

The study design was structured as a prospective, interventional, placebo-controlled, single-blind, longitudinal study, involving 69 patients divided into two groups - 41 patients with applied high-energy laser radiation and 28 patients with "imitating" laser treatment (placebo group). Adequate clinical and electrophysiological methods were used to evaluate patients - 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.

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. The values of the monitored indicators after the treatment prove a statistically significant effect in the experimental group 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.

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

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 Dr Lili Yordanova Yosifova is a well-structured and excellently conducted and analyzed scientific study on the effect of high-energy laser radiation in patients with diabetic polyneuropathy. It contains results and conclusions with an ingenious contribution to science and 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 Dr. Yosifova, has acquired in-depth theoretical and clinical knowledge and demonstrates that she has qualities and skills for independent conduct of

valuable scientific research, because of which I confidently vote in favor of awarding the academic research degree „doctor“ to Dr. Lili Yordanova Yosifova.

Date: 20th October 2022

Assos. Prof. Dr. Kosta Kostov, PhD

