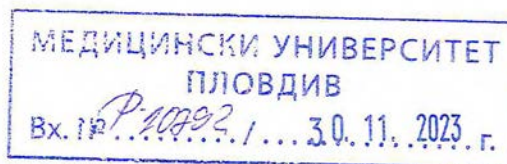


To the Scientific Jury
Constituted by the Rector
of MU Plovdiv

By order № P- 3012 / 18.10.2023



OPINION

From Assoc. Prof. Teodora Nedeva, MD, PhD

Rousse University "Angel Kanchev", FOPHHC, Department of "Medical, clinical and diagnostic activities";

COC- Ruse, Department of AIC- medical doctor

Subject: Dissertation on "Life-threatening hyperglycemic disorders in patients with diabetes mellitus in the intensive care unit", in the doctoral program "Anesthesiology and Intensive Care Medicine", scientific specialty "Anesthesiology and intensive care", Professional field 7.1 Medicine.

Doctoral student: Angel Petrov Prodanov, MD, of independent training at CAEIM, MF, MU Plovdiv

Scientific supervisor: Prof. Chavdar Stefanov Stefanov, MD, DSc, Head of the Department of Anesthesiology, Emergency and Intensive Medicine, Faculty of Medicine, Medical University - Plovdiv.

Dear Colleagues,

I received a set of documents which contained: orders, declarations, CV, abstract of doctoral thesis, list of publications and dissertation of Angel Petrov Prodanov, MD. Their type and volume completely fulfill the requirements for the development of the academic staff in MU Plovdiv and awarding PhD. According to the order of the Rector of MU Plovdiv, with № P- 3012 / 18.10.2023, I am a part of the Scientific Jury. I am appointed to prepare an opinion on the dissertation.

- 1. Brief biography of the researcher:** Angel Petrov Prodanov, MD, was born on February 20, 1985. in the city of Pazardzhik. Graduated in 2004 his secondary education at "Nesho Bonchev" School of Panagyurishte. Since 2005 until 2011 he studied Medicine at the Medical University of Plovdiv. Since 2011 until now he works as an anesthesiologist in CAIC of UMBAL "St. Georgi". In 2014, he won the competition for "Assistant" at CAEIM, MU-Plovdiv. In 2016 acquired a specialty in Anesthesiology and intensive care. From 2018 to the present, he is the procurator of MBAL "Uni Hospital". In 2020 obtained a master's degree in "Health Management" at MU-Plovdiv. As a member of the CAEIM team, he participates in scientific projects and has good computer skills and is fluent in English.
- 2. Annotation of the problem:** Glycemic control is essential for the critically ill. Multiple studies have demonstrated a negative relationship between hyperglycemia and the clinical course and outcome of patients. On the other hand, diabetes, which is most often associated with hyperglycemic complications, is a socially significant disease not only for Bulgarian patients. Generally known facts are: that its expression is associated with many predisposing and risk factors; a large part of its pathophysiological mechanisms cause serious organ damage that deepens the patient's suffering, significantly disables him over time, worsens his quality of life,

is a reason for hospital admissions and treatment, including in emergency/intensive wards, and increases premature death.

Managing carbohydrate metabolism and glycemic levels is not always easy. It creates problems and poses questions for clinical teams. For intensivists, acute metabolic disorders, occurring with hyperglycemia, hyperketonemia, disturbances in the alkaline-acid balance, dyselectrolytemia, tissue hypoperfusion, are important and are the subject of discussions and research, due to their clinical diversity, complications and challenges in their therapeutic impact. Glycemic control of critically ill patients with hyperglycemia and DM is an actual problem of modern intensive care medicine. Advances have been made in the understanding of metabolic disorders, the schemes, doses and method of insulin administration, rehydration, the reduction of multiple organ damage and the improvement of clinical outcome. Algorithms for treatment, monitoring and intensive care have been created worldwide for this patient population, which can be successfully adapted and applied in Bulgarian conditions as well. The medical community faces a number of questions to resolve, which is a good reason for future research, observation and development of unified strategies for the management of hyperglycemic conditions.

Based on the above, I believe that the topic of Angel Petrov Prodanov's dissertation is current, dissertable, perspective and practically significant, since at the moment there have been no similar scientific studies of anesthesiologists in Bulgaria.

- 3. Analysis and evaluation of the dissertation:** I approach the work of my colleague with the clear awareness that dissertations are usually unique works, without strictly fixed frameworks, but they follow exemplary models established over time by the scientific community. This is followed in the dissertation proposed for evaluation.

General volume and structure: The present dissertation contains a total of 170 standard pages. The author's research and literature data are presented to the readers in 10 sections and the second, fourth, fifth and sixth of them have subsections. It is illustrated with 25 tables and 27 figures. The distribution of information is as follows: List of figures and tables – 4 pages, Abbreviations used in the text - 2 page, Literature review - 41 pages, Goal and objectives of the dissertation project - 1 page, Clinical study objects and methods - 22 pages, Results - 55 pages, Discussion - 16 pages, Conclusions - 2 pages, Contributions - 1 page, Bibliography - 22 pages.

Format and content of the sections: My assessment is that the work is generally written intelligibly, with good style, but there are some places with rather long, clumsy sentences and unclear word order, which makes it a little difficult to understand their meaning. In the "Contents" tab, the pages of the various sections are indicated, which makes it possible to find them easily and without problems. The arrangement and formatting of the pages ensures a relatively good readability of the information in them, which shows the author's interest in the problem. All tables and figures have clearly formulated explanations, which makes it easier to understand the presented results. The different sections are titled according to generally accepted scientific models

Section "Literature review": the main characteristics of the researched problem and the author's position regarding his choice to research this specific topic are presented.

For me, the fact that hyperglycemic conditions - DKA and HHC are presented with definition, reference values, the essence, pathophysiological features, criteria for treatment in EU/ICU, possible diagnostic methods and techniques for monitoring the critically ill, related to treatment of hyperglycemia potential organ complications and outcome. Studies and positions of various foreign authors are presented. Special emphasis is placed on the differences in diagnostic criteria and treatment strategies of the main UK and USA (ADA) guideline documents. It is evident that Dr. Prodanov has approached thoroughly and knows well the literature data and the results published by other authors. Intensive monitoring and treatment of patients with hyperglycemia and DM is a current issue and will continue to be the subject of research and discussion. This is determined by many factors: complex endocrine,

immune and metabolic changes in the body and the associated adverse consequences; multiple organ and tissue damage; the diagnostic and therapeutic challenges in the management of these patients; pharmacological and economic cost of hospital stay; hospital mortality in this patients cohort. The analysis of the literary data made a good impression on me, from which the main goal and tasks that the dissertation student sets at the beginning of the research are naturally and logically derived. It is accepted that the literature review is about 30% of the total volume of work. In the current one, this is not fully respected.

Goal and objectives of the dissertation project: developed as required. The main purpose of the study and the four tasks related to it are formulated clearly and concisely and I fully accept them in this form.

Section "Clinical study object and methods": The work was developed on the basis of a retrospective observational study, for the period January 2019 - January 2022. 623 disease histories were included in the screening. 123 hospital records met the inclusion criteria in the study - the patients had life-threatening hyperglycemic conditions, complete data on the intensive therapy performed, the types, dosage regimens and method of insulin administration were available in the patients' documentation. These 123 patients were over 18 years of age, with proven hyperglycemia over 11 mmol/l, metabolic acidosis with pH below 7.2 and ketonuria, hyperosmolar hyperglycemic state, over 48 h stay in ICU, proven DM.

The following are detailed: the methods of clinical monitoring (physical examination and monitoring, apparatus monitoring of the respiratory and cardiovascular system, hourly monitoring of diuresis, assessment of volemia); clinical - laboratory tests (hemo-indicators, biochemistry, electrolytes, blood-sugar profile, urine-sugar profile, KGA); principles of therapeutic control (diagnosis of DKA and HHC; volemia control; dyselectrolytemia correction; insulin therapy); detailed definitions and indicators. Patients in ICU, according to the achieved glycemic target at the 24th hour of hospitalization, are divided into 2 groups: 55 people with "strict" (target blood sugar values 4 - 9 mmol/l) and 68 - with "liberal" glycemic control (target blood sugar values 7 - 13 mmol/l). For me, this distribution, given the overlap of some values in the two groups, e.g. patients with blood sugar 8, is unclear.

The data were processed with up-to-date statistical software products, including classical and newer methods of data processing and analysis.

My personal judgment is that the value of the work would be higher if there was also a prospective group of patients, but I do not mean it with the idea that it is a disadvantage. I accept that the design of any scientific study is an individual choice of the researcher, his supervisor and team. It can always be built upon with future research.

"Results" section: on 55 pages, the results obtained by the dissertation are reflected in tabular, graphic and narrative form. They meet the tasks set.

"Discussion" section: compare own with world results. The solution of the set tasks is presented in fulfillment of the main objective of the research. I believe that the obtained results are important for our daily practice and it would be appropriate to present the research to a wider audience so that they are useful for the daily work of the anesthesiology community in our country. The author presents a Protocol for the treatment of life-threatening hyperglycemic conditions in surgical and therapeutic patients, which is the most valuable in his work.

"Conclusions" section: 6 conclusions are clearly and concisely formulated. I accept them without any remarks.

"Contributions" section: are divided into 2 groups, as is accepted in common practice: theoretical and practical. They are clearly described and logical and I accept them all. 3 of them have an original character.

"References" section: 246 sources are cited, which are sufficient for a detailed study of the experience of different researchers. They are arranged in order of citation in the text. There are no posts in Cyrillic. Regarding the publication period of the literature used, most publications are published before 2018. Only 5 of the titles were printed in the last 5 years.

The author presents 3 scientific publications on the topic of the dissertation. They are published in the journal Anesthesiology and Intensive Care, which is referenced in the global SCOPUS database. Dr.

Prodanov is the first author in all of them. According to the minimum requirements of the MU Plovdiv, this is sufficient scientific activity to acquire PhD.

Abstract: According to some scholars, it is considered an independent publishing activity. According to others, it is an integral part of the dissertation and should be analyzed together with it. The information in the abstract is presented on 57 pages. In a compressed version, the readers are offered the content of the dissertation. In my opinion, this is appropriate because it allows the reader to get acquainted with the basic thesis of the scientific research along with quick and easy introduction to the results and conclusions.

Conclusion: related to the aforementioned, I think that the presented dissertation is very valuable in practical and scientific terms.

I am thus certain in granting POSITIVE assessment of the scientific thesis. I also propose to the honorable scientific jury to award the educational and scientific degree "PhD" to Angel Petrov Prodanov, MD, in the doctoral program in "Anesthesiology and Intensive Care Medicine".

28.11.2023

Prepared the opinion:

/ Assoc. Prof. Teodora Nedeva, MD ,PhD/

Заличено на основание
Чл.5 §1, б."В" Регламент (ЕС)2016/679