

TO THE CHAIRMAN OF THE SCIENTIFIC JURY
DESIGNATED BY A WRITTEN ORDER Nr. R-109-207/17.07.2024
OF THE RECTOR OF MEDICAL UNIVERSITY OF VARNA

R E V I E W

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On doctoral thesis "**CONTROLLED ARTERIAL HYPOTENSION IN SHOULDER SURGERY**" for awarding educational and scientific degree "Doctor of Philosophy" in doctoral program in Anesthesiology and Intensive Care.

Doctoral candidate: Dr. Zdravka Ivanova Ivanova- Department of Anesthesiology, Emergency and Intensive Care Medicine, Medical Faculty, Medical University of Varna

Scientific Supervisor: Prof. Viliyan Hristov Platikanov, MD, PhD- Department of Anesthesiology, Emergency and Intensive Care Medicine, Medical Faculty, Medical University of Varna

1. General presentation of the procedure and the doctoral student.

The PhD student was enrolled by a written order of the Rector of the Medical University of Varna No. R-109-501/04.11.2020 and dismissed with the right to defense by a decision of the Faculty Council, Faculty of Medicine, Medical University of Varna (Protocol No. 24/08.07.2024 and a written order of the Rector of the Medical University of Varna No. R-109-207/17.07.2024).

The submitted set of materials on paper and electronic media is in accordance with the requirements specified in Article 69 of the Regulations for academic staff development in the Medical University of Varna.

The PhD student has submitted 2 (two) full-text scientific publications in reference to the PhD thesis.

2. Short Biography of the PhD Student

Dr. Zdravka Ivanova Ivanova was born in 1991 in Varna. She graduated his Master's degree in Medicine from Medical University of Varna in 2016. In the same year she started her medical practice as a resident in the Department of Anesthesiology and Intensive Care at University Hospital "St. Marina"-Varna, where she is still working so far. In 2021 after successfully passing the state exam Dr. Zdravka Ivanova was recognized as a specialist in Anesthesiology and intensive care medicine. Since 2020 she has been a full-time doctoral student at the Department of Anesthesiology, Emergency and Intensive Medicine at the Faculty of Medicine of Medical University of Varna. She is fluent in English and Spanish.

3. Relevance of the topic

Operative interventions of the shoulder and proximal humerus represent a serious challenge for the anesthesiologist with the intense pain stimulation and related autonomic manifestations, the

specific positioning of the patients and the associated risks of critical disruption of cerebral perfusion, as well as increasingly widespread application of endoscopic techniques requiring a bloodless operative field. This necessitates the development of a complex approach which, along with the principles of adequate balanced multimodal anesthesia, should also include an effective multimodal strategy for pain control, precise monitoring and adequate management of hemodynamics, as well as application of strategies to control intraoperative bleeding. In this aspect, controlled hypotension is a key component of the complex anesthetic approach in shoulder surgery, ensuring effective control of intraoperative bleeding, "clean" operative field and optimal operative conditions. Various methods and techniques have been described to achieve and maintain controlled hypotension, each with its own advantages and disadvantages. At present, there is still no consensus on a universal, preferred, or best method of controlled hypotension. There is even less definitive opinion on the possibilities of applying peripheral nerve blocks to achieve controlled hypotension in shoulder and proximal humerus surgery. Proceeding from the above, I strongly believe that the topic of Dr. Zdravka Ivanova Ivanova's PhD Thesis is an actual, promising and practically significant problem, which has not yet been the subject of scientific research in Bulgaria.

4. Understanding of the Problem

The construction of the dissertation is dedicated to the solution of a significant problem, which undoubtedly enhances the significance of the scientific development. In the "Literature review" the doctoral student shows that she is well acquainted with the nature, advantages and importance of controlled hypotension, the indications, the techniques for achieving it and the associated risks and complications. It can be seen that Dr. Ivanova has a thorough knowledge of the problems and the results published so far on the subject of the dissertation work. The cited sources are selected appropriately and are sufficiently informative. The literature review presents the PhD student as a researcher with the ability to interpret and critically evaluate the scientific information.

5. Methodology of the Study

The scientific research is planned and conducted correctly. The obtained results are reliably reported and subjected to detailed statistical analysis. It is noteworthy that Dr. Ivanova has mastered and used appropriately specialized software products for analysis and statistical processing of primary data.

6. Characteristics and Evaluation of the Doctoral Thesis

The thesis represents a completed scientific work. It is properly constructed and includes all the relevant sections following the established specific form. It is written in an understandable grammatically correct Bulgarian in accordance with the scientific nature of the paper. The following sections are included in the thesis: Contents - 2 pages; Abbreviations - 1 page; Introduction - 2 pages; Literature Review - 37 pages; Aim and Tasks - 1 page; Materials and Methods - 14 pages; Results and Discussion - 42 pages; Conclusions - 1 page; Contributions - 1 page; Scientific Publications in Connection with the Dissertation - 1 page; References - 8 pages. Appendices to the PhD Thesis are missing. The doctoral thesis is written on a total of 113 pages. It is well illustrated with 36 figures and 13 tables.

The bibliographic reference covers 186 titles of which 6 in Cyrillic and 180 in Latin. It is in alphabetical order. Only 53 (28%) of the cited publications are from the last 10 years.

The title is clearly formulated and sufficiently informative. It reflects adequately the content of the research and corresponds to the presented data and conclusions.

Literature review – it covers 37 pages which represents 33% of the volume of the dissertation work. It shows good knowledge of the problem and creative analysis of the cited literature. It

systematically and comprehensively presents the problem that is the object of scientific research and fixes the controversial and unsolved issues in the world and national clinical practice. It is written in short and comprehensible sentences and provides sufficient information about the physiological aspects of hemodynamics, its changes under general anesthesia and operative stress, the nature, indications, advantages, techniques, contraindications and complications of controlled hypotension. The literature review also presents the specific features of shoulder surgery, as well as the indications, contraindications, technique, side effects and complications of the interscalene plexus block and its potential to be used as a method to achieve controlled hypotension. The presented literature review allows the author to analyze various aspects of the problem as well as to determine the main goal and the priorities of the scientific research.

Main goal - it has been stated correctly, clearly and accurately formulated in harmony with the title of the dissertation and corresponds to the further development of scientific research.

The tasks are formulated correctly and precisely. Six tasks are set, aimed at the implementation of the set goal, describing the necessary actions.

The section "Materials and Methods" presents the subject, the object and the design of the study are. It is properly structured and presented and covers 14 pages. 162 patients are included in the study. They are divided into two groups of 81 patients each. The first group, called experimental, is prospective and includes patients undergoing surgery of the shoulder and proximal humerus over a period of 4 years, in which an interscalene plexus block was applied to the usual protocol of controlled arterial hypotension. The second group, called the control group, is retrospective and includes patients undergoing surgery of the shoulder and proximal humerus over a period of 4 years, in which the usual protocol of controlled hypotension was applied without the application of an interscalene plexus block. The inclusion and exclusion criteria are correctly formulated. Clinical research methods include documentary method, clinical, instrumental, laboratory and treatment methods. The treatment methods, in turn, are divided into surgical and anesthetic one. A wide range of modern and accurate statistical tests has been used for statistical processing which guarantees the reliability of the obtained results and the conclusions.

In my opinion, as the most important component of the dissertation work, this section should be further elaborated with a more detailed and thorough description of the study design.

I would like to point out some critical remarks and recommendations:

- Definitions of basic concepts and classifications are missing.
- The main technical specifications and characteristics of the equipment used for general anesthesia, for ultrasound guidance of interscalene plexus block, as well as the "standard automatic vital signs monitoring system" are not presented.
- There is no description of the underlying basic physical principles of monitoring techniques used, especially for hemodynamic monitoring.
- In the subsection "Anesthesiological methods" it is indicated that "hypotensive, multimodal, general anesthesia with endotracheal intubation was applied to all patients according to the rules and protocols adopted in the Department of Anesthesiology and Intensive Care of University Hospital "St. Marina" - city of Varna". It would be appropriate for these protocols to be comprehensively described and even presented as appendices at the end of the dissertation.
- It is not clear from the described methodology of general anesthesia what the target values of the alveolar concentration of the used inhalation anesthetic are, since in both groups of patients "higher doses of inhalation anesthetic" were used as the main method for achieving controlled hypotension.

- Nowhere in the research methodology, and subsequently in the presented results, are target values of systemic arterial pressures indicated for the main patients categories and positions on the operating table, which I consider absolutely necessary based on the topic of the PhD Thesis.
- Based on the topic of the dissertation work, I believe that it would be appropriate to include invasive measurement of systemic arterial pressures in the hemodynamic monitoring.
- In the same subsection, it is stated "the monitoring of the depth of anesthesia was carried out by the values of MAC...", as well as "the value of the MAC of the inhalation anesthetic and its changes we tracked and reflected...". MAC is a standardized indicator for quantitative assessment of the anesthetic potency of inhalational anesthetics. The MAC has a single value for each specific patient, which is mainly determined by his age and can be modified by various physiological and pathological conditions, use of other medications, etc. But the MAC of the inhalation anesthetic for each specific patient does not change over time of anesthesia, does not vary within a certain reference interval and has no minimum or maximum value. One of the possibilities for evaluating the depth of inhalation anesthesia is the monitoring of the achieved real alveolar concentration of the used inhalation anesthetic by means of measuring its concentration at the end of expiration. It is expressed in volume percentages and/or as a percentage ratio to MAC for the specific age group to which the patient belongs. The actual alveolar concentration of the inhalation anesthetic, as well as its fluctuations, cannot and should not be indicated as MAC, MACmin and MACmax. Such terminological inaccuracy is unacceptable for a scientific work such as the dissertation.
- I believe that, in addition to determining the number of patients to whom nitroglycerin was administered intraoperatively, the assessment of the consumption of antihypertensive medication would be much more correct by determining and comparing the administered dose and the duration of infusion of the preparation.

The obtained results correspond to the set tasks. Their description is supported by rich graphical and tabular material with accompanying detailed textual descriptions. When discussing her own results, the doctoral student offers generalisations, systematization and comparison with the results of other authors and teams postulating his own hypotheses.

When describing and discussing the results related to monitoring the alveolar concentration of the inhalation anesthetic, numerical values are presented without specifying units of measurement, i.e. it is unclear whether the values given are the actual concentration expressed as volume percentages, or whether the values given are percentage ratio of the measured true alveolar concentration relative to the MAC of the inhalation anesthetic (which I consider more likely). In the first case, this would raise the question of the adequacy of the depth of hypnosis and the associated risk of awareness during anesthesia, as well as contradict the statement in the study methodology that the main method of achieving controlled hypotension was the administration of "higher doses of inhalation anaesthetic".

Based on the analysis of the obtained results, the doctoral student develops and offers an easy-to-use algorithm for the application of controlled hypotension and postoperative pain control during surgery of the shoulder and proximal humerus. The proposed algorithm is actually the most significant contribution of Dr. Ivanova's dissertation, as it offers an opportunity to optimize care, increase the quality of medical care and improve the outcome. The purpose of any protocol, however, is to standardize and unify a certain practice, and therefore each of its components must be written sufficiently clearly, in detail and specifically. The algorithm developed by Dr. Ivanova is presented too schematically and generally. Apart from the drugs for premedication and their doses, it does not indicate the specific medications and their doses for induction and maintenance of general anesthesia, it does not indicate the local anesthetic of choice with the recommended concentration, dose and volume of the solution to achieve an interscalene brachial plexus block, target values of systemic arterial pressures, target values of alveolar concentration of the inhalation anesthetic, etc.

The dissertation concludes with the formulation of **eight (8) conclusions**. The conclusions are clear and informative and reflect the essence of the research. I accept them as content and personal achievement of the doctoral student. I appreciate the fact that they follow the specific tasks and present the results of the study convincingly and systematically.

7. Contributions and Significance of the Dissertation for Science and Practice

Five theoretical and 3 practical contributions have been formulated. They are quite sufficient for such a thesis. I accept contributions without objection.

8. Publications Related to Doctoral Thesis

Dr. Zdravka Ivanova has presented 2 publications in which she is the first author. The one article was published in "Anesthesiology and Intensive Care" journal, and the second one- in "Varna Medical Forum" journal. Both journals are currently not refereed and indexed in the world-reknown scientific information databases Scopus or Web of Science. I believe that the PhD student should prepare and publish scientific articles in peer-reviewed scientific journals, indexed and referenced in world-renowned databases (Scopus & Web of Science). The scientific works meet the minimum requirements for acquisition of the educational and scientific degree "Doctor of Philosophy" according to the Regulations for the academic staff development in the Medical University of Varna.

9. Personal contribution of the doctoral student

Taking into account the professional competences of Dr. Zdravka Ivanova as a specialist in anesthesiology and intensive care medicine and the upgraded scientific capacity I am entirely convinced that the doctoral thesis is his personal achievement under the skillful guidance of his scientific supervisor.

10. Abstract

The abstract is prepared following standard guidelines and accurately reflects the content of the dissertation. It is prepared in accordance with the requirements of the Regulations of Medical University of Varna. It is written on 60 pages and is very well structured and illustrated. The abstract reflects the aim, tasks, materials, methods and logically presents the results related to the conclusions and contributions of the dissertation work. I have no further critical remarks on its content.

11. Critical Remarks and Recommendations

All critical remarks and recommendations are explained in detail in the assessment of specific sections of the dissertation work.

CONCLUSION

Despite the critical remarks, the PhD thesis "**Controlled arterial hypotension in shoulder surgery**" by Dr. Zdravka Ivanova contains scientific and applied results that constitute an original contribution to the field of science and meet all the requirements of the Law on Academic Staff Development in Republic of Bulgaria, the Regulations for its implementation and the Regulations of the Medical University of Varna. The presented materials and the dissertation results are fully completed according to the specific requirements of the Medical University of Varna.

The doctoral thesis shows that the PhD student - Dr. Zdravka Ivanova Ivanova, possesses in-depth theoretical knowledge and professional skills in the scientific specialty "Anesthesiology and Intensive Care Medicine" by demonstrating qualities and skills for independent conduction of scientific research.

Taking into account all the above-mentioned facts I grant my positive assessment of the study presented by the reviewed doctoral thesis, abstract, results and contributions, proposing to the members of the honorable Scientific Jury to give their positive vote for awarding the educational and scientific degree "Doctor of Philosophy" to Dr. Zdravka Ivanova Ivanova in doctoral program "Anesthesiology and Intensive Care".

September 18, 2024

Reviewer:

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
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