To the Chairman of the scientific jury

determined with Order № P-109-337/09.08.2021

of the Rector of the Medical University-Varna

REVIEW

From assoc. prof. Magdalena Spasova Kondeva-Burdina, PhD

Department "Pharmaology, Pharmacotherapy and Toxicology"

Faculty of Pharmacy, Medical University-Sofia

included in the composition of the Scientific jury, according order № P-109-337/09.08.2021 of the Rector of MU-Varna and elected for reviewer on the first meeting of the scientific jury, which took place on the 20.08.2021 (Protocol № 1).

Concerning:

Procedure for the award of educational and scientific degree "Doctor" in the area of high education 7. **"Healthcare and sport"**, professional direction 7.3. **"Pharmacy"** and PhD program **"Toxicology"**, with candidate **Stanislava Angelova Georgieva.**

Topic of the PhD thesis: **Characteristics of acute medicinal poisoning cases in Varna district over a 30-year period.**

Sientific supervisors: Prof. Dr. Peko Penkov Marinov, MD

Prof. Antoaneta Zdravkova Tsvetkova, MD, PhD

Career development of the candidate

1. Education

September 2010 – December 2015 – received educational degree "Master", specialty "Pharmacy" to the MU-Varna.

September 2005 – July 2008 – received educational degree "Professional bachelor", specialty "Assistant pharmacist" to the Medical College-Varna.

2. Professional activity

April 2017 – UNTILL NOW – Master of Pharmacy, Head of Pharmacy "Medunipharm";

January 2016 – April 2017 – Master of Pharmacy, Sashka Todorova EOOD, Pharmacy "Seiba";

June 2011 – December 2015 – Assistant pharmacist, Sashka Todorova EOOD, Pharmacy "Seiba";

May 2007 – July 2008 – Assistant pharmacist, Galena EOOD, Pharmacy "Pharma Plus"

Evaluation of the topic relevance

Poisoning is a significant public health problem. According to WHO data, in 2016 more than 1,206,000 people died as a result of accidental poisoning. Of these deaths, 84% occured in low and middle-income countries.

The World Health Organization (WHO) estimates the total number of acute accidental poisonings worldwide at 2-3 million cases per year, of which 1 million severe poisonings, leading to 20,000 deaths per year. The estimated number of intentional poisonings is about 2 million, of which approximately 200,000 are suicides.

The high frequency of accidental or intentional poisonings with drugs from different groups are a prerequisite for the development of specific programs for diagnosis, treatment and prevention of poisoning in different countries. The main elements of these programs are the identification of toxic hazards that exist at the local level (in order to establish preventive measures), the diagnosis of poisoning and the treatment of patients.

Currently, in developed countries the most common acute exogenous intoxications are drugs (60%), which can be explained by the fact of their easy availability and their presence in every home.

At her PhD thesis, the candidate made a depth analysis of the epidemiology and marked the main characteristics of the acute drug poisoning cases in Varna region, registered in Clinic for intensive treatment of acute poisoning and toxicoallergies at the Military Medical Academy in Varna for the period 1991-2020 to improve measures for their prevention.

The structure of the PhD thesis

The dissertation includes 160 pages, 25 figures and 20 tables. The bibliography covers 260 titles.

The Literary review in details revealed the problems, connected with the acute medicated poisonings World Wide and in particular the poisonings in Varna district for an extensive period.

The Purpose and tasks are correctly formulated.

The Methods are presented in details. Their diversity showed the high methodological preparation of the candidate. These methods provide receiving depth information, which helps to reach the scientific aims and solving the formulated tasks.

The main methods include:

- Summarizing the acute medicated intoxications data using descriptive statistics.

- Approach to reporting data uncertainty.

- Approach to using regression analysis.

- The documentary method is used for analysis of literature sources, documents and regulations.

- Statistical methods - descriptive analysis.

The candidate developed a proposed system for training classifiers of text from patient documents for the purposes of automated risk assessment in a poison control coordination center.

The Results are presented systematically and followed a logical order. They are exhaustively illustrated with tables and graphics, which are enough clear and informative.

The Discussion of the results is very informative and presented in depth. The candidate managed to summarize the data and to compare them correctly with the literature information.

Acute drug intoxications are divided by etiology into 11 groups - benzodiazepines, hypnotics, neuroleptics, antidepressants, anticonvulsants, nonsteroidal anti-inflammatory drugs /NSAIDs/, opiates, cardiovascular, mixed drug intoxications / drug intoxication and intoxication with antibiotics, vitamins, hormones, etc./

Data on the overall pattern of poisoning in each geographical region are important for preventing and reducing morbidity and mortality. The presented retrospective study of drug poisoning in the Varna region shows the number of patients admitted to the Clinic for treatment of acute poisoning and toxicoallergies and burns MMA Hospital - 6977. They represent 37.85% of all acute intoxications. Drug intoxications are more common in women - 71.4%. Men are 28.6%, the ratio of women:men is 2.50:1. Intentional self-poisoning for suicide is 5914. Between

1991-2015, the highest relative share of benzodiazepine intoxications - 26.5%, followed by mixed acute medicinal intoxications - 24.2%, while between 2016-2020 the percentage of combined drug intoxications increased - 36.76%, followed by 12.24% of combined intakes with alcohol and 10.56% of benzodiazepines. Fatal outcome was registered in 50 patients - 0.71%.

Acute medical intoxications are most often the result of suicide attempts - 5914 (89.6%). Medications are the mainstay of suicide poisoning, and sedatives, antidepressants, and analgesics are most commonly used because of their availability.

Following the dynamics in the etiology of acute medical intoxications, it was found that some drug intoxications do not significantly change their frequency and relative share over the years, although the period under consideration is long - benzodiazepines, neuroleptics, anticonvulsants, cardiovascular, opiates, other drugs and drugs.

Other drug intoxications increase their number slightly - antidepressants, NSAIDs.

The frequency of mixed drug intoxications increases significantly, at the expense of reducing the frequency of single poisoning with benzodiazepines, sedatives and hypnotics.

From the presented analysis, a number of benefits can be derived from identifying high-risk patients to perform suicide attempts for drug poisoning. These are women up to 24 years of age. In order to prevent future events, it is of paramount importance to determine the motivation(s) of at-risk patients. To this end, preventive measures can be taken, including educational, regulatory and management approaches. Media and educational campaigns on the topic of acute poisoning are needed, as well as the active participation of general practitioners, nurses, pharmacists, teachers and pedagogical councils.

Another possible role of the pharmacist in the control of poisoning is the establishment of a civic information and coordination unit at the municipal, national and international level.

The Poison Coordination Center can be based on the extremely rich experience of Bulgarian physicians and pharmacists from the Varna region and provide information on the toxicity, risk and treatment of various types of substances.

I receive ***the Conclusions***, which the candidate made at her PhD thesis. They are presented clearly and correctly revealed the achieved results, connected with the aim and tasks of the work.

I agree with ***the Contributions***, which are summarized as follow:

Contributions of confirmatory, scientifically applied and original nature:

- For the first time, a description of acute drug poisoning in the Varna region for a period of 30 years (1991-2020) was made and a statistical analysis was prepared in terms of demographic and etiological indicators, on the basis of which measures can be taken to improve and optimize of medical care for the population, as well as the development of effective preventive measures, as well as those for rehabilitation, aimed at reducing the impact of toxic factors as a cause of preventable morbidity and mortality.
- The typical toxicodromes in drug poisoning and treatment methods are summarized. A specific emergency form and selection of therapeutically effective dosage forms can be proposed and developed in any modern treatment center, as well as advanced training of pharmacists in order to assess and prevent cases of poisoning or refer intentional cases of poisoning to a psychologist or psychiatrist, specific educational programs.
- For the first time, an approach has been developed and a platform for anonymization of clinical data of patients compliant with the EU regulation on personal data protection (GDPR) has been proposed and an approach for analysis and prerequisites for implementation of a software application for visualization of clinical data has been proposed.
- For the first time, an approach for training a model and classifiers for patient documents containing text in natural language has been proposed, which has the ability to assess the possible risk of combined drug intoxication and an algorithm for building a mobile application with trained models has been proposed. Development of classifiers to a poisoning coordination center of international and national importance.
- For the first time, the roles of pharmacists as consultants in poisoning, data annotation and assessment of toxicity risk models are presented, and

additional training of pharmacists and pharmacy students is needed on prevention and prevention of suicide trials with medicinal products.

The Abstract of the PhD thesis is very comprehensive, created according the requirements and revealed the main results, receiving from the scientific development.

CONCLUSION

The dissertation of Stanislava Angelova Georgieva is with current character and contribution to the scientific data, which are connected with the search of new approaches for evaluation of the possible risk from combined drug intoxication. On the base of the made analysis of her PhD thesis: "Characteristics of acute medicinal poisoning cases in Varna district over a 30-year period", I can give my POSITIVE EVALUATION and recommend to the Scientific jury to award to Stanislava Angelova Georgieva the educational and scientific degree "Doctor" to the PhD program "Toxicology", professional direction 7.3. "Pharmacy" in the area of high education 7. "Healthcare and sport".

07.11.2021

Sofia

Reviewer:

/assoc. prof. Magdalena Spasova Kondeva-Burdina, PhD/