

To
Chairman of the Scientific Jury
Appointed by
Order of the Rector of MU-Varna,
№R-109-337 /09.08.2021.

REVIEW

from

Assoc. Prof. Dr. Evgenia Ivanova Barzashka - Hristova, MD

Head of Toxicology Clinic

at UMBAL "Dr. Georgi Stranski" EAD Pleven Medical University – Pleven

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concerning

The dissertation for awarding the educational and scientific degree "DOCTOR"

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Scientific specialty: Toxicology

on the topic:

" CHARACTERISTICS OF ACUTE MEDICINAL POISONING IN VARNA DISTRICT OVER A 30-YEAR PERIOD "

by

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The topic of the dissertation is relevant because it treats one of the most serious problems in clinical toxicology - drug poisoning, which is increasing with the intensive development of the pharmaceutical industry.

In the modern world of developed countries, acute exogenous drug intoxications account for over 60% of all acute poisonings, the leading ones being those with cerebrototoxic drugs, used mainly in psychiatric and neurological practice.

The latest WHO data show that acute exogenous drug intoxications are formed as a new pathology in toxicology, with rapid increase of cases, more aggressive in nature, covering all age groups and with a severe clinical picture. Their peculiarity is the development of "combined" poisonings as a result of simultaneous administration in high doses of several types of drugs.

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The literature review sheds light on the competence in working with medicinal products in clinical practice, which is important not only for patient safety, but also for monitoring the safety of medicines.

The aim and tasks in the dissertation on the topic " CHARACTERISTICS OF ACUTE MEDICINAL POISONING IN VARNA DISTRICT OVER A 30-YEAR PERIOD " are well formulated, substantiated and related to the presented literature data.

The set goal determines the need to study and analyze the main characteristics and epidemiology of acute drug poisoning in Varna region, registered in Intensive Care Clinic for Acute Poisoning and Toxic Allergies at MMA-MHAT Varna for the period 1991-2020 to improve measures for their prevention.

To achieve this aim, 8 main tasks are well formulated, each of which explains what is sought and how to do it. This allows one to choose the right approach and algorithm for conducting research, to analyze and summarize the results with the relevant conclusions and to indicate the need for a modern approach to solving problems.

The materials, methods and tools of the research are directly related to the purpose and implementation of the tasks. They are very well described, explained and illustrated.

The dissertation includes:

1. Rich clinical material, processed retrospectively on the basis of the medical documentation of the Clinic for intensive treatment of acute poisonings and toxicallergies at the Military Medical Academy - MHAT - Varna - over a 30-year period.
2. The methods used in the analysis of clinical data are processed by: "Automated analysis approach for retrieving content from medical documents available to the patient." This chapter describes a proposed approach using NLP / natural language processing / for creating a mathematical model for assessing the risk of drug intoxication depending on the medicinal products taken by the patient, food supplements in combination with or without ethanol.
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The study was conducted with toxicological patients treated in the city of Varna, and the author used an analysis of medical histories and personal ambulatory cards of patients admitted to poisoning in the Clinic for Intensive Care of Acute Poisoning and Toxoallergies at MMA-MHAT-Varna. For this purpose, permission was obtained from the Chairman of the Ethics Commission at the Military Medical Academy-MHAT-Varna.

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In the section "Results" the own results of the researches are presented in detail and scientifically substantiated, which are well interpreted.

The results cover retrospective processing of a huge amount of material from 6977 patients with acute drug poisoning, treated in the Clinic for intensive treatment of acute poisoning and toxoallergies at the MMA - Varna. It covers a 30-year period - 1991 - 2020.

The studied contingent is divided on different grounds - gender, age, as the studied period is divided into two subperiods - 1991-2015. and 2016-2020.

In the first 15-year subperiod, patients from the younger age group up to 44 years predominate, and in the second - the older contingent over 60 years. It is worrying that, both in percentage terms and in absolute terms, although declining, young people and people of working age maintain high values.

The frequency, dynamics and structure of acute exogenous drug intoxications are determined, in regional aspect - Varna region.

The results of the research allow to build the socio-demographic, clinical profile of the patients. It is extremely important to emphasize that determining the dynamics, structure and frequency of acute exogenous intoxications and suicide trials with drugs in the Varna region for the period 1991 - 2020, allows to analyze the emerging trend in both sexes. Females predominate in a significant percentage of 71.4%, which correlates with the literature data.

The clinical profile of the patient is established by determining the leading etiological groups of drugs, which is an indicator of the most used drugs in medical practice.

According to this sign, acute drug poisonings are divided into 11 groups, with the largest relative share of benzodiazepine intoxications, followed by mixed drug poisonings, and in third place are drugs intended for the treatment of cardiovascular diseases. The very low relative share of opium poisoning is only 0.52% in the Varna tourist region.

The peculiarities of the clinical course of intoxication, the assessment of the severity of poisoning and the outcome thereof are described.

The existing standardized scale for grading the severity of poisonings is presented, allowing a qualitative assessment of the morbidity, better identification of the real risks and comparability of the data. These data are based on a program developed on the basis of international documents - by the European Association of Poison Centers and Clinical Toxicologists, the International Chemical Safety Program and the European Commission in the 1990s.

Determining the severity of poisoning, serves to classify cases of poisoning in adults and children, the type of toxic noxa and their dosage.

A comparative analysis establishes the clinical profile of the patient, determining the leading etiological groups of drugs, the nature and type of concomitant drugs and / or psychoactive substances in acute exogenous drug intoxications.

It is clear from the study that toxicological trauma affects the active structural unit of society. In the first subperiod covering the years 1991-2015 intoxications of the young age up to 24 years prevail, and in the next subperiod -2016-2020 the patients with the largest relative share are over 60 years of age, which correlates with the socio- economic development of the country.

Undoubtedly, the most significant practical contribution is to determine the percentage of different drugs in the studied patients, giving an idea of the profile and the combination of drugs and drugs that are used in everyday practice.

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Master of Pharmacy Stanislava Angelova Georgieva was born on September 21, 1986 in the town of Malko Tarnovo, Burgas region. She graduated from the Medical University - Varna,

Faculty of Pharmacy, ACS - Master in 2015, and before that he was a graduate of the Medical College-Varna, specialty "Assistant Pharmacist" - with ACS "Professional Bachelor", graduated in 2008.

In 2018 she was enrolled as a doctoral student in a regular form of education for acquiring the educational and scientific degree "DOCTOR" in the field of higher education: 7. Health and sports; Professional field: 7.3. Pharmacy; Scientific specialty: Toxicology.

The professional experience of the doctoral student is related to the pharmaceutical activity in the field - pharmacies "Ceiba"; Pharma Plus; Meduinpharm. She skillfully combines pharmaceutical practice and scientific work.

The dissertation submitted for review on the topic "CHARACTERISTICS OF ACUTE MEDICINAL POISONING IN VARNA DISTRICT OVER A 30-YEAR PERIOD" examines the most common acute exogenous drug intoxications, which are mainly due to their widespread use in medical practice and relatively unrestricted accessibility.

The topic of the dissertation is relevant because it treats one of the most serious problems in clinical toxicology - drug poisoning, which is increasing with the intensive development of the pharmaceutical industry.

In the modern world of developed countries, acute exogenous drug intoxications account for over 60% of all acute poisonings, the leading ones being those with cerebrototoxic drugs, used mainly in psychiatric and neurological practice.

The latest WHO data show that acute exogenous drug intoxications are formed as a new pathology in toxicology, with rapid increase of cases, more aggressive in nature, covering all age groups and with a severe clinical picture. Their peculiarity is the development of "combined" poisonings as a result of simultaneous administration in high doses of several types of drugs.

The need for epidemiological study in the dynamics for a 30-year period of acute exogenous drug intoxications, in regional terms is related to the frequency and severity of this pathology, as well as the premature loss of human potential through chemical trauma.

This complements the relevance of the topic of modern toxicology. The Bulgarian nation, as a user of medicines, needs a serious informational explanation on the issues of this medicinal disease, as well as in general for awareness of the problem, as well as for its early recognition and overcoming. Of interest to the medical community are modern concepts of multiorgan damage to the body by drugs in daily use; the role of a certain package of prognostic parameters to establish the development of the disease. It is also important to change them both in dynamics and individually, as well as in the overall aspect, during the period of treatment and overcoming of toxic reactions and pharmacological influence of symptoms.

The development of therapeutic treatments worldwide, especially in the process of detoxification, has been carried out in separate combinations, but not in a complete

therapeutic package. Despite the numerous publications, opinions about the place of detoxification, the pharmacological influence of the symptoms, the choice of medications, the choice of dosage regimens, and the correct moment of their application are insufficient and contradictory.

The obtained results reveal possibilities and development of therapeutic schemes for cerebrototoxic lesions as well as lesions of the parenchymal organs and the peripheral nervous system. Moreover, some of them may have a diagnostic-prognostic character and serve as a guide for the course of the therapeutic process.

The dissertation of Stanislava Angelova Georgieva contains a total of 160 pages and is illustrated with 20 tables and 25 figures.

The numbers of the figures and tables in the abstract correspond to the numbers of the figures and tables in the dissertation, which facilitates the parallel reading and evaluation of the scientific value of the work.

It is written in clear literary Bulgarian in a scientific style.

The dissertation is structured correctly according to the requirements and includes: introduction; Literature review; purpose, tasks, object of the research, inclusion criteria, methods and tools of the research, with an approach for automated analysis for extracting content from natural language medical documents available to the patient. There are well-described results and discussion, conclusions and contributions.

In structural terms, the dissertation is developed in the following chapters: Introduction - 2 pages; Literary review - 48 pages; Purpose and tasks - 1 page; Object of the research - 1 page; Methods and tools - 8 pages; Results - 75 pages; Discussion - 2 pages; Conclusions - 1 page; Conclusion - 1 page; Contributions - 1 page; Publications related to the dissertation - 1 p.

The bibliographic reference covers 260 sources, in Latin, most of them after 2000. It presents a contemporary view on issues related to the direction of research, European and global trends.

The literature review is presented on 48 pages, and an in-depth analysis of the publications related to the topic has been made, both in Bulgaria and in foreign literature. It is presented in several sections:

- Historical overview
- Definitions of poison and poisoning
- Classification of toxins

The literature includes clinical and paraclinical evaluation of the various drug toxic noxa, respectively the emerging syndromes.

The methods of treatment are described: conventional and extracorporeal, the antidote treatment, which is defined as the best and effective therapy for severe poisoning. A characteristic of the mechanism of action of the antidotes is made.

The role of the pharmacist in the prevention and participation in coordination initiatives for control and management of poisonings with drugs sold in the pharmacy network is described. With regard to the preventive aspect, knowledge of toxicology, pharmacology, pharmacognosy, as well as pharmaceutical care serve to improve the pharmacist's relationship with patients in the pharmacy network and to ensure a more efficient and economical supply of drugs.

The literature review sheds light on the competence in working with medicinal products in clinical practice, which is important not only for patient safety, but also for monitoring the safety of medicines.

The aim and tasks in the dissertation on the topic " CHARACTERISTICS OF ACUTE MEDICINAL POISONING IN VARNA DISTRICT OVER A 30-YEAR PERIOD " are well formulated, substantiated and related to the presented literature data.

The set goal determines the need to study and analyze the main characteristics and epidemiology of acute drug poisoning in Varna region, registered in Intensive Care Clinic for Acute Poisoning and Toxic Allergies at MMA-MHAT Varna for the period 1991-2020 to improve measures for their prevention.

To achieve this aim, 8 main tasks are well formulated, each of which explains what is sought and how to do it. This allows one to choose the right approach and algorithm for conducting research, to analyze and summarize the results with the relevant conclusions and to indicate the need for a modern approach to solving problems.

The materials, methods and tools of the research are directly related to the purpose and implementation of the tasks. They are very well described, explained and illustrated.

The dissertation includes:

1. Rich clinical material, processed retrospectively on the basis of the medical documentation of the Clinic for intensive treatment of acute poisonings and toxicallergies at the Military Medical Academy - MHAT - Varna - over a 30-year period.
2. The methods used in the analysis of clinical data are processed by: "Automated analysis approach for retrieving content from medical documents available to the patient." This chapter describes a proposed approach using NLP / natural language processing / for creating a mathematical model for assessing the risk of drug intoxication depending on the medicinal products taken by the patient, food supplements in combination with or without ethanol.
3. Summary of AMI data was done using descriptive and inferential statistics.

The study time and the criteria for inclusion of patients in data processing are described.

The study was conducted with toxicological patients treated in the city of Varna, and the author used an analysis of medical histories and personal ambulatory cards of patients admitted to poisoning in the Clinic for Intensive Care of Acute Poisoning and Toxoallergies at MMA-MHAT-Varna. For this purpose, permission was obtained from the Chairman of the Ethics Commission at the Military Medical Academy-MHAT-Varna.

In the section "Results" the own results of the researches are presented in detail and scientifically substantiated, which are well interpreted.

The results cover retrospective processing of a huge amount of material from 6977 patients with acute drug poisoning, treated in the Clinic for intensive treatment of acute poisoning and toxoallergies at the MMA - Varna. It covers a 30-year period - 1991 - 2020.

The studied contingent is divided on different grounds - gender, age, as the studied period is divided into two subperiods - 1991-2015. and 2016-2020.

In the first 15-year subperiod, patients from the younger age group up to 44 years predominate, and in the second - the older contingent over 60 years. It is worrying that, both in percentage terms and in absolute terms, although declining, young people and people of working age maintain high values.

The frequency, dynamics and structure of acute exogenous drug intoxications are determined, in regional aspect - Varna region.

The results of the research allow to build the socio-demographic, clinical profile of the patients. It is extremely important to emphasize that determining the dynamics, structure and frequency of acute exogenous intoxications and suicide trials with drugs in the Varna region for the period 1991 - 2020, allows to analyze the emerging trend in both sexes. Females predominate in a significant percentage of 71.4%, which correlates with the literature data.

The clinical profile of the patient is established by determining the leading etiological groups of drugs, which is an indicator of the most used drugs in medical practice.

According to this sign, acute drug poisonings are divided into 11 groups, with the largest relative share of benzodiazepine intoxications, followed by mixed drug poisonings, and in third place are drugs intended for the treatment of cardiovascular diseases. The very low relative share of opium poisoning is only 0.52% in the Varna tourist region.

The peculiarities of the clinical course of intoxication, the assessment of the severity of poisoning and the outcome thereof are described.

The existing standardized scale for grading the severity of poisonings is presented, allowing a qualitative assessment of the morbidity, better identification of the real risks and comparability of the data. These data are based on a program developed on the basis of international documents - by the European Association of Poison Centers and Clinical Toxicologists, the International Chemical Safety Program and the European Commission in the 1990s.

Determining the severity of poisoning, serves to classify cases of poisoning in adults and children, the type of toxic noxa and their dosage.

A comparative analysis establishes the clinical profile of the patient, determining the leading etiological groups of drugs, the nature and type of concomitant drugs and / or psychoactive substances in acute exogenous drug intoxications.

It is clear from the study that toxicological trauma affects the active structural unit of society. In the first subperiod covering the years 1991-2015 intoxications of the young age up to 24 years prevail, and in the next subperiod -2016-2020 the patients with the largest relative share are over 60 years of age, which correlates with the socio- economic development of the country.

Undoubtedly, the most significant practical contribution is to determine the percentage of different drugs in the studied patients, giving an idea of the profile and the combination of drugs and drugs that are used in everyday practice.

The results are well illustrated and analyzed.

Critical notes

In the examined indicators presented graphically and / or in a table, the statistical package of processing of the results is not marked and the respective statistically significant difference is not described. The tables do not present the mean values and standard deviations of all studied indicators. Modern statistical processing of the results guarantees a good interpretation of the conclusions made and the contributions received, which is essential for the value of the work.

The inclusion criteria indicate an age group over 13 years, and then the following age groups are defined:

up to 24 years; 25-44; 45 - 60 years; over 60 years;

It should be borne in mind that according to the Charter of the Rights of the Child, "Every living being between the ages of 0 and 18 is a child." Children have specific age characteristics, on the basis of which the periods in childhood are formed and patients up to 18 years of age must be separated into a separate group. It is not clear here who is the youngest and who is the oldest patient. The critical remarks made do not diminish the value of the dissertation, as a large amount of factual material has been processed.

The conclusions are 7 and are based on the processed material and the obtained results.

5 contributions of scientific-applied and confirmatory nature have been identified.

The abstract is designed according to the requirements, adequately reflecting the content of the dissertation.

In connection with the topic, 3 publications in scientific journals, 4 participations in scientific forums related to the dissertation are covered.

CONCLUSION

The dissertation on the topic " CHARACTERISTICS OF ACUTE MEDICINAL POISONING IN VARNA DISTRICT OVER A 30-YEAR PERIOD " treats a current medical, toxicological and pharmacological problem.

The scientific value derives from the processing of large clinical and pharmacological material, the conclusions made, as well as from the scientific and applied contributions.

I believe that the dissertation presented in this way meets the requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria and the Regulations for the Development of the Academic Staff and the terms and conditions for acquiring scientific degrees and holding academic positions at MU - Varna.

This gives me reason to give my positive assessment and to recommend to the esteemed jury to award a master's degree in pharmacy Stanislava Angelova Georgieva educational and scientific degree "DOCTOR", in the field of higher education: 7. Health and Sports; Professional field: 7.3. Pharmacy; Scientific specialty: Toxicology

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