REVIEW

by Assoc. Prof. Violeta Silvi Chernodrinska, MD, PhD member of Scientific Juri

regarding

the dissertation defense

to Dr Maria Rumenova Boyadzhieva MD

Topic of the PhD thesis:

"Live microstructural analysis of rare eye diseases with modern technologies"

for conferment of an educational and scientific degree "Doctor (PhD)" in the field of scientific specialty "Ophthalmology", code 03.01.36.

Scientific supervisor: Corresponding member Prof. Dr. Hristina Nikolova Grupcheva, MD, FEBO, FICO(Hon), FBCLA, FIACLE

Biographical data

Dr. Maria Rumenova Boyadzhieva was born on 30.12.1983. in the city of Sofia. In 2009, she graduated from Medical University-Varna "Prof. Dr. Paraskev Stoyanov", after which she worked in the Emergency department and Intensive respiratory department of the "St. Marina" Hospital-Varna. In 2016 began specialization in eye diseases at SBOBAL - Varna, and in 2020 acquired a specialty in ophthalmology. She has participated in numerous scientific meetings, congresses, courses and specializations, among which a course in orthokeratology - Paris (2019) and a Summer School in Linskopin under the guidance of Prof. Neil Lagalli (2017). She has over 17 scientific publications in national and international journals and 19 citations.

Timeliness of the problem

So-called "rare diseases" are diseases that affect a small number of people compared to the general population. More than 7,000 rare diseases are known, from which more than 300 million people suffer. Currently, the European list of rare diseases includes 53 ophthalmic conditions that are classified as rare diseases and another 103 systemic diseases with ophthalmic involvement. Nowadays, the multidisciplinary approach has a decisive role in their diagnosis and management. A large percentage of them do not have an FDA-approved treatment. Last but not least, advances in technology and genetic engineering offer hope for improving the quality of health care for patients with rare diseases.

In Bulgaria the problem of rare diseases is extremely topical due to the characteristics of the population and the limited resources of the health system. Dr. Boyadzhieva researches a topic that has not only a medical but also an exceptional social aspect. The paper provides a unique algorithm for tracking and treating rare eye diseases based on an analysis of the health policy of countries with established practices in the field.

General characteristics of the dissertation work

The structure of the dissertation is in accordance with modern standards and requirements. The dissertation is written on 157 standard pages and illustrated with 14 tables and 46 figures. The paper includes the following sections: Contents – 1 page, Introduction – 3 pages, Abbreviations used – 1 pages, Summary – 3 pages, Abstract – 3 pages, List of figures and tables – 5 pages, Literature review – 36 pages. , Aim, tasks and hypotheses- 1 p., Materials and methods- 31 p. Results- 38 p., Discussion- 7 p., Conclusions- 2 p., Contributions- 1 p., Bibliography- 8 p., Appendices- 14 p. ., List of publications - 1 page.

The literature reference includes 125 literary sources in Latin, most of which were published after 2012. and 17 literary sources in Cyrillic.

The literature review is comprehensive, comprehensive and demonstrates detailed knowledge of the subject. Covers about 1/3 of the dissertation work (36 pages). The literature review is divided into:

1. Definition of a rare disease
2. Sources of information and data on rare diseases
3. Clinical picture of rare diseases
4. Diagnosis, treatment and prevention of rare diseases
5. Rare eye diseases
6. Classification of rare eye diseases
7. Treatment of rare eye diseases
8. Summary

Purpose, tasks and hypothesis of the dissertation

The goal is adequately formulated - to follow the path of patients with rare eye diseases, to evaluate the registration regime, the process of including eye diseases in the national registry for rare

diseases, and to create a model for a clinical registry for the benefit of everyday ophthalmological practice.

To achieve the set goal, 6 tasks have been set:

1. To carry out a review of the European rules and registration regimes for rare diseases and rare eye diseases. View the national register.

2. To assess the knowledge of rare diseases among ophthalmologists.

3. To create a model for the registration of a rare eye disease - Aniridia.

4. To make a clinical assessment of rare eye diseases according to the Orphanet classification.

5. To create a model for a publicly accessible national register for rare eye diseases in Bulgaria.

6. To develop a plan to create an expert center for rare eye diseases in Bulgaria.

Materials and methods

An algorithm for registering the disease aniridia and one for creating an expert center for rare eye diseases and a national registry have been developed. Publicly available data on rare eye diseases, clinical data from prospectively followed patients as well as established methodologies for managing patients with rare eye diseases were used for the analyses.

The study was conducted at the Department of Eye Diseases and Visual Sciences of the Medical University - Varna, on the territory of SBOBAL - Varna, over a period of 5 years. Dr. Boyadzhieva points out that all clinical studies were performed with the latest generation technology allowing microstructural analysis. A questionnaire is attached to test the knowledge about rare eye diseases of specialists and specialists in Eye Diseases.

Results

The indicated results demonstrate that to date there is no expert center for rare eye diseases and a register of patients with rare eye diseases in Bulgaria. An algorithm was created for the registration of an expert center and a national registry for rare eye diseases, and the need to include aniridia in them was indicated.

The analysis of the questionnaires (out of 110 sent, correctly filled in and 74 returned) regarding the awareness of Bulgarian ophthalmologists and residents in ophthalmology, shows that nearly half of the respondents meet a patient with a rare eye disease every month, but only 39.47%

of those who filled out the questionnaire treat these patients. It is interesting to note that nearly 60% of the participants are of the opinion that Bulgarian specialists do not receive professional training for the prevention, diagnosis and treatment of rare diseases, although 60% of the respondents share that during their training they had specific classes/ lectures devoted to these diseases.

Prospectively followed were 39 patients according to the algorithms created in the present study for tracking rare eye diseases. The author points out that the created algorithms would help to collect qualitative and analytical data, implement control over the disease, report the effect of the treatment carried out - a basis for creating standards for good medical practice.

Dr. Boyadzhieva makes 10 well-founded conclusions, namely:

1. The study confirms the need to create an expert reference center for rare eye diseases.

2. Based on the conducted in-depth and analytical analysis of the data, it is proven necessary to include more rare eye diseases in the National List of Rare Diseases.

3. The need to build a new national program for rare diseases, supporting the National Register of patients with rare diseases and updating Regulation No. 16 of 2014, is demonstrated. of the Ministry of Health in line with European legislation.

4. It is proven that the creation of an up-to-date, accessible and functional registry for rare eye diseases is not only possible, but can represent a step forward in epidemiological and clinical studies in this field - the lack of reliable epidemiological and clinical data generated in local settings, is a significant obstacle to effective planning and management of health care costs for any country, including Bulgaria.

5. The need for the participation of Bulgaria and the Bulgarian expert center for eye diseases in the European reference networks for improving the care and diagnosis of rare eye diseases is confirmed.

6. It is necessary to update the standard on "Medical genetics", Ordinance No. 26 of the Ministry of Health and the diagnostic algorithms and indications for conducting genetic and genomic research - the establishment of a precise molecular diagnosis for any genetic eye disease can only be achieved through genetic research and this will allow the clinician to stratify clinical risk in terms of prognosis, comorbidities, treatment options, and/or participation in clinical trials. The financing of diagnostic genetic tests now takes place only within the framework of Ordinance 26 of the Ministry of Health - children up to the age of 18 are examined free of charge. For patients over 18 years of age with rare diseases, genetic diagnosis is practically not provided within the current clinical pathways, and these patients remain in a large number of cases undiagnosed and inadequately treated.

7. It is necessary to improve prevention, diagnosis and care for patients with rare diseases, including rare eye diseases, as well as providing equal access to therapies with orphan drugs and innovative therapies for these patients in Bulgaria.

8. The need to raise awareness of rare eye diseases among the population and medical specialists is confirmed.

9. The need to create algorithms for good practices and care for patients with rare eye diseases is proven, including the preparation of files on rare eye diseases in Bulgarian, to be accessible to specialists, patients, patient organizations, etc.

10. It is proven imperative to build a comprehensive health policy for patients with rare diseases, including rare eye diseases, and to make changes in social policy.

List of publications related to the dissertation

1. Kristiyan D Vasilev, Yana M Manolova, Mariya Boyadzieva, A Typical Clinical Case of Uveitis Combined With Central Serous Chorioretinopathy and Optic Disc Edema, IJITE – Issue45, Volume 28, Number 01, Published On: april 2017;

2. Davide Borroni MD, Mohit Parekh PhD, Maria Boyadzhieva MD, Stefano Ferrari PhD, Sajjad Ahmad MD and Bogumil Wowra MD, Simple Limbal Epithelial Transplantation (SLET): A review on current approach and future directions, May 2018, Survey of Ophthalmology

3. Maria Boyadzhieva, Hristina Grupcheva, A new approach for management of the anterior eye surface with the oldest in terms of design contact lenses, Bulgarian ophthalmological review, issue 3, 2018, Maria Boyadzhieva, Hristina Grupcheva, A new approach for management of the anterior eye surface using the "oldest" contact lenses concept, Bulgarian Review of Ophthalmology 62 (3), 16-24

Conclusion

The presented dissertation is structured according to the Law on the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB) and the criteria for acquiring the educational and scientific degree "doctor" at the Department of "Ocular Diseases and Vision Sciences" at the Medical University - Varna. In-depth knowledge and hard work on the given problem are observed in the scientific development. I give a positive assessment to the dissertation work of Dr. Maria Rumenova Boyadzhieva and allow myself to propose to the respected members of the Scientific Jury to vote positively for awarding the scientific and educational degree "Doctor (PhD)" to Dr. Boyadzhieva in the scientific specialty "Ophthalmology".

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