Opinion

By Assoc. Prof. Violeta Chernodrinska, MD

regarding the defense of the dissertation

of Dr. Silvia Nikolaeva Nikolova

on the topic

“Approach to uveitis in Bulgaria”

for awarding the educational and scientific degree “DOCTOR” in the scientific specialty

“Ophthalmology”, code 03.01.36

with scientific supervisor Assoc. Prof. Dr. Binna Nikolaeva Nencheva, MD

Biographical data

Dr. Silvia Nikolaeva Nikolova was born on 18/08/1983 in the town of Aytos. In 2001, she graduated the “Ivan Vazov” Secondary School in Burgas. During the period 2002-2009, she was a medical student at “Prof. Dr. Paraskev Stoyanov” Medical University – Varna. After graduation, she worked as a medical representative (2009-2018) and as a resident physician at Burgas. In 2018, she acquired a specialty in "eye diseases" from MU-Varna. Since 2021, she has been a part-time assistant at the Department of "Eye Diseases and Visual Sciences" of MU-Varna, a full-time lecturer for the "Medical Optician" department and a specialist ophthalmologist at USBOBAL- Varna. She is also part of the team of specialists at the Varna's ocular medical center and the Dr. Grupchevi Vision Center. Her scientific interests are focused on the treatment and monitoring of patients with uveitis, surgical treatment of the anterior segment of the eye and its appendages, treatment and monitoring patients with glaucoma. Dr. Nikolaeva is constantly improving her qualifications by annually attending courses conferences, for which she has presented a detailed list. Among them are “Modern methods research of structural changes in the retina (FA and OCT)”, 2019, “Lasers in ophthalmology - treatment of eye diseases”, 2019, “Surgery of the vitreous body and retina”, 2020, “Ultrasound diagnostics in ophthalmology”, 2020, “Amniotic membrane”, 2020, “Intravitreal administration of medications”, 2020, “Strabology”, 2020. She is a member of the Bulgarian Medical Union and the Bulgarian Society of Ophthalmology. She speaks Russian and English and has very good computer literacy.

Relevance of the problem

Uveitis is a disease, caused by disorders of various etiologies - infectious and non-infectious agents and can lead to impaired vision, blindness and reduced quality of life. Uveitis is among the leading causes of blindness in developed countries, ranking in 5th or 6th position. Patients often develop depression, anxiety and choose self-isolation for problems related to disorders and lack of vision. Trends in

therapeutic approaches to uveitis are developing continuously, with an increasing share of biological and immunosuppressive therapy; increased adaptation of intraocular implants for the release of medications with prolonged action; a personalized approach from the individual ophthalmological practice; integrationof artificial intelligence and telemedicine systems. The successful treatment of uveitis is a complex series of in-depth examination, detailed history taking, performance of highly specialized examinations, correct and timely diagnosis, precise choice of treatment and monitoring of the response to it.

General characteristics of the dissertation work

The structure of the dissertation work is in line with modern standards and requirements. The dissertation work contains 212 pages, including 22 tables and 60 figures. 217 literary sources are cited. 5 chapters are presented, corresponding to the aim and the objectives set and meeting the requirements for the layout of the dissertation work. The literature review includes 57 literary sources in Latin and none in Cyrillic. There are 3 publications related to the dissertation work. The literature review is comprehensive, thorough and demonstrates detailed knowledge of the matter. It covers about 1/3 of the dissertation work. The literature review is divided into:

1. Anatomy of the uvea

2. Anatomical and pathoanatomical considerations

3. Classification of uveitis

4. Epidemiology and risk factors

5. Etiology

6. Diagnosis and laboratory tests in uveitis

7. Ophthalmological tests for patients with uveitis

8. Bacterial uveitis

9. Treatment of uveitis

10. New trends in the treatment of uveitis

11. Complications.

Aim, objectives and hypothesis of the dissertation

The aim is adequately formulated - assessment of socio-demographic characteristics, diagnostic and therapeutic algorithms and complications in patients with uveitis, based retrospective analysis and prospective follow-up for a period of 8 years.

To achieve the aim, 6 objectives have been set:

1) to conduct a review of publications in the literature and evaluate modern diagnostic approaches in patients with uveitis and the therapeutic approaches applicable to them;

2) to study and analyze the socio-demographic characteristics and etiology of patients with uveitis for a period of 8 years;

3) to analyze the course of uveitis, diagnostic approaches and therapeutic algorithms in patients with uveitis who underwent treatment at USBOBAL-Varna;

4) to assess the complications of the course of the disease, concomitant diseases and side effects of the therapy;

5) to analyze the duration and course of the disease (relapses, remission intervals);

6) to create a risk profile of the studied patients with uveitis and predict the risk of relapse and an algorithm for behavior in patients with infectious and non-infectious uveitis.

Materials and methods

The present study was conducted on the territory of the University Specialized Hospital for Eye Diseases for Active Treatment – Varna for a period of 8 years - 2014-2018 and 2019-2021. 219 patients who underwent treatment in hospital and outpatient care were studied. The selection of patients was based on precisely defined criteria - patients with uveitis as an independent or accompanying disease in patients, under and over 18 years of age and who completed an informed consent form. Exclusion criteria were patients without uveitis, patients with other ophthalmological diseases not accompanied by uveitis, patients with uveitis and mental disabilities and those who did not complete an informed consent form.

The methodology of the study includes:

1.Documentary method through research and analysis of the published scientific literature regarding the prevalence and risk factors of the disease, diagnostic methods and therapeutic algorithms.

2.Sociological method through the creation of a questionnaire that meets the objectives of the study and the conduct of a survey among patients.

3.Clinical method - performing examinations such as - autorefractometry, tonometry, biomicroscopy, ophthalmoscopy, optical coherence tomography, fluorescein angiography and taking anamnesis.

4.Statistical methods - analysis of variance (ANOVA, MANOVA), variation, correlation, regression and comparative analysis and risk assessment analysis (OR, RR). In all analyses, an acceptable level of significance of $p<0.05$, $p<0.01$, $p<0.001$ at a confidence interval CI 95% is assumed. The data was statistically processed using SPSS v.20, using descriptive indicators for quantitative and qualitative variables and is presented in tabular and graphical form.

Results and Discussion

The mean age of the patients in this study (54.2 years) is higher than that reported in a study by a number of researchers from Brazil (32.1 years), Colombia (31.7 years), Tunisia (34.0 years), North America (45.0 years) and Southeast Brazil (41.0 years). Dr. Nikolova's study confirms the hypothesis of the specificity of the disease, according to which uveitis covers different age groups. The data support the findings of population studies, which describe an increasing incidence of uveitis with increasing age. Regarding the results compared to other developed countries, the data from the reviewed dissertation is consistent with the reported results from Spain, Greece and Germany, where the incidence of the disease increases with age and uveitis in children and adolescents is not so common. No difference was found between the incidence between the two sexes. The most common localization of uveitis worldwide is anterior uveitis. The results of the present study confirm this fact - anterior uveitis accounts for 91.2% of the cases studied. In the present study, idiopathic uveitis was found in 42.2% of cases and acute anterior uveitis was diagnosed in 44.7% of cases. Onchocerciasis is not typical for our latitudes. Increasing life expectancy determines a more frequent encounter with various infectious disease agents. Certain professions carry a risk of developing certain infections and on the other hand, poor socio-economic status affects the solvency of patients in case of need for expensive tests and medications. Last but not least, the state of the healthcare system is also important in relation to the possibility of expensive examinations and treatment being covered by the state. Close collaboration with other specialists is necessary, both when interpreting the results of the examinations and when carrying out the treatment, therefore we can safely say that uveitis is an interdisciplinary problem.

Dr. Silvia Nikolova makes 10 well-founded conclusions, namely:

1. A trend towards an increase in the frequency and recurrence of the incidence of uveitis has been established, which passes from chronic to acute form, with a rejuvenation in the age of the patients with the disease observed mainly in men and people from rural regions.

2. Male gender emerges as a risk factor (OR=3.9) for binocular involvement in patients with uveitis.

3. The localization of uveitis correlates with the age of the patients and the severity of the disease.

4. Idiopathic uveitis predominates, with the most common causes being herpes zoster (6.9%), ankylosing spondylitis (5.1%), herpes simplex (4.6%) and rheumatoid arthritis (2.3%).

5. The results of the findings established during the biomicroscopy show a significant difference in the two periods in all studied segments.

6. A significant difference was established regarding the drug treatment of uveitis, with the first period being dominated by patients treated with corticosteroids, NSAIDs and mydriatics, while the use of biological drugs increases in the second period.

7. The results of the study of the treatment of uveitis show that biological drugs are applied primarily in patients with moderate and severe forms of the disease.

8. The use of systemic NSAIDs increases with the severity of uveitis and immunosuppressants are only used in patients with severe form of the disease.

9. Rheumatoid arthritis, herpes simplex, and ankylosing spondylitis have been identified as risk factors for recurrence of uveitis, with their severity decreasing in the second studied period, which can be explained by improved disease control through the application of biological therapy.

The risk profile of patients with uveitis for disease recurrence and development of severe form of the disease includes the presence of systemic diseases (psoriasis vulgaris), autoimmune diseases (ankylosing spondylitis and rheumatoid arthritis) and viral agents (herpes zoster), binocular involvement and residence in a rural region.

Contributions

The contributions of Dr. NIKOLOVA are: contributions of a scientific and applied nature, of a cognitive nature and contributions of a practical nature.

In my opinion, the most useful of which in practice are the creation of a risk profile of patients with uveitis and prognosis of relapses and the creation of a brochure with guidelines for general practitioners for the purpose of early diagnosis of the disease.

Conclusion

The presented dissertation is structured in accordance with the Law on the State of the Republic of Bulgaria and the criteria for acquiring the educational and scientific degree "doctor" at the Department of "Eye Diseases and Visual Sciences" at the Medical University - Varna. The scientific work demonstrates in-depth knowledge and hard work on the given problem. I give a positive assessment of the dissertation work of Dr. Silvia Nikolaeva Nikolova on the topic "Approach to uveitis in Bulgaria". I propose to the esteemed members of the Scientific Jury to vote positively for awarding the scientific and educational degree "doctor" to Dr. Silvia Nikolaeva Nikolova in the scientific specialty "Ophthalmology".

28.12.2024 Assoc. Prof. Dr. Violeta Chernodrinska DM

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