

OPINION

By Assoc. Prof. Violeta Chernodrinska, MD, PhD

regarding

dissertation thesis defense

of Anna Nedyalkova Ilieva- Krusteva on theme

**„Screening program of retinopathy of prematurity –
regional application, analysis of results and
perspectives“**

For aquisition of educational and scientific degree “DOCTOR” in scientific specialty
“Ophthalmology”, code 03.01.36

With research supervisor Assoc. Prof. Yana
Manolova, MD, PhD

Relevance of the problem

Retinopathy of prematurity is a leading cause of preventable childhood blindness.

It has been estimated that by 2010, globally, almost 185 000 premature infants had developed ROP, 20 000 had lost vision and a further 12 300 had developed mild to moderate visual impairment. 65% of children with visual impairment are in developing economies, which includes Bulgaria. Worldwide, there are 50 000 children under the age of 15 who have lost their sight due to this disease.

The development of digital technology offers new fast, convenient methods of diagnosis, including at a distance. Problems for diagnosis and timely treatment of the disease are: the small number of specialists trained to work with this specific pathology and the distance of intensive care units for premature children from ophthalmology units, the need for coordination between specialists from separate

medical structures.

The increasing number of children who are affected, as well as the legal aspects - claims by parents in the event of an unfavourable outcome, shape many of the problems facing doctors. Meanwhile, children around the world continue to lose their sight, with all the social and economic consequences this entails.

General characteristics of the thesis

The structure of the dissertation is in line with modern standards and requirements. The dissertation has 202 standard pages and is illustrated with 34 figures and 17 tables. The bibliography includes 481 references, of which 13 in Cyrillic and 468 in Latin. There are 4 publications related to the dissertation.

The literature review is comprehensive, thorough and demonstrates a detailed knowledge of the subject matter. It covers about 1/3 of the dissertation (64 pages) and comprehensively discusses all aspects of etiology, pathogenesis, classifications and treatment of the disease, as well as screening criteria for children at risk.

Aim, tasks and hypothesis of dissertation thesis

The aim is well formulated - To establish the epidemiological and clinical characteristics of ROP among premature infants in the Varna region according to the current screening program for ROP adopted in the Republic of Bulgaria, as well as to offer a platform to improve the awareness of parents and medical professionals about this disease. In order to achieve the set goal, 6 tasks have been set:

1. To determine the frequency and characteristics of ROP in premature infants screened at the Neonatology Department of the Specialized Hospital of Obstetrics and Gynecology "Prof. Dr. Dimitar Stamatov" - Varna and "University Specialized Hospital of Eye Diseases for Active Treatment - Varna"-Ltd.;
2. To analyze the risk factors on the fetal side, which could be related to the development and progression of the disease;
3. To analyse the maternal risk factors that could be relevant to the development and progression of the disease;
4. To monitor the early post-therapeutic effect of intravitreal administration of anti-VEGF medication;
5. To determine the place of ROP as a cause of severe visual impairment and blindness among the students at the Special School for Students with Visual Impairment "Prof. Dr. Ivan Shishmanov", Varna;
6. To propose an internet-based information portal for ROP.

Materials and Methods

The clinical material includes 124 preterm children, who were screened for ROP through the Hospital "Prof. Dimitar Stamatov" - Varna and followed up in the Hospital for Prematurity - Varna for the period January 2017 - December 2020.

The inclusion criteria for the study are consistent with the standard adopted at the National Workshop on Screening and Treatment of ROP in Bulgaria in 2009:

The study methodology includes:

Diagnostic methods: identification of preterm infants to be screened; examination of medical records - current medical history, birth certificates, and neonatal units where the child was treated.

Standard methods of examination for ROP: ensuring maximum medicated mydriasis; topical anaesthesia and blepharostat placement; examination by binocular indirect ophthalmoscopy at the Specialized hospital for Obstetrics and Gynecology "Prof. Dr. Dimitar Stamatov" and/or photodocumentation of clinical findings with RETCAM at the University Hospital of eye diseases for active treatment-Varna;

Determination of management- follow-up or treatment

Treatment methods: laser therapy, cryotherapy, intravitreal application of anti-VEGF medications. Statistical methods: descriptive analysis, comparative analysis, linear regression analysis.

In the study concerning the incidence of ROP in the School for visually impaired children "Prof. Dr. Ivan Shishmanov" in the city of Varna. 145 children were included. Data on age, sex and cause of visual impairment according to the available medical information of students with visual impairment attending the school in the school year 2022/2023.

Results and Discussion

For the study period, data of ROP were found in 86 children (69.4% of all children studied), with 25 of them (20.2% of all children studied)

the disease progressed to ROP requiring treatment. The remaining 61 children (49.2% of all children studied) showed signs of spontaneous disease regression.

After comparison with a similar study 15 years ago in the same institutions, the incidence of the disease was found to be significantly lower compared with the present study. Dr. Ilieva draws attention to the fact that despite the high incidence of diagnosed ROP cases in the present study, most of them had a mild form of the disease in which spontaneous regression was observed. One possible explanation is that the mean TR and GW in this previous study were significantly higher compared to the current criteria. Improved neonatal care in recent years has resulted in the survival of many more high-risk infants, increasing the chance of developing ROP. The present results confirm this worldwide trend.

From the multivariate analysis applied, the role of low Birth weight, prolonged ventilatory support, neonatal anaemia and stage III IVC as independent factors for the development of ROP was confirmed. Regarding disease progression, low birth weight and stage III IVC were determined as independent risk factors. Regarding maternal risk factors, a significant association was found between the factor in vitro fertilization and the development of ROP, but not for the progression of already developed disease.

The early post-therapeutic effect of anti-VEGF medication was investigated, and ROP regression was achieved in more than 80% of children.

Through the development of a web-based information portal with the address: www.rop-info.com, the awareness of parents and medical professionals has been improved at national level.

Dr. Anna Nedyalkova Ilieva-Krusteva draws 10 well-founded conclusions, namely:

1. The incidence of ROP among premature infants treated in the Intensive Neonatology Unit at the Hospital "Prof. Dimitar Stamatov" - Varna and screened for the disease is high - 69.4%.

The incidence of ROP in the Varna region is significantly higher than in the Plovdiv region (30.3%), Sofia region (22.8%) and Stara Zagora region.

(5,4%).

3. The incidence of preterm infants with ROP in the Varna region requiring treatment is 20.2%, which again significantly exceeds the previously reported incidence, for example in the Sofia region - 7.4%.

4. Low birth weight, invasive ventilatory support, grade III IVH and the presence of neonatal anaemia are significant and independent risk factors for the development of ROP.

5. Low birth weight and grade III IVH are significant and independent risk factors for disease progression.

6. Small GA, presence of HMB; performing more than 2 hemotransfusions; exogenous surfactant administration; grade I IVH, low 1-min APGAR are statistically significant but not independent risk factors for the development of ROP.

7. Low GA, presence of neonatal anemia, HMB, exogenous surfactant administration; low APGAR at 1st and 5th minute are statistically significant but not independent risk factors for progression of ROP to stages requiring treatment.

8. Of the maternal risk factors examined, we found IVF to be significant for the development of ROP but not for disease progression. In regression analysis, IVF was dropped as a significant risk factor for the development of ROP.

9. Studying the etiological causes of vision loss among students of the school for visually impaired children "Prof. Dr. Ivan Shishmanov", Varna, shows that diseases of the optic nerve and retina are the leading causes of severe visual impairment and blindness, and among the studied students ROP takes second place after optic nerve

atrophy as an etiological cause of vision loss.

10. Timely treatment with intravitreal administration of anti-VEGF medication for type 1 prethreshold disease has a good early anatomic outcome.

Contributions

The contributions of Dr. Anna Nedyalkova Ilieva-Krusteva are: contributions of scientific and applied nature, contributions of cognitive nature and contributions of practical nature.

In my opinion, the most useful in practice are: the update of the current trends concerning the diagnosis, treatment and follow-up of ROP, as well as the implementation of an online-based information portal dedicated to ROP, the purpose of which is to assist parents and medical professionals.

Conclusion

The presented dissertation is structured in accordance with the Law for the Acquisition of Educational and Scientific Degree "Doctor" at the Department of Ophthalmology and Visual Sciences, Medical University - Varna. In the scientific work, thorough knowledge and work on the given problem are observed. I give a positive evaluation to the dissertation work of Dr. Anna Nedyalkova Ilieva-Krusteva entitled "Screening program for retinopathy of prematurity - regional application, analysis of results and perspectives."

I propose to the distinguished members of the Scientific Jury to vote positively for the award of the scientific and educational degree "Doctor" to Dr. Anna Nedyalkova Ilieva-Krusteva in the scientific specialty "Ophthalmology".

28.12.2024r

City of Sofia

Assoc. Prof. Violeta Chernodrinska, MD, PhD

A handwritten signature in black ink, consisting of a large, stylized capital letter 'V' followed by a cursive 'C' and a series of loops and strokes that form the rest of the name.

