

REVIEW

from

Prof. Miroslava Kadurina, PhD

Acibadem City Clinic – Sofia

Of Thesis on

„INFANTILE HAEMANGIOMAS – EPIDEMIOLOGICAL CHARACTERISTICS AND MANAGEMENT APPROACH”

for the award of the educational and scientific degree „Doctor of Philosophy“

To Dr Kristina Vassileva Semkova

Professional domain: 7.1. Medicine

Higher education: 7. Health care and sports

PhD programme: 03.01.21 ‘Dermatology and Venereology’

1. General presentation of the procedure and the PhD student

Biography: Dr. Kristina Vassileva Semkova is a specialist in dermatology and venereology. She completed her higher medical education at the Medical Faculty at MU - Sofia and specialized in the Department of Dermatology and Venereology at MU - Sofia under the supervision of Prof. Sonya Marina. She acquired a specialty in 2013, and since 2015 had a two-year training in dermatopathology.

The presented set of materials in paper and electronic form is in accordance with the requirements of the Medical University of Varna.

Dr Semkova presents a dissertation written on 131 pages, a summary written on 77 pages and 4 publications, 3 of which are referenced and indexed accordingly in the world's WOS/S bases.

2. Topicality of the problem

Hemangiomas are the most common vascular anomalies on infants and may be associated with life-threatening complications and functional changes. The discovery of an innovative therapeutic method for their treatment has put hemangiomas back in the focus of clinical trials, and the topic remains relevant worldwide. The dissertation on "INFANTILE HAEMANGIOMAS IN INFANTS AND CHILDREN - EPIDEMIOLOGICAL CHARACTERISTICS AND THERAPEUTIC APPROACH" has an important practical significance and answers contemporary questions.

This dissertation is the first of its kind in the Republic of Bulgaria and gives a clear idea of the specifics for the Bulgarian population, in addition to contributing to the international database for topical treatment of infantile hemangiomas with beta blockers.

The dissertation is presented on 131 pages and is illustrated with 27 figures (18 photos and 9 diagrams), 9 tables and 3 appendices.

3. Understanding of the topic

Dr. Semkova has extensive theoretical knowledge and practical skills and shows in-depth knowledge of the problem and issues related to the treatment and diagnosis of hemangiomas in infants and children

4. Methodology of the study

Dr. Semkova proposes research and statistical methods suitable for the purpose of the dissertation, and the proposed methodologies of the various studies are suitable for obtaining a satisfactory and informative answer regarding the set goals and objectives.

5. Characteristics and evaluation of the dissertation work and contributions

The thesis is structured according to the requirements of the Medical University - Varna and contains an introduction, purpose and tasks, material and methods, results, discussion, conclusions, contributions and bibliography. Publications, related to this thesis, are presented at the end of the dissertation.

The chapter "Literature Review" introduces the the problem in details focusing on the epidemiology, risk factors, localization and therapy of infantile hemangiomas. Particular attention is paid to the risk factors for their occurrence, as well as to current methods of treatment.

The goals and tasks are clearly defined, and the tasks are adequate to achieve the goal of the dissertation.

The section "Material and methods" describes in detail the clinical and epidemiological studies; the materials used; statistical methods and ethical aspects. The study group was large enough to achieve statistical significance of the results and to draw conclusions, as 304 children of both sexes were studied, followed for a sufficient period of time to assess the effect of treatment and the psychosocial impact on the family.

The dissertation includes the following own studies:

- Epidemiological study to assess prenatal and postnatal factors associated with an increased risk of developing hemangiomas in infancy and childhood in the Bulgarian population
- Development of a scale for assessing the activity and severity of hemangiomas, which is suitable for initial assessment and follow-up of treatment
- Prospective study of the therapeutic effect and safety profile of a new drug for topical treatment of hemangiomas in infants and children - topically applied timolol maleate.
- Study of the efficacy and safety of timolol maleate 1% emulsion / gel
- A study to assess parents' perceptions of the psychosocial effect of childhood hemangiomas on family quality of life.

The studies were conducted according to a strict protocol with adequate inclusion and exclusion criteria. The "Discussion" section analyzes the results of the studies, which confirm the data from the world literature and provide data on the Bulgarian population. The studies are unique to the Bulgarian population and highlight some specific characteristics. Assisted reproduction by the in vitro method (including intracytoplasmic sperm injection / ICSI) and intrauterine insemination are not associated with an increased incidence of hemangiomas in the Bulgarian population, as only 8.2% of the study group with hemangiomas were conceived by the in vitro method, compared to 5.5% of the control group. Globally, there are significant differences in the statistical significance of this association, with some studies showing a link that is not established in other studies.

The introduction of an innovative and original evaluation system is a significant practical contribution, and the results are promising for its application in practice and unification of the therapeutic approach. The study for the development and validation of this rating scale was published in a peer reviewed international journal with an impact factor, which also shows its importance.

The study of topical administration of timolol maleate as a treatment for hemangiomas in infants and children is of paramount importance. Such a study is being conducted for the first time in Bulgaria and Dr. Semkova and her team were the first to introduce this treatment as a standard for small and

superficial haemangiomas. The study is also one of the first in the world with this treatment, which is confirmed by the significant number of citations that can be found in global databases. The treatment is well tolerated and effective, showing significant improvement at 12 and 24 weeks of initiation.

Also of interest is the introduction of a new formulation of the preparation - emulgel, which is a relatively new and innovative form, combining the properties and advantages of emulsion and gel.

No less important is the study of quality of life in the families of children with hemangiomas. The questionnaire used is adequate for the needs of the survey. The results highlight the significant effect of hemangiomas on the psychosocial functions of the daily lives of patients and their parents and provide a basis for developing additional interventions and involving psychologists and their assistance in a comprehensive approach to the treatment of these vascular lesions.

The thesis contains 7 conclusions based on the results of the studies. All conclusions are significant and contribute to the knowledge of the problem nationally and globally. This work provides 11 contributions, of which 5 contributions are original, 2 are of scientific-theoretical nature and 4 contributions are of scientific-applied nature.

I do not find elements of plagiarism and I find the presented data to be original, interesting and extremely important for the development of our understanding of this common dermatological condition.

The bibliography includes 168 literature sources.

6. Summary

The summary contains 77 pages and includes in an abbreviated form the main sections of the dissertation. It is structured according to the requirements. The content and quality of the abstract reflects the main results achieved in the dissertation

7. Assessment of the scientific criteria

Four publications (3 as the first author in indexed international publications with impact factor) and 10 scientific papers at Bulgarian and international forums were presented in relation to this thesis work.

Dr. Semkova fully meets the required scientific criteria of the Medical University - Varna according to the regulations for the development of the academic staff of MU-Varna for obtaining the scientific degree "Doctor of Philosophy".

8. Conclusion

With this innovative and original work, Dr. Semkova demonstrates in-depth theoretical knowledge and professional qualities and skills in the field of Dermatology and Venereology and on the topic of the dissertation, as well as skills for conducting and analyzing scientific research. The dissertation of Dr. Semkova on "INFANTILE HAEMANGIOMAS - EPIDEMIOLOGICAL CHARACTERISTICS AND THERAPEUTIC APPROACH" for the award of 'Doctor of Philosophy' degree shows theoretical and scientific contributions that enrich the knowledge of pediatric hemangiomas nationally and globally. The dissertation work meets all the requirements of the Law for development of the academic staff in the Republic of Bulgaria (ZRASRB), the Regulations for application of ZRASRB and the Regulations of MU-Varna.

Based on the above review, I confidently give my positive assessment of the study presented by the above peer-reviewed dissertation, abstract, results and contributions, and I invite the esteemed scientific jury to award the educational and scientific degree 'Doctor of Philosophy' to Dr. Kristina Vassileva Semkova in a doctoral program in Dermatology and Venereology.

01.07.2021г.

Рецензент:

Проф. М. Кадурина, дм