

# **REVIEW**

**from**

**Prof. Nikolay Tsankov, PhD**

Acibadem City Clinic Tokuda Hospital – 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**

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

According to the requirements, Dr Semkova presents: dissertation written on 131 pages; summary written on 77 pages; 3 publications in international scientific journals and 1 publication in a Bulgarian scientific journal, all related to the topic of thesis. Of the scientific publications presented, 3 are published in journals with impact factor and are of course referenced and indexed accordingly in the world's WOS/S bases.

### **2. Topicality of the problem**

The dissertation work on ‘Infantile haemangiomas – epidemiological characteristics and management approach’ addresses serious questions related to vascular tumours in childhood. Infantile haemangiomas are the most common benign tumors in children up to the age of 1 year, but their etiopathogenesis is insufficiently understood. There are various hypotheses, which accordingly are the basis of modern treatment modalities.

Propranolol and its analogues are now convincingly established as a method for systematic treatment of infantile hemangiomas associated with functional disorders or with potential life-threatening complications. Topical treatment of hemangiomas with beta-blockers is suitable for small lesions, but the treatment regimen, type of preparation and duration of therapy are still the subject of scientific clarification. The current dissertation work makes a serious contribution in this direction, helping to establish the effect of treatment with topical beta blockers and also determining the impact that this type of vascular abnormalities have on the life of the family.

### **3. Understanding of the topic**

The dissertation shows that Dr Semkova has in depth theoretical knowledge and professional skills. It is illustrated with 3 appendices, 9 tables and 27 figures. The understanding of the topic is shown not only in the detailed literature review, but also in the three publications on the subject of the thesis with impact factor and in the 10 presentations given by the PhD student at international symposiums and congresses in the USA and Europe

### **4. Methodology of the study**

The methodology of the study includes clinical methods, therapeutic methods, statistical methods and ethical aspects. Very interesting is the Hemangioma Family Burden method, which is applied for the first time in Bulgaria and has been analyzed in 186 children. The contribution of the PhD student is the creation of the scale for assessing the activity and severity of the hemangioma and the effect of treatment. This scale was also applied to 186 children and was developed as part of the study.

### **5. Characteristics and evaluation of the dissertation work and contributions**

The PhD student, Dr. Kristina Vassileva Semkova presents a thesis that is structured according to the requirements and contains an introduction, literature review, purpose and tasks, materials and methods, results, discussion, conclusions, contributions, published scientific papers and bibliography.

The literature review is written on 30 pages and includes as separate sections the clinical picture of hemangiomas, their etiology and pathogenesis, provoking factors, diagnostic studies and relevant therapeutic methods, which are divided into conventional and modern.

The objective and the 11 tasks are clearly defined. I find that the well-defined tasks could lead to the achievement of the set objective.

A total of 304 children of both sexes selected over an 11-year period aged between 2 and 48 months were included in the various studies. The main criterion for inclusion was the presence of infantile haemangioma. The main criterion for exclusion from the active treatment study was a haemangioma in the latest stages of spontaneous resolution.

The results of the own studies are divided into 6 subsections:

- ✓ Study of epidemiological factors, assessing their frequency and comparing data on the Bulgarian population with literature data on frequency worldwide.
- ✓ Development of a scale for assessing hemangiomas, by defining main parameters that characterize their severity and activity
- ✓ Prospective study of the therapeutic effect of topically administered timolol maleate, optimisation of the schedule of administration and identification of side effects
- ✓ Study on the efficacy and safety of administration of a bulgarian topical preparation – timolol maleate 1% emulgel
- ✓ Study of the influence of hemangioma on the quality of life of the family (hemangioma Family Burden Questionnaire)
- ✓ Description of interesting cases

The section "Discussion of results" highlights the significant correlation of data in the Bulgarian and global populations on pre- and perinatal risk factors for the occurrence of hemangiomas. Low body weight at birth and the degree of prematurity were identified as the main risk factors in the study. The HASI method developed and validated by the PhD student is suitable for use by dermatologists and pediatricians who treat children with haemangiomas. The study of topical therapy with betablockers is the first of its kind in the Republic of Bulgaria. Treatment with timolol in the study group showed higher effectiveness in flat lesions compared to nodular lesions and, as expected, better results during the proliferation phase versus the involution phase. Timolol maleate has a good safety profile, despite significant systemic absorption, even with the administration of negligibly low doses. The study showed exceptionally good tolerability, effectiveness and safety of administration of timolol maleate 1% emulgel. A special guidance was devised about the place of timolol in the treatment scheme of infantile hemangiomas. 48 families filled in a questionnaire to assess the overall impact of hemangiomas on the family, including the psychosocial influence on individual family members. The obtained results fully support the concept of a significant impact of hemangiomas on the psychosocial functions of the daily lives of patients and their parents.

Seven conclusions have been drawn based on the results of the dissertation work. The presented conclusions correspond to the material presented in the chapter "Results". Of great practical importance are conclusions 5 and 6, which define the treatment with timolol maleate and, accordingly, the mode of titration of the drug and the follow-up of patients.

The contributions of the dissertation work are 11, divided into three sections – original (5 contributions); scientifically theoretical (2 contributions) and scientific and practical and confirmatory (4 contributions).

I find no elements of plagiarism and find the presented data to be original and interesting.

The bibliography includes 168 literature sources in English. The Bulgarian publication on the topic with main participation of the PhD student, is the Bulgarian consensus on the treatment of hemangiomas in nursing and childhood and are presented separately.

## **6. Assessment of the scientific criteria**

Four articles in relation to this dissertation work have been published in the literature and the PhD student is the first author in 3 of them. There have also been 10 scientific presentations at Bulgarian and international forums.

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

## **7. Summary**

The summary contains 77 pages and includes in abbreviated form the main sections of the dissertation work. The content and quality of the summary reflects the main results presented in the dissertation.

## **8. Conclusion**

The thesis of Dr Kristina Vassileva Semkova, „ **INFANTILE HAEMANGIOMAS – EPIDEMIOLOGICAL CHARACTERISTICS AND MANAGEMENT APPROACH**” for the award of the educational and scientific degree „Doctor of Philosophy “ contains scientific and theoretical and scientific and applied results, which represent an original contribution to science and meet all the requirements of the Law on development of academic staff in the Republic of Bulgaria, the Regulations for implementation of the latter and the Regulations of MU-Varna.

In view of the above, I am confidently giving my positive assessment of the studies and their results presented by this thesis and summary as reviewed above. I propose to the honorable scientific jury to award the educational and scientific degree "Doctor of Philosophy" to Dr Kristina Semkova in the PhD Program in "Dermatology and Venerology".

**23.06.2021г.**

**Reviewer: .....**  
**Prof. Nikolay Tsankov, PhD.**