

REVIEW

on the dissertation and abstract on

Hemangiomas in infancy and early childhood - innovative treatment and follow-up

Presented for public defense before a scientific jury for the award of the degree of Doctor of Science and Education in the field of higher education. 7 Health and Sport, professional field 7.1. Medical Sciences, Doctoral Programme "Dermatology and Venereology"

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The dissertation of Dr. Radka Tsokova Maslarska is written in 150 pages, divided in the following chapters:

- Introduction - 3 pages
- Literature review - 41 pages
- Objectives and methodology - 5 pages
- Results of the study - 56 pages
- Results and Discussion - 5 pages
- Recommendations - 2 pages
- Conclusions - 2 pages
- Contributions - 2 pages
- References- 19 pages
- Appendix - 9 pages

The dissertation is illustrated with 32 tables and 80 figures. There are also 4 appendices.

The literature review shows that infantile hemangiomas are the most common benign vascular tumors in children under 1 year of age. Without treatment some hemangiomas do not fully regress and thus can result in residual skin changes and sometimes functional impairment.

The prevalence, etiopathogenesis, current classification, clinical forms, diagnosis, and indications for treatment are discussed with emphasis on the therapy of infantile hemangiomas.

Special attention is paid to local treatment as well as localization of hemangiomas.

In chapter two "Aim and methodology of the study" the aim of the dissertation is precisely stated "Retrospective analysis of infantile haemangiomas treated with Propranolol and establishment of a standard therapy and follow-up scheme in Bulgaria". As a result, 6 objectives were defined, which are consistently discussed in the course of the dissertation.

The results of the own clinical studies cover the distribution of 276 patients by sex (84 boys and 192 girls) and gestational age, as well as the age at initiation of treatment, the clinical characteristics of

the disease and the effect of the treatment. It is noteworthy that 154 children(68,1%) of children born after cesarean section were diagnosed with hemangiomas.

The results of the clinical studies are demonstrated in 26 tables, 31 figures, a summary and a photographic follow-up of 10 clinical cases from 2020 and 10 clinical cases from 2021. The results are in line with the recommendations of the “ Consensus of the Bulgarian Expert Group on the Treatment of haemangiomas.“.

The discussion of the results indicates that Propranolol is the first choice of treatment for children with infantile hemangioma.

The contraindications of Propranolol therapy are presented. A follow-up strategy for these children is demonstrated.

The conclusion section consists of 11 points and reflects the results of all clinical studies of the doctoral candidate.

The bibliography consists of 163 scientific articles- 2 in Cyrillic and 161 in Latin

General presentation of the procedure and the doctoral candidate.

The set of materials is presented on paper and its content is in full compliance with the conditions and procedures for the award of the degree of Doctor of Education and Research.

The dissertation has been approved unanimously and the formal public defense has been initiated with the Order No. 15-05-25 dated 06.06.2023 of Acibadem-CityClinic-Tokuda Hospital.

Teaching background

Dr. Radka Maslarska has a long-time teaching experience with medical residents in the field of neonatology as well as obstetrics and gynecology. She participates as a lecturer in highly specialized courses on transfontanal and abdominal ultrasonography and neonatal intensive care. She is a lecturer at the Faculty of Public Health at the Medical University of Sofia. The doctoral candidate is a major and active participant in a wide range of parent education modules regarding follow-up and treatment of neonates and children with hemangiomas.

Medical relevance of the dissertation topic

Infantile hemangiomas are the most common benign vascular tumors in children under 1 year of age. Propranolol is the betablocker, approved in 2014 by the EMA and FDA for the treatment of infantile hemangiomas. The approved dosage form is a standardized solution, administered orally.

The doctoral candidate was one of the first in the country to start treatment of infantile hemangiomas with Propranolol. The topic of this dissertation is a guideline for clinical research around the world.

Knowledge of the medical issue

The doctoral candidate started her research on the problem in 2016 and is one of the most theoretically trained researchers, as well as a physician with the most clinical experience in Propranolol treatment in our country.

Methodology and results of the study

The methodology achieves the aim of this clinical study and provides answers to the objectives, defined in the dissertation.

A diagnostic and therapeutic algorithm for different types of hemangiomas according to their number, anatomical localization and size was developed.

The etiological factors associated with the development of hemangiomas in infancy and early childhood are explored: preterm birth, preeclampsia, gestational diabetes, thrombophilia, multiple pregnancy, use of anticoagulants.

Ulcerations in hemangiomas were detected in 7 (2.5%) children out of 276 examined and infantile life-threatening hemangiomas were detected in 2.9% of the analyzed group.

The doctoral candidate emphasizes the need for an interdisciplinary approach, based on her own studies and a thorough literature search.

It is stressed that Propranolol is the first choice of treatment in children with infantile childhood haemangioma based on the the following findings in the dissertation:

- minimal side effects
- peripherally mediated vasoconstriction
- inhibits hemangioma stem cell proliferation and induces apoptosis
- reduces vascular density of infantile hemangiomas

The statistical methods (descriptive statistics, Kolmogorov-Smirnov test, Chi-square test, non-parametric test, Kruskal Wallis and Wilcoxon signed-rank test) present the obtained results in an objective and correct manner.

Characteristics and evaluation of the thesis and contributions

Contributions of the dissertation are qualified as "methodological" - 5 in number and "practical-applied" - 4 in number.

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

Scientiometric criteria

The doctoral candidate presents 3 publications on the topic of the dissertation - 2 in Bulgaria and 1 abroad, which summarize the research in the dissertation.

Abstract

The abstract is written in 66 pages and includes in abridged form the main sections of the dissertation. The content of the abstract meets the requirements for a dissertation.

Critical notes

1. Only 2 references in Cyrillic are cited.
2. The two literature sources in Bulgarian are not cited correctly according to the established standard.
3. The dissertation of Dr. Kristina Semkova "Haemangiomas in infancy and childhood - epidemiological characteristics and therapeutic management" (Medical University of Varna), which for the first time in our country presents the topic of local application of beta-blockers in infantile haemangiomas, is not cited.

4. It is surprising that with such a large number of clinical studie, the doctoral candidate has published only three scientific articles.

The critical remarks made do not diminish the value of this dissertation and its contributions to the management of infantile and early childhood haemangiomas.

Conclusion

Having read the materials provided to me on the professional and scientific development of Dr. Radka Tsekova Maslarska and her dissertation work "Hemangiomas in infancy and early childhood - innovative treatment and follow-up", I believe that the dissertation work contains theoretical and practical results, some of which represent an original contribution to this important scientific topic. These results meet all the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria (LADAB) and the Regulations for the Implementation of the LADAB for the Award of the Educational and Scientific Degree "Doctor".

I confidently give a positive assessment of the submitted dissertation, the results and contributions and propose the Honourable Scientific Jury to award the degree of Doctor of Education and Science to Dr. Radka Tsokova Maslarska.

23.06.2023

Reviewed by

Prof. Nikolay Konstantinov Tsankov, MD