

REVIEW

by

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**External member of the Scientific Jury, determined by order № P-109-153 /
14.04.2022 of the Rector of the Medical University „Prof. Dr. Paraskev
Stoyanov” – Varna**

Subject: the dissertation on the topic:

**„Genitourinary syndrome of menopause in women after hormonal, surgical
and radiation castration”**

Scientific adviser Prof. Dr. Yavor Kornovski DSc

For awarding educational and scientific degree „DOCTOR”

*Field of higher education: 7. Health and sport, professional field 7.1 Medicine,
scientific specialty „Obstetrics and gynecology”*

of Dr. Pavel Petrov Dobrev

Brief biographical data and career profile

Dr. Pavel Petrov Dobrev was born on June 23, 1986. He graduated from the Vasil Levski School for Foreign Languages in Burgas. He studied at the Medical University „Prof. Dr. Paraskev Stoyanov” - Varna and in 2011 he graduated in Medicine. In 2016 he acquired the specialty „Obstetrics and Gynecology”. His professional training in the field of operative gynecology, oncogynecology and minimally invasive surgery takes place at the Oncogynecology Clinic, University Hospital „Dr. Georgi Stranski” in Pleven. In 2016 he started working in Complex Oncology Center - Burgas, and since 2019 he is head of the

Department of Oncogynecology. In 2021 he was enrolled as a doctoral student in an independent form of education at the Medical University „Prof. Dr. Paraskev Stoyanov” - Varna. He is a member of the Scientific Society of Obstetrics and Gynecology and of the Bulgarian Medical Union. He is fluent in written and spoken English and Russian.

Relevance of the dissertation

Dr. Pavel Dobrev has developed a topical and socially significant health problem. Genitourinary menopausal syndrome is a hypoestrogenic disorder of morphology and function of the external genitalia. Its manifestations include a wide range of urological and sexual complaints and affect over 50% of postmenopausal women. They are based on urogenital atrophy. Only ¼ of women with genitourinary syndrome share their complaints with a doctor. Surgical, hormonal or radiation castration in the treatment of cancer in young women leads to the rapid onset and development of genitourinary disorders. Early detection and individualized pharmacological and physiotherapeutic treatment is important to prevent the progression of symptoms and to improve quality of life.

Literature review

From the literature review it is evident that Dr. Dobrev has thoroughly and precisely acquainted with the scientific literature on the subject. It is presented on 47 pages, citing 167 sources, mostly by foreign authors. The embryonic development of the female urogenital system, the histological structure and physiology of the vagina are discussed in detail. The changes that occur in estrogen deficiency have been studied. The clinical picture and the frequency of symptoms of genitourinary atrophy have been studied in detail. The pathoanatomical, biochemical and microbiological aspects of atrophic vaginitis in postmenopausal women are presented. Significant place is given to the role of lactobacilli in vaginal microecology. Vascular anatomy and age-related changes in vaginal blood flow in women are discussed. In theoretical and practical aspect, the modern possibilities for treatment of atrophic vaginitis and genitourinary syndrome are presented. These include topical estrogen administration, intravaginal dehydroepiandrosterone, systemic hormone replacement therapy, SERM, Tibulone, Oxytocin gel. Laser therapies are a modern and effective means of treating genitourinary syndrome.

Structure of the dissertation

The presented work has a volume of 122 standard pages. It is illustrated with 16 tables and 14 colored figures. The bibliography includes 167 literary sources, 2 of which are by Bulgarian authors, the remaining 14 are in Russian and 151 in Latin. The topics discussed show the depth of the analysis and emphasize the modernity of the problem. The dissertation is properly structured, its content meets the requirements. The proportion between the individual sections is observed. It includes: literature review - 47 pages, purpose and tasks - 2 pages, clinical material and methods - 30 pages, results and discussion - 21 pages, conclusions - 1 page, contributions - 2 pages, bibliography - 15 pages.

Purpose and tasks

The aim is to study the frequency and various manifestations of the genitourinary atrophy syndrome after surgical and drug (hormonal and chemotherapy) castration. The goal is clearly and precisely formulated, which is a prerequisite for quality work and obtaining adequate results. To achieve it, 8 tasks have been set.

Material and methods

A prospective clinical and epidemiological study involving 67 patients was conducted. The studied clinical contingent has an average age of 40.27 ± 3.90 years in the range of 30-45 years. The main diseases of the studied patients are Ca gl. mammae, Ca ovarii and Ca colli uteri. The patients are divided into two main groups. 35 (52.2%) have surgical castration and 32 (47.8%) have drug castration (chemo and /or hormone therapy). The participants in the study were selected with the help of pre-developed inclusion and exclusion criteria, which are strictly observed. The inclusion and exclusion criteria are clearly and precisely formulated. The research methods and methodology are carefully selected. Various research methods have been used: clinical, hardware, laboratory. The main assessment was made on the basis of vaginal pH; vaginal cleanliness; amount of lactobacilli. A Questionnaire has been developed to assess the frequency of subjective symptoms related to the vaginal component of

genitourinary syndrome in menopause (GSM) - dyspareunia, vaginal dryness and pruritus vulvae after both types of castration (surgical and medical). Indicators of urinary symptoms are also included.

Statistical processing of the results was performed with statistical packages IBM SPSS Statistics 25.0 and MedCalc Version 19.6.3. 9 well-established modern methods for mathematical analysis of the processed results were used.

Evaluation of the results

The obtained results are presented sequentially in a logical order according to the set tasks. For each task the results are analyzed, which is the basis for correct conclusions.

- The first task shows that patients with surgical castration have a higher percentage of missing lactobacilli, while those with drug castration - a normal and reduced amount. Most (65.7%) were participants in the study with vaginal dryness, followed by those with dyspareunia (50.7%). The least patients are without such symptoms - 19.4%, and those with Pruritus vulvae are completely absent. Leading in the subjective symptoms related to the urinary component of the genitourinary syndrome (GSM) in menopause is nocturia with 56.7%, followed by mixed incontinence with 23.9%. Last is the imperative incontinence with 4.5%.
- The second task found that patients with surgical castration have a higher percentage of missing lactobacilli and alkaline vaginal pH, while those with drug castration - normal /reduced amount and acidic pH.
- The results of the third task include the fact that patients with surgical castration have a higher rate of dyspareunia and vaginal dryness, while those with drug castration lack subjective symptoms associated with the vaginal component of genitourinary syndrome in menopause.
- Regarding the urinary component of GSM, studied in the fourth task, it was found that women with surgical castration have a higher rate of nocturia, pollakiuria, imperative and stress incontinence. Those with drug castration have dysuria and mixed incontinence.
- An important result is the prognostic importance of age, type of castration and type of cancer for dyspareunia, vaginal dryness, pruritus vulvae, vaginal pH, vaginal purity and amount of lactobacilli. They are derived according to the fifth task.

- The prognostic significance of the same factors with respect to the urinary component of GSM is presented in the solution of the sixth task.
- On the seventh and eighth tasks a comparative analysis was made between the two types of castration - surgical and medical in terms of symptoms of the two components of GSM - vaginal and urinary. These results, supported by adequate statistical processing, are well illustrated in tables.

Evaluation of the conclusions

The conclusions in the dissertation are 9 in number, and they are accurately and clearly presented according to the results of the study. They are strongly supported by statistical data. The obtained results and conclusions can serve as a basis for the behavior and treatment of genitourinary syndrome after castration due to cancer.

Evaluation of the dissertation contributions

7 contributions are indicated, which are of a confirmatory nature and of an original nature. They reflect the real scientific value of the research done and the results obtained. The contributions have scientific and practical value. They can serve as a basis for an individual approach to reduce the frequency of subjective complaints of patients with genitourinary syndrome and to improve quality of life.

Scientific activity

Dr. Dobrev has participated in a research project and has cited two publications in foreign and two in Bulgarian journals.

Conclusion

The dissertation of Dr. Dobrev is an in-depth and useful study for gynecological science and practice. The complex evaluation of this work gives me grounds to recommend to the esteemed Scientific Jury to award the educational and scientific degree „Doctor” in the professional field „Medicine” in the scientific specialty „Obstetrics and Gynecology” by Dr. Pavel Petrov Dobrev.

Date: June 9, 2022

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Signature:.....

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