OPINION

from

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Department of Periodontology and oral mucosa diseases, FDM, MU - Plovdiv

Appointed by order No. R-109-393/07.09.2023 as a member of a scientific jury in the procedure for acquiring the educational and scientific degree "doctor" in the doctoral program "Therapeutic Dentistry", professional direction 7.2. Dental Medicine

Author: Tsvetalina Ivanova Gerova-Vatsova

Form of doctoral study: regular form of study

Department: Periodontology and Dental Implantology, FDM, MU "Prof. Dr. Paraskev Stoyanov" - Varna

Topic: STUDYING THE RESULTS OF THE APPLICATION OF AUTOGENOUS, PLATELET-RICH PLASMA AT REGENERATIVE THERAPY OF VERTICAL BONE DEFECTS

Supervisor: PROF. DR. STEFAN VASILEV PEEV,PhD

1. General presentation of the procedure and the doctoral student

The review of the documents shows that the procedure for deducting the doctoral student and the procedure for announcing the defense have been followed, the documents have been prepared in accordance with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Rules for its Application and the Rules for the Terms and Conditions for Acquisition of scientific degrees and occupation of academic positions at Medical University - Varna. The PhD student has attached the required three full-text publications.

2. Brief biographical data for the doctoral student

Dr. TSVETALINA IVANOVA GEROVA-VATSOVA graduated in 2017 from the FDM at the Medical University - Varna, acquiring the Master's degree in Dental Medicine. From the same year, she worked as an assistant at the Department of Periodontology and Dental Implantology of the Faculty of Medicine at the University of Varna. In the period 2017-2023, Dr. Gerova specializes in periodontology and diseases of the oral mucosa at the "Prof. Dr. Paraskev Stoyanov" Medical

University, Varna, FDM. In 2019, she was enrolled as a full-time doctoral student at the Department of Periodontology and Dental Implantology, FDM, MU-Varna. In connection with the dissertation, the candidate participated in a scientific project and published 5 full-text articles, 4 of which she was the first author.

3. Relevance of the topic and appropriateness of the set goals and tasks

Vertical bone defects are a serious factor that develops as a result of periodontitis and affects both the determination of the severity of the periodontal disease and the progression of the disease, the complexity of the future treatment and the prognosis of the corresponding tooth. The presence of intraosseous periodontal pockets, persistent over time, leads to the presence of a continuous source of infection, complicating the course of treatment of periodontitis. That is why the treatment of intraosseous defects and vertical bone defects is essential to restore the health and function of the dentition. This treatment requires surgical interventions after achieving control of the inflammation from the initial hygiene phase of periodontal disease therapy, and is subject to regenerative periodontal surgery. A number of materials have been proposed over the years to support regeneration processes and lead to the formation of new attachment, periodontal ligament and bone. This includes barrier membranes, various types of bone replacement materials of autogenous, allogeneic, xenogenic or alloplastic origin. The use of guided tissue regeneration (GTR) with resorbable barrier membranes, as well as the increasingly frequently applied enamel matrix derivatives (EMD), have proven their effectiveness in the regenerative periodontal therapy of intraosseous defects. In recent years, the possibility of applying platelet-rich plasma (PRP) has been increasingly discussed, and the latest recommendations of the European Federation of Periodontology for conducting clinical studies include the additional investigation this possibility for the regeneration of vertical bone defects. Bearing in mind the above, the topic of the current dissertation is extremely relevant and there is a significant need to conduct clinical research in this area. The purpose of the study is clearly formulated and supported by specific clinical tasks to investigate the effectiveness of the application of autogenous platelet-rich plasma in the regenerative therapy of vertical bone defects.

4. Knowing the problem

The literature review for the dissertation is sufficiently voluminous, informative and up-to-date. In its first part, Dr. Gerova consistently examines the theoretical basis of regenerative periodontal therapy. The following pages of the literature review are devoted to the different types of materials – membranes, bone substitutes and enamel matrix derivatives – that are used in the regenerative procedures of intraosseous defects. The advantages and disadvantages of each of them are described in detail, a detailed classification of all types of materials is presented, and the review is supported by a sufficient number of citations of literature reviews and clinical studies examining these materials.

In the second part of the literature review, Dr. Gerova examines the possibilities of CBCT imaging in relation to its application in periodontology. The principles of the CBCT study are described in detail, as well as its advantages over conventional X-ray diagnostics with two-dimensional segmental X-rays. The specific periodontal indications for the use of computed tomography are indicated, underlining clearly that this type of imaging is not a standard in periodontal examination, but rather its supplement.

5. Research methodology

The goal is clearly stated. Although only three clinical tasks were formulated, they represent a sufficient volume of clinical research. The methodology was chosen according to the way of conducting a similar type of clinical research, and one inaccuracy was admitted. Dr. Gerova points out that a reassessment of the patients' condition "after a waiting period of 6 weeks to 6 months" is registered. Data from the literature are controversial regarding the time interval in which surgical periodontal treatment should be applied after the initial one, but all patients are subject to maintenance periodontal therapy, which is carried out for a precisely defined period of time. The intervals of control visits must be specifically defined!

The selected statistical evaluation methods are a prerequisite for the reliability of the conclusions drawn, but a larger set of analyzes could be applied to offer a more detailed evaluation of the results.

6. Characterization and evaluation of the dissertation work

The dissertation is written on 230 standard pages and illustrated with 86 figures and 93 tables and 26 appendices. The literary reference includes 396 literary sources - 6 in Bulgarian and 390 in Latin.
The literature review for the dissertation is sufficiently voluminous, informative and up-to-date.
However, there are some inaccuracies that should be mentioned.
The literature review begins with a definition of periodontitis and a citation of the latest classification of periodontal diseases and conditions from 2017. There is an inaccuracy in the citation of the classification, with the author stating that "The current classification we use today is Caton et al. This statement is inaccurate, as the classification is presented in an article first authored by Jack G. Caton, but is the result of the work of a large team of scientists who are members of the American Academy of Periodontology and the European Federation of Periodontology.
The pathogenesis of periodontitis is described in detail, clarifying the mechanisms of destruction in the periodontal structures, but a significant inaccuracy was admitted in determining the etiological factor. The author states that "microorganisms" are "the only cause of periodontal diseases". Modern concepts of the etiology of periodontal diseases are based on the presence of a dental biofilm with certain characteristics, and the onset of the disease is associated with dysbiotic relationships between the periodontopathogenic representatives of this biofilm and the macroorganism.
The treatment plan for periodontal diseases is consistently presented, but inaccuracy in the parameters determining the success of periodontal treatment is admitted. Dr. Gerova states that "Improvement in periodontal health was observed with reductions in PD, BoP and mobility and increases in CAL." An increase in clinical attachment was more associated with disease progression, while a gain in CAL expressing is in the negative reduction, is a positive clinical criterion. A similar error was made later in the exposition.
In the following parts of the literature review, Dr. Gerova examines vertical bone defects. A significant inaccuracy was made regarding the description of the bone defects. The author mentions the presence of supraosseous bone defects ("there are two types of bone defects: supraosseous (suprabony) defects and infraosseous (infrabony) defects."). This type of bone defects does not exist. In their article, Goldman and Cohen defined the presence of supra-osseous or supra-crestal and infra-osseous or sub-crestal periodontal pockets depending on the location of the bottom of the pocket relative to the alveolar bone margin. Furthermore, in the representation of the intraosseous defects,

the description of the proximal bony walls is omitted, taking into account only the presence or absence of buccal and lingual cortical bone.

At the end of the literature review, there is no concluding part, which would summarize the limitations of the literature data so far and, accordingly, conclude the purpose of the present dissertation work and the need to conduct subsequent research.

After formulating the goal and the two tasks, the dissertation student presents in detail the materials and methods used in the dissertation work. Dr. Gerova applies modern methods of diagnosis and therapy of vertical bone defects.

Among the inclusion criteria for patient selection, the dissertation offers satisfactory personal oral hygiene. It would be better to specify this inclusion criterion by specifying specific bleeding and plaque index values. From the presentation of the selection of patients, it is not clear what the periodontal diagnosis of the patients is, whether it concerns localized or generalized periodontitis, as well as the stage and class of disease progression. In the exclusion criteria, Dr. Gerova indicates uncontrolled systemic diseases, which means that patients with controlled diabetes mellitus could be included in the study. According to modern concepts, the presence of this disease modifies the degree of progression of periodontitis and at the same time influences the course of healing.

In the presentation of the materials, the bleeding index of Animo&Bay, 1975 is presented as the gingival index. This is a significant inaccuracy, since this index does not evaluate the color and consistency of the gingiva, but only the presence of bleeding on probing. The equipment used for scaling and polishing is no better.

Dr. Gerova describes in detail the tests carried out to assess the periodontal status, but it is not clear from the presentation what criteria the teeth subjected to root surface debridement meet. They should be clearly defined.

The methodology does not indicate specific intervals of maintenance periodontal therapy and periodontal status assessment.

Task 1 investigated the effectiveness of platelet-rich plasma (PRP) administration in the regenerative therapy of intraosseous defects. In the task for treated 12 intraosseous defects from 7 patients. The results show a statistically significant reduction in: the depth of probing, the level of clinical attachment, the distance from the enamel-cement border to the bottom of the bone defect (determined on CBCT), the distance from the ECG to the highest part of the bone crest (determined on CVST). These results convincingly demonstrate the effectiveness of the application of platelet-rich plasma (PRP) in the regenerative therapy of intraosseous defects. Regarding the plaque index and the bleeding index, Dr. Gerova reported a statistically significant increase in these indicators 6 months after the operative intervention compared to the baseline data before the operation. It is possible that this is due to inefficiently performed supportive periodontal therapy, since the surgical intervention was performed at a different time interval after the initial hygiene phase for all patients and it was not precisely defined in the task description. In addition, other follow-up visits to the patients (for example, after 1 and 3 months) after the surgical intervention, in which to control the values of the plaque and bleeding and to re-motivate and re-instruct the patients to maintain adequate oral hygiene, were not commented on. . In addition, in the postoperative period, the duration of systemic antibiotic and anti-inflammatory treatment, the duration of mouthwash use, and the other hygiene measures that are recommended to patients are not described. Tables 3 through 18 should be reformatted by combining pairs into one common table that emphasizes the mean, standard deviation, t-value, and statistical significance, rather than presenting them in two separate tables.

My critical notes are similar to the rest of the tasks. In tasks 2 and 3, a statistically significant improvement of the main clinical parameters such as depth of probing and level of clinical attachment, but a deterioration of the parameters assessing the inflammation and oral hygiene of the patients was again established. My comments on the results of these two problems and their tabulation are the same as for problem 1.
In the discussion of the results, Dr. Gerova presented results from a comparative intergroup analysis of the data, which showed no significance between the different types of materials used in the regenerative therapy of vertical bone defects. However, it is clear that the clinical attachment gain was most significant in the group of defects treated with a combination of PRP and membrane (mean 4.5 mm), followed by the groups treated with EMD alone (4.00 mm) and PRP (3.92 mm). The smallest clinical attachment gain was recorded in the group treated with GTR alone (3.84 mm).
The comparison of the obtained results with similar studies in the literature is insufficient, and I recommend that a more detailed analysis of the data be carried out.
The conclusions are reliable and reflect the results obtained from the tasks in the dissertation work. They lead logically to the contributions of the dissertation work.

7. Contributions and significance of the development for science and practice
Specific contributions have been formulated for the three tasks, some of which I accept as original for the country and of a confirmatory nature for the world.
For the first time in the world and in Bulgaria, the application of autogenous platelet-rich plasma in the treatment of vertical bone defects is investigated and the effectiveness of PRP and EMD in the regenerative therapy of vertical bone defects is evaluated clinically and through CBCT.

8. Evaluation of publications on the dissertation work
Dr. Gerova presents 5 full-text publications in connection with his dissertation work. All publications present an overview of the literature on various issues - application of platelet-rich plasma in periodontology, application of barrier membranes in guided tissue regeneration, use of bone-restorative materials in guided tissue regeneration, application of two-dimensional X-ray and CBCT diagnostics in periodontology , and the importance of CBCT diagnostics in periodontology.
I recommend Dr. Gerova to publish his own results of the dissertation work after a detailed statistical analysis.

9. Personal participation of the doctoral student
Dr. Gerova personally participated in the conduct of the clinical studies, the formulation of the results and the contributions from them. During the course of the studies, the dissertation student learns clinical techniques and methods of working with highly specialized diagnostic studies such as CBCT.

10. Abstract
The presented abstract reflects in a synthesized form the structure and content of the dissertation development.

11. Critical remarks and recommendations
The critical remarks and recommendations were presented in the separate points of the opinion as follows - in point 5 regarding the research methodology, in point 6 regarding the literature review,

materials and methods, results and discussion, in point 8 regarding the publications on the dissertation work.

12. Recommendations for future use of dissertation contributions and results

I believe that the doctoral student gives the foundations for evaluating the clinical and paraclinical effectiveness of the regenerative therapy of vertical defects with autogenous platelet-rich plasma. I recommend longer-term follow-up of patients, their inclusion in adequate supportive periodontal therapy, and reporting of the results.

CONCLUSION

The dissertation contains scientific and applied results, which represent a contribution to science and meet all the requirements of the law on the development of the academic staff in the republic of bulgaria, the regulations for its implementation and the corresponding regulations of the MU - Varna. The presented materials and dissertation results fully correspond to the specific requirements of the MU - Varna.

The dissertation shows that the doctoral student Tsvetalina Ivanova Gerova-Vatsova possesses theoretical knowledge and professional skills, demonstrating the qualities of independent conduct of scientific research.

Due to the above and despite the comments and criticisms that I address to the dissertation work, I give my positive assessment of the conducted research, presented by the above-reviewed dissertation work, abstract, achieved results and contributions, and I propose to the honorable scientific jury to award the educational and scientific degree "doctor" of Tsvetalina Ivanova Gerova-Vatsova in the doctoral program "therapeutic dentistry".

10. 11. 2023 г.
Plovdiv

Reviewer: .....
Assoc. Prof. Blagovesta Yaneva, PhD