

OPINION

From Ass. Professor dr. Elena Firkova, PhD, DDS

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Member of the scientific jury with order by the Rector of MU – Varna Prof. V.
Ignatov № P – 109 – 85/ 11.03.2021

Concerning: PhD thesis for awarding an educational and scientific degree
“Doctor”; professional field 7.2 Dental Medicine, PhD program “Oral surgery”.

Theme: Treatment of medication-related osteonecrosis of the jaws with
application of platelet rich fibrin PRF

Author: d-r Rosen Bozhidarov Tsolov

Form of the doctoral study: Self-training in the department “Oral surgery”, FDM,
MU – Varna

Scientific advisor: Prof. Dr. Tihomir Georgiev, DDS, PhD

1. General presentation of the procedure and the candidate

Electronically presented set of documents includes the following:

- PhD thesis;
- A list with the scientific publications, related to the dissertation theme and their copies;
- Curriculum Vitae;
- Application to the Rector of MU – Varna for opening the procedure.
- Declaration for authenticity of the documents;
- Declaration for originality of the PhD thesis, which is not a part of a teams’ project;
- Declaration for Dr. Tsolov registration in scientific data bases – ORCID and Google Scholar;
- Scanned diplomas Dr. Tsolov degrees.

The abstract and the order of the Rector for deduction with the right to defend the Phd: № P – 109 – 85/ 11.03.2021 is presented in paper.

The set of documents is in accordance with Procedure for Acquisition of educational and scientific degree “Doctor” in MU – Varna from 2018 (69:1 and 2).

Dr. Rosen Tsolov graduated with a master’s degree from Faculty of Dental Medicine, MU – Plovdiv in 2005. He has also a master’s degree for public health and health management from 2016. Since 2006 till now he works in the Maxillofacial clinic of UMBAL “Sv. Georgi” – Plovdiv. r. The candidate knows English language.

The dissertation is presented on 180 pages and includes 30 tables and 90 figures. The reference list contains 200 publications, most of them are from the last decade.

2. Relevance of the topic

The frequency of the medication-related osteonecrosis of the jaws (MRONJ) is comparatively low in the world – it affects about 7% of patients on intravenous bisphosphonates and 0.2% of patients with oral administration. However, the tendency is towards an increase based on the the increased number of indications and administration of bisphosphonates, antiresorptive and antiangiogenic medications. And while diagnosing MRONJ is not difficult when the classification criteria of the American Association of Oral and Maxillofacial Surgeons is applied, the treatment is still controversial, without definitive consensus when and how the conservative or surgical treatment should be applied to ensure better treatment outcomes. In this regard, the dissertation thesis is relevant for the scientific community and would be beneficial for fully understanding the mechanisms and treatment options. The application of biologically active growth factors adjunct to the surgical treatment allows for better and faster wound healing in the affected tissues as well as functional rehabilitation of patients.

The PhD thesis is properly structured. It contains the basic acknowledged elements: introduction, literature review, aim and tasks, material and methods, results and discussion, summary, conclusions, contributions, references, and additional documents, related to the studies.

3. Knowledge of the problem

The literature review presents the frequency and etiology of MRONJ, the risk factors and risk classes for patients based on the main systemic disease and the

medication administration, as well as the modern treatment approaches – conservative and surgical – based on the stage of the lesion. There is information about current alternatives/adjuncts – recombinant human parathormone, hyperbaric oxygenation, laser phototherapy and biologically active growth factors. The character, biological effects, and application of platelet rich fibrin in dental practice is also discussed. Its main advantages and disadvantages are discussed, based on the analysis of a significant number of publications.

The literature review is informative and analytical. It finishes with a discussion of unsolved problems and leads to the aim of the study.

4. Research methodology

The aim of the dissertation is well defined – to perform a comparative evaluation of the clinical and radiographic results after conservative and surgical treatment, combined with PRF application in patients with MRONJ. The tasks for it are 4 – logically following the main purpose and enough for a clinical research. Selected materials and methods correspond to the tasks for achieving the goal. They are enough and suitable for statistical analyses and validity of the results, the conclusions, and summaries.

Task #1 is a retrospective study of the frequency of MRONJ among the Bulgarian population for 2015 – 2018. The official data from National Health Insurance system are used. The dissertation would have more value if the author had used the data for complete 2018, not only the first 6 months. The statistical analysis demonstrates an increase in the frequency with almost 9% for the time observed. A higher frequency among patients on ibandronic acid, compared to those receiving alendronic acid was found out.

A huge number of patients diagnosed with MRONJ (237) was included in Tasks #2, 3 and 4, within the time of evaluation – from 2013 to 2017. The inclusion criteria had to be set and described more precisely. The patients had to be randomized in groups based on the MRONJ stage – 2 or 3 (according to the classification system of the American Association of Oral and Maxillofacial Surgeons). The criteria and decision tree, which define the treatment approach had to be determined, depending on the initial clinical and radiographic signs and symptoms.

Task #2 evaluates the characteristic radiographic finding in patients with MRONJ. These parameters include osteolysis and bone loss, bone density, buccal and lingual width of the bone surrounding the lesion immediately after the surgical procedure. Computer tomography is used and the scans are included. I must point out that maybe because of a technical mistake, the author wrote that the method used is orthopantomography.

Task #3 includes a comparative analysis of parameters such as anatomotopographic location of the osteonecrosis lesions, size, dimensions, and intensity of the radiographic image, its homogeneity and eventual presence of sequestrum formation 6 months after treatment. The goal of this evaluation is to observe the long-term results and structural characteristics of the affected areas. The treatment approaches – conservative or surgical, with additional application of PRF membranes in the osteonecrosis lesions are described in detail with many clinical photographs. This is the method, which objectively demonstrates the healing process in the alveolar bone after both treatment modalities.

Task #4 assesses the healing process using some clinical parameters such as hyperemia, swelling, formation of healthy granulation tissue and epithelization. These subjectively evaluated parameters are monitored immediately after the procedure and on days 7, 14, 30 and 90 – only for the extent of epithelization. It was not necessary to monitor these parameters on day 30 – as a rule, the uneventful healing process in the soft tissues would resolve these signs. Instead of them, some other parameters would be used, including restoration of life quality of the patients, using specific indices. The author claims the degree of epithelization in the PRF-treated patients was faster on day 14, while in the group of conservatively treated patients 13% did not show signs of epithelialization.

The results are well interpreted and illustrated by a significant number of tables and figures. The statistical methods used are tailored with for the parameters and the necessary correlations. Each task ends with a discussion of the results and a summary. However, it briefly repeats the results already listed. The final conclusions at the end do not differ from the conclusions after each task – that could be formulated in another way.

5. Characteristics and evaluation of the dissertation and the contributions

The epidemiologic survey on the frequency of MRONJ based on official data comprising a period of 2,5 years is impressive. The detailed surgical protocol, combined with autologous growth factors in the PRF membranes, together with the good quality clinical photographs is another advantage of the thesis. The conclusion, based on the research that patients could benefit from the application of PRF membranes, leading to better treatment outcomes, also has a certain value.

Contributions with original scientific value and applicable to the practice are as follows:

1. The frequency of MRONJ and the correlation with the administered medications among Bulgarian population has been estimated for the first time.
2. The PRF membrane, adjunct to the surgical protocol, has been used and evaluated for the first time.
3. A comparative clinical evaluation for the ability of PRF membrane demonstrating the stimulation of the healing process of soft and hard tissues after surgical treatment of patients with MRONJ has been performed.
4. A comparative radiographic evaluation of the bone density after application of PRF membranes was performed, the results were compared with those in the conservatively treated patients.
5. A 6-months comparative computer-tomography study was performed for evaluation of the alveolar bone condition and density in patients with MRONJ and surgically treated with adjunct usage of PRF membranes.

6. Assessment of the publications and the personal contribution of the PhD-student.

Obviously, the PhD thesis is an original research of the author.

Dr. Tsolov presents 3 full-text published articles. In all of them he is the first author. There is no evidence for citations of the presented articles.

7. The abstract

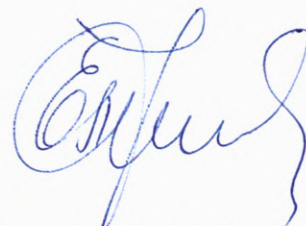
The content of the abstract corresponds to the PhD. It meets the requirements of MU – Varna. It comprehensively represents the dissertation itself.

CONCLUSION

The dissertation named “Treatment of medication-related osteonecrosis of the jaws with application of platelet rich fibrin PRF” with author dr. Rosen Bozidarov Tsolov contains scientific and scientifically applied results, which possesses contribution to the science and meet the requirements of the Regulations of the Law for the promotion of academic scientists in Bulgaria, and the Regulations of MU – Varna.

The dissertation thesis is a proof, that dr. Tsolov has in-depth theoretical knowledge, and professional skills in the specialty “Oral surgery”. He can perform a scientific research and has the skills and knowledge to interpret the results and summarize the scientific data. Based on the arguments stated above, I can offer to the esteemed scientific jury to award the educational and scientific degree” Doctor” to Dr. Rosen Bozhidarov Tsolov in the PhD program “Oral surgery”.

The opinion is prepared by:



8.04.2021 г.

Assoc. Prof. Elena Firkova, Phd, DDS