

REVIEW



From: Assoc. Prof. Dr. Deyan Zdravkov Neychev, PhD, Department of Oral Surgery, Faculty of Dental Medicine, Medical University - Plovdiv, member and chairman of the Scientific Jury, included by order № P-66 / 18.01.2021 of the Rector of MU-Plovdiv

Subject: Dissertation on "*Non-pharmacological strategies for pain and anxiety control associated with local analgesia in children*" for the award of educational and scientific degree "**Doctor of Philosophy - PhD**" in the doctoral program "Pediatric Dentistry", professional field 7.2 Dentistry, higher education education 7. Health and sports

Author: Dr. Elitsa Romanova Veneva-Raichinova, PhD student in self-study at the Department of Pediatric Dental Medicine, Faculty of Dental Medicine, Medical University - Plovdiv, after preliminary discussion by the extended Department Council (ex. № 134/ 17.12.2020) and acceptance by the Faculty Council (ex. № 8/ 21.12.2020) of the Faculty of Dental Medicine of the developed dissertation.

Scientific supervisor: Prof. Dr. Ani Belcheva-Krivorova, PhD

1. General presentation of the procedure and the doctoral student

The presented set of materials on the procedure on paper and electronic media are prepared correctly, complying with the requirements of the Law for the development of the academic staff in the Republic of Bulgaria and regulations of MU-Plovdiv from 06.11.2014 and includes the following documents:

- Abstract, dissertation, publications and documents of the doctoral student - a copy of the publications related to the topic of the dissertation; autobiography; a copy of the diploma for completed Master's degree; copy of diploma for specialty; enrollment order; doctoral minimum exam report; deduction order with the right to public defense; protocol from the Department council with a positive decision on the readiness for defense; declaration of originality; list of publications related to the topic - 3 publications; declaration of authenticity of the submitted documents.

Dr. Elitsa Romanova Veneva - Raichinova was born on May 1, 1988 in the town of Kyustendil. She graduated from high school in 2007 at the Plovdiv Language High School with intensive study of German and English. In 2013 she graduated from the FDM of MU-Plovdiv, and in 2017 through a competition she was selected as a full-time assistant in the Department of Pediatric Dentistry at the FDM of MU-Plovdiv, where she still works today.

Dr. Veneva participates in the teaching of students in Bulgarian and English. She speaks English and German with level C1.

2. Topicality of the dissertation

Pain control in dentistry and in pediatric dentistry in particular is a serious challenge. In 1975, the IASP (International Association for the Study of Pain) adopted a definition that corresponded to Descartes' vision and rehabilitated his understanding of the brain-body relationship. The definition adopted by the IASP was made in 1964 by Merskey in defense of a doctoral thesis. He describes pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or an experience described in connection with such damage." The IASP definition avoids linking pain to a specific stimulus. Knowledge of the mechanisms of pain provides many methods and tools for its control, which is especially important in the treatment of children.

In 1965, Ronald Melzack and Charles Patrick Wall proposed a theory that was revolutionary for the study of pain - the "Gate control theory". The model presented by the two authors suggests that the signals originating in the main afferent elements of skin stimulation are transmitted to three areas in the spinal cord: SG, the dorsal column, and to a group of cells called transmission. According to the authors, the portal in question in the spinal cord is Substantia gelatinosa in the posterior horns, which modulates the transmission of sensory information from the main afferent neurons to the transmission cells in the spinal cord. This portal mechanism is controlled by the activity of thick and thin fibers.

In addition, there are structures in the brain that have an antinociceptive effect. The areas of the brainstem involved in reducing pain are two: the gray matter around the aqueduct (PAG) and the nucleus raphe magnus (NRM). The key neurotransmitters involved in downward suppression are two: norepinephrine and 5HT (serotonin). The establishment of a phenomenon such as "central sensitization", first described in 1983 by Clifford J. Woolf, changed the perception of pain as a peripheral reaction and gave it a central character. Central sensitization is a persistent post-traumatic change in the CNS that results in hypersensitivity to pain.

In recent years, based on improving knowledge of the anatomical structures and mechanisms associated with the emergence, conduct and suppression of pain perception, many methods and tools have emerged for improved control of pain - preemptive analgesia, and several innovative products for dental use have been developed based on of this theory - Accupal, DentalVibe, Vibraject and others. Their action is expressed in the principle of masking the pain of the needle penetration by applying pressure, vibration, microoscillations or a combination thereof.

There is a wealth of literature data based on clinical trials that defines the hypothesis that vibration from devices not only relieves needle puncture pain, but could also reduce infiltration pain by physically facilitating the distribution of anesthetic fluid.

The study of DentalVibe as a new non-pharmacological agent for achieving painless local anesthesia, as well as the application of laser preemptive analgesia, are pain control agents with a relatively small number of clinical trials.

These data define the topic of the dissertation as relevant and significant. Knowledge of non-pharmacological techniques for pain control, especially in childhood, is particularly important in this era of a quiet epidemic of allergic reactions to many pharmacologically active agents.

3. Knowledge of the problem

In her dissertation, Dr. Elitsa Veneva demonstrates in-depth knowledge of the developed topic. The literature review is presented on 37 pages. The doctoral student has made a thorough review of the literature related to the various means and methods of pain control. An in-depth review of the recommendations of the European (EAPD) and American Academy (AAPD) in Pediatric Dentistry from 2017 and 2007 is made.

The **literature review** provides up-to-date data on the problem under consideration, as over 50% of the authors are from the last 10 years. This determines the dissertation's awareness of the problem and directs the research in the right direction.

After the critical analysis of the literature, the dissertation has formulated the unsolved problems in the last part of the literature review.

The aim of the dissertation, developed by Dr. Veneva, is precisely and clearly formulated, namely: "to study the possibilities for non-pharmacological management of pain and anxiety associated with local analgesia in pediatric patients."

The realization of the set goal is achieved by performing five set tasks, as the fourth task has two subtasks.

The defined **objectives** are: Study of the effectiveness of the DentalVibe device for reducing anxiety and pain during local infiltrative anesthesia in pediatric patients; Study of the efficacy of a virtual reality device for reducing anxiety and pain during local infiltrative anesthesia in pediatric patients; Comparison of the efficacy of two non-pharmacological methods for distraction - through DentalVibe and virtual reality, to reduce pain and anxiety during local injection anesthesia (LA) in childhood; Study of the possibility of photobiomodulation with Er: YAG laser to achieve safe

preemptive laser analgesia in pediatric patients; Development of recommendations for non-pharmacological control of pain and anxiety associated with local analgesia in dental patients in childhood.

4. Methodology of the investigations

The **methods** used by Dr. Veneva are aimed at each of the set objectives. The inclusion criteria for patient selection are described in detail, as well as the methods used to obtain statistically reliable results.

Task 1: The subjects of the study are 41 children aged 8 to 12 years and they must meet certain inclusion criteria.

Task 2: The subjects of the study are 40 children aged 8 to 12 years.

Task 3: The objects of observation, as well as the inclusion and exclusion criteria are identical to the first two tasks.

For tasks 1, 2 and 3, a visual analog scale (VAS) was used, consisting of a Wong-Baker FACES scale with facial expressions and a nominal scale (0 - 10). To assess subjective anxiety during local anesthesia, the Facial Image scale (FIS) was used - self-assessment using a picture scale with faces. The dynamics of the heart rhythm was also registered - by using a pulse oximeter.

Self-assessment of dental fear was investigated using a questionnaire before each visit - a dental subscale of the scale for assessing children's fear - Dental Subscale of Children's fear Survey Schedule (CFSS-DS), consisting of 15 questions related to various aspects of dental treatment, including fear of injections.

Task 4: This task is divided into two subtasks, considering two important aspects: Study of the morphology of the enamel surface after laser analgesia with Er:YAG - study of a scanning electron microscope and study of the efficiency of a modified protocol with Er:YAG laser to achieve of preemptive laser analgesia in pediatric patients.

Task 5: Development of recommendations for non-pharmacological control of pain and anxiety associated with local analgesia in dental patients in childhood. An overview and acquaintance with the state of the discussed problems in a number of countries worldwide was made.

Impressive is the extremely systematic and detailed description of the methodology of the clinical protocol for each task, which provides control at each stage of the study and repeatability of the study.

The systematization, processing and analysis of the primary data in the form of quantitative and qualitative variables is realized with the statistical package of the software for social sciences IBM SPSS Statistics v. 22. A significance level of $p < 0.05$ was assumed for all tests. The graphical analysis was performed in the environment of MS Office 2013 using Excel.

Results

The results of the first task show that after successful completion of both manipulations - control and experimental, patients were examined for their preference for a method of analgesia - traditional or DentalVibe-assisted injection (DV). Of the patients studied $n = 34$, most prefer analgesia accompanied by the DentalVibe device - 85.3%.

The results of the second task show that of the studied patients $n = 32$, most prefer analgesia accompanied by VR-device - 71.87%. There was no statistically significant difference between the first, third and fourth time points - in terms of heart rate. Hierarchical multiple regression established relationships between heart rate and "subjective pain during LA" and subjective anxiety according to FIS at the first visit.

The results of the third task - of the studied patients $n = 67$, most (82.5%) prefer analgesia, assisted by one of the two applied non-pharmacological methods.

Fourth task

First subtask - It can be concluded that the laser settings of 0.75 W/ 15 Hz / 50mJ/ 12 J/cm² and greater can be considered ablative from a distance of 10 mm even with a maximum water spray.

Second subtask - When placebo analgesia was administered at the first visit, the model was found to be statistically significant. When using laser preemptive analgesia at the second visit, the measured mean heart rate differed statistically significantly between the four time points.

The results of the fifth task

Recommendations have been made to: parents, dentists, professional organizations and to the faculties of dentistry.

The presented results are thoroughly discussed. The demonstrated systematics of the scientific search can be highly admired, as well as the illustration of each of the tasks.

The material used is sufficient to obtain statistically reliable results. The methodologies are correctly selected and focused on each of the set tasks. All this provides a solution to the problems defined in the dissertation.

5. Characteristics and evaluation of the dissertation

Dr. Veneva's dissertation is properly structured, containing all the main elements for presenting a dissertation: content, abbreviations used, introduction, literature review, purpose and tasks, material and methods, results and discussion, summary, conclusions, contributions, bibliography and applications. The presented dissertation is written on 193 pages. It is illustrated with 17 tables, 37 figures and 7 appendices. The bibliography includes 214 literary sources, of which 16 in Cyrillic and 198 in Latin. The exhibition is presented accessible and concise.

Own research and discussion are 105 pages long. The results are accurately and correctly described, fully analyzed with subsequent interpretation and illustration with tables and figures. A discussion of each task is made, as the author compares the results obtained by him with data from the literature. The performed critical analysis allows Dr. Veneva to evaluate the used methods and to define four generalizing conclusions. The formulated conclusions correspond to the set goals and objectives.

6. Contributions and significance of development for science and practice.

3 groups of contributions are presented:

Scientific-theoretical contributions - the effect of laser settings used for preemptive laser analgesia with Er: YAG on the surface morphology of the enamel by scanning electron microscopy is studied, determining laser parameters for laser analgesia that do not damage its integrity.

Methodological contributions - For the first time in the world, a methodology of a clinical protocol for preemptive laser analgesia is being developed, which has been proven to be safe, reproducible and publicly available before the results of the study are published.

Scientific and applied contributions - For the first time in our country the possibilities for non-pharmacological influence of pain and anxiety during local anesthesia through vibrotactile device and virtual reality are proved, without establishing superiority of one method over the other, which allows the clinician the choice to the appropriate means to the patient.

Recommendations for non-pharmacological control of pain and anxiety related to local analgesia in dental patients in childhood have been developed, aimed at parents, dentists and institutions responsible for the oral health of children in Bulgaria.

7. Evaluation of the dissertation publications

Dr. Veneva presents three publications related to the dissertation, which fully cover the legal requirements. The dissertation also has 11 participations in Bulgarian and international forums, where she is a leading author.

8. Personal participation of the doctoral student

The conducted research and observations of patients and the subsequent results, conclusions and contributions in the dissertation are the personal work of the author.

9. Abstract

The content and quality of the author's abstract corresponds to the developed work and is made according to the requirements of MU-Plovdiv. It has the following parts: introduction, purpose and tasks, materials and methods, results and discussion, conclusions, contributions and publications related to the dissertation. It reflects the main results achieved in the dissertation, the conclusions and contributions, publications and scientific reports in Bulgarian and international congresses.

CONCLUSION

The dissertation submitted to me for review **meets the requirements** of the Law for the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for its implementation and the Regulations of MU - Plovdiv.

The dissertation shows that the doctoral student Dr. Elitsa Romanova Veneva - Raychinova has theoretical knowledge and professional skills in the scientific specialty "Pediatric Dentistry". After the analysis, I give a **positive assessment** for a dissertation on "*Non-pharmacological strategies for control of pain and anxiety associated with local analgesia in children*" and will vote "yes" for the award of educational and scientific degree "Doctor of Philosophy - PhD" in the scientific specialty "Pediatric Dentistry" **by Dr. Elitsa Romanova Veneva - Raychinova.**

Plovdiv

Assoc. Prof. Dr. Deyan Neychev, PhD

20.01.2021

