

ANNOTATION

on PhD thesis of Dilbarkhanov Bassymbek entitled «Peculiarities of dental implantation to patients with post-menopausal osteoporosis» presented as an application for PhD degree on the specialty «6D110100–Medicine»

Relevance of the research topic.

In modern conditions, dental implantation continues to be the best method for stomatological rehabilitation of secondary adentia patients to recover their chewing function and aesthetics (Kulakov A.A., 2011; Timofeyev A.A., 2012; Temmerman A., 2017; Weitzmann M.N., 2016; Albrektsson T., 2005; Szymanska J., 2007). At the same time, in order to extend the indications for conducting dental implantation, the problem of reducing the risk of developing complications becomes relevant. According to the research data (Hao L., 2017; Chen H., 2013; Guiglia R., 2013; Temmerman A., 2017; Palattella P., 2008), among the most important causes of complications are the presence of general somatic pathology in patients.

According to the results of the carried on studies (Dvorak G., 2011; Yuan Y., 2020; Siebert T., 2015; Gao A., 2020), the causes of rejection of dental implants are often unexplained, especially in the older age group and more often in women.

According to the World Health Organization, osteoporosis is considered to be one of the most important health problems, ranking fourth in its importance after cardiovascular diseases, cancer and diabetes mellitus (WHO, 2016).

It has been found out (Lee J.W., 2019; Brown B.N., 2017) that at the early stages of its occurrence osteoporosis has asymptomatic course; generally, women do not complain and feel themselves “practically healthy”, i.e., they do not fall into the group where dental implantation is contraindicated. However it is in these patients that an unforeseen dental implant rejection may develop due to post-menopausal osteoporosis, which can affect their osteointegration in the bones of the jaws.

It is known that osteoporosis is a disease of multiple-factor nature, the frequency of which increases with ageing. Human life expectancy in the 21-st century becomes higher, resulting in increasing the number of people in the older age group with a predominance of the female population with an active working life. Furthermore, the hypoestrogenia that occurs in their menopause causes an intense loss of bone mass due to the reduction of the mineral component and the protein matrix. Along with other manifestations of osteoporosis, women in the post-menopausal period often have the secondary adentia with various degree of manifestation of the alveolar bone atrophy, which significantly impairs the quality of patients' life (Garcia-Fernandez L., 2018).

The above stated data suggest that implants rejection may be associated with the systemic disorders of bone tissue metabolism and, in particular, with the developing post-menopausal osteoporosis, where the pathological changes also occur in the bone tissue of the jaws in the form of the increased resorption, osteopenia and osteoporosis.

It is a proven fact (Brankston G., 2007; Laheij A.M., 2012; Grisa A., 2018) that applying dental implants is the best overall opportunity for further high-quality

stomatological prosthetics. The high rate of patients needing the assistance of an orthopaedic dentist indicates the necessity for improvement of this type of stomatological care. In this regard, the wider application of technical and constructive possibilities provided by modern dental implantology as well as one of the progressive methods of eliminating the defects of dentition is a current method to improve dental care for the population, including patients with post-menopausal osteoporosis.

The availability of the above-mentioned pathogenetic mechanisms and the probability of developing osteoporosis in patients with post-menopausal osteoporosis require a thorough examination as a part of the pre-operative preparation prior to surgery.

Unfortunately, there is no systematized source of information on the stomatological status of post-menopausal osteoporosis patients during the dental implantation. Thus, for the development of possible complications, it seems extremely important to develop tactics of pre-operative and post-operative care of patients with this type of pathology before dental implantation, which determined the need for this research.

The objective of the thesis is:

to increase the efficacy of dental implantation osteosynthesis in the post-menopausal osteoporosis patients.

Subjects of the study:

-patients with post-menopausal osteoporosis with indications to dental implantation;

-retrospective analysis of medical (stomatological) documentation.

Units of observation:

- for determining the structural and functional state of bone tissue in women at the post-menopausal period, 144 women, who applied for dental aid to the Department of Internship on Stomatology of NJSC « S.D.Asfendiyarov KazNMU » and the Dental Clinic «Stóminvést and K» were chosen. Among them 59 women between 25 and 68 years of age completely met all selection criteria according to cross-sectional study data;

- for the analysis of archival materials, medical documentation of 4395 patients consulted and examined at the dental clinic of the S.D.Asfendiyarov Kazakh National Medical University and at the StomInvest & K Dental Clinic LLP for the period from 2018 to 2019 was selected.

-for the pre-operative examination of patients, 60 patients, who applied for dental aid to the Department of Internship on Stomatology of NJSC « S.D.Asfendiyarov KazNMU » were selected.

-for clinical studies 100 patients, who applied for dental aid to the Department of Internship on Stomatology of NJSC « S.D.Asfendiyarov KazNMU » and the Dental Clinic «Stóminvést and K» were selected.

The amount of analyzed information material is 2 monographs, 5 dissertations, 6 textbooks and textbooks, 2 analytical reports, 6 methodological recommendations of the WHO and the Ministry of Health of the Republic of Kazakhstan, 137 scientific articles in English.

The object of the research is the studying of osteointegration processes in patients with post-menopausal osteoporosis, depending on the degree of bone tissue mineralization.

Place of study: Department of Dental Internship on stomatology, Dental Clinic of the NJSC “ S.D.Asfendiyarov Kazakh National Medical University » and LLP «StomInvest and K” Dental Clinic» (Almaty).

Research objectives:

1. to study the informative value of diagnostic study methods in the planning and implementation of dental implantation in post-menopausal osteoporosis patients.

2. to evaluate the metabolism and bone density of the jaws in patients with post-menopausal osteoporosis according to laboratory studies, ultrasonic densitometry, X-rays and conus-radial computed tomography (CRCT).

3. to substantiate the criteria for selecting the post-menopausal osteoporosis patients for dental implantation.

4. to develop a surgical protocol for dental implantation in post-menopausal osteoporosis.

5. to evaluate the efficacy of osteointegration and indicators of stability of intra-bone implants at the stages of dental implantation in patients with post-menopausal osteoporosis.

Methods of the study:

-basic (survey, inspection, probing, percussion, palpation);

-additional (oral hygiene index)

-special (X-ray, orthopantomography, CRCT, periotestometry, densitometry);

-laboratory tests (biochemical analysis of blood and urine with determining specific markers of bone tissue formation and resorption);

- statistical analysis with elements of evidence-based medicine.

Key findings of the study.

1. The literature review has shown that dental care is considered to be one of the most demanded and mass medical activities due to the high incidence of major dental diseases. Practically, up to 70-90 per cent of children and 100 per cent of adult population suffer from the certain dental diseases. In the adult population, the incidence of dental problems is 95.0-96.0 per cent, and in the age groups over 35, the incidence of dental problems takes the first place with the need for prosthodontics reaching 60-100%. As of 2018, there were 1,817 dental organizations operating in the Republic of Kazakhstan, of which: 596 (33%) have a state form of ownership and 1,221 (67%) have a non-state form. Compared to the previous years, the number of State-owned organizations has increased by 10 per cent as a result of the opening of new dental units in schools and in rural areas, which is the evidence of the growing accessibility to dental care by the general population, especially dental implantology.

2. The results of the analysis of the medical records from the archive materials showed that the majority of those who need dental aid (74.1 per cent) were persons between 41 and 60 years of age. Dental implant treatment was rendered to 916 patients, accounting 20.8%.

The analysis of dental implantation results for various types of jaw bones architectonics showed that in patients with osteoporosis between 1.5 and 10 years or more after the operation of intra-bone implantation, only 66% of implants remained functional, while in cases of normal type of jaw bones architectonics, the efficacy of implantation was 95%. A study of the influence of the degree of mineralization on the processes of osteolysis in the peri-implant zone has shown the following: the smallest dimensions of vertical and horizontal gum line osteolysis were observed in patients with a decrease in mineralization of not more than 30% of the physiological norm.

Thus, in women in the post-menopausal period, against a plausibly higher remodeling of bone tissue (osteocalcin: $p = 0.005$, β -CTx: $p = 0.002$), there is observed the increased destruction of the alveolar process of the upper and lower jaws, but the changes were statistically unreliable against the background of a statistically significant and reliable increase in the level of Ca ($p=0.009$).

3. Our dental examination showed that the average PGA index was 24.2 ± 1.5 in Group I, 22.9 ± 1.8 in Group II and 15.7 ± 1.2 in Group III. Thus, the intensity of caries was 1.5 times higher in osteoporosis patients than in somatic healthy individuals ($p < 0.05$).

According to the results of the X-ray study, in 23 (79.3%) patients with systemic osteoporosis of group I, a IV type of bone tissue was observed (figure 18), as the area of tooth defects had a thin cortical layer and loose sponge bone. In 13.8% of the cases, the bone tissue of the alveolar processes was of the III-d type of bone tissue where a thin compact layer covered a sponge layer of sufficient density. In 6.9% of the cases, the bone tissue of the alveolar processes matched the II type of bone tissue - when a thick compact layer and a dense sponge bone were preserved.

In processing the information, CT studies showed that the average height of bone in the suspected implantation sites in patients with osteoporosis in Group I was 10.1 ± 0.9 mm, and in Group II - 12.2 ± 1.1 mm. In group III (control) patients, it was definitely higher - 13.6 ± 0.7 mm ($p < 0.05$). The following data were obtained from the linear densitometry of the image with the calculation of average values: the optical density of the sponge substance of the alveolar processes in patients of group I was 150.20 HU. (Hounsfield units), which indicated a low-mineralized bone tissue in the jaws, with patients in Group II having 234.85 HU. Patients in Group III have 428.150 HU. Thus, despite the wide variation in the indicators within the examined groups, the data show a decrease in the quantity of bone substance in the units of volume in patients of Group I and II, and a change in the quality substance of bone i.e. ratio of organic and mineral components.

The analysis of the results of the ultrasound densitometric study revealed a significant variation in the indicators within the examined groups. The results obtained from patients with osteoporosis in Group I revealed that the rate of sound waves was reduced on average by 41.6% compared to a group of persons without systemic pathology of bone tissue. In patients with osteoporosis of group II, the average echodensity of bone tissue was lower by 31.1% compared to the group of persons without systemic pathology of bone tissue. The obtained data show a decrease in the quantity of bone substance of the jaws in the units of volume of

osteoporosis patients and a change in the quality of the bone substance - the ratio of organic and mineral components.

Biochemical studies have shown that in patients with osteoporosis of group I, the concentration of oxyproline in daily urine was 32.8 ± 2.6 ng/day, and in patients of group II was 29.4 ± 2.2 ng/day, which exceeded the normal values. In group III patients, the level of oxyproline was within the normal parameters of 22.4 ± 2.1 ng/day. In 5 patients of group I (33.3%), the activity rate of bone alkaline phosphatase was within the normal range, in 4 ones (26.7%) - a decrease in this index and in 6 (40.0%) of the examined ones - an increase were marked. In group II, 18 people, or 81.8%, had a decrease in alkaline phosphatase activity. In the remaining 4 examined patients (18.2%) the alkaline phosphatase activity in this group was within the normal limits. In Group III, the activity of bone alkaline phosphatase in all patients was within the normal limits.

4. We have developed a clinical protocol that is designed for type IV bone with weak mineralization of bone tissue. This clinical protocol describes step by step each stage of dental implant installation. In addition, a method for installing dental implants in menopausal osteoporosis has been developed.

Dynamic examination of patients with dental implantation with post-menopausal osteoporosis showed that 72 (93.5%) of the installed dental implants achieved the primary stability, 5 dental implants showed the results of «Periotest S» within the limits from +10 to +19. The data from the «Periotest S» apparatus showed that 73 (94.8%) dental implants had stability in terms from -08 to +07 (stable). At the same time 2 (2.6%) ones showed +14- +19 that was considered as slightly mobile. 2 (2.6%) dental implants showed +28-+29, that was evaluated as significantly mobile. An analysis of the stability of the dental implants six months after the surgery showed that in the compared group I 29 (93.5%) dental implants had the values of periotestometry from -08 to +7, which indicated the stability of the given dental implants. Meanwhile in this group 2 (6.5%) dental implants had values +43 - +49, indicating a lack of stability of the dental implants. The data from the compared group II showed that 23 (92%) dental implants reached strong osteointegration of -08- +07. The index in one (4%) dental implant was +12, which corresponded to the index of «slightly mobile». Besides one (4%) dental implant showed the value of +46, indicating that there was no osteosynthesis of the dental implant with the bone.

In the examined patients of the control group the results of periotestometry were found from -08 to -06, indicating strong osteosynthesis in 21 dental implants (100%, which is determined by the number of dental implants applied in this group). The results of group I (group of comparison 1) showed between -08 and +09, indicating strong osteointegration in 29 dental implants (93.5% which is pointed out by the number of dental implants applied in this group), the osteointegration was not revealed in 2 dental implants with the values of +46 and +48 (6.5% which is indicated by the number of dental implants applied in this group). The results of group II (group of comparison 2) showed between -08 and +09 in 24 dental implants (96% which is indicated by the number of the applied dental implants in this group). One dental implant showed a result of +33, indicating no osteointegration.

The results of the dental implant placement study showed that the use of a new surgical protocol and a method for installing dental implants improved both the results of primary stabilization of the dental implant and the integration of the dental implant with the bone tissue of the jaws in patients with postmenopausal osteoporosis and the quality of life in general.

Scientific novelty.

The scientific novelty of the study is that for the first time:

-the priority and informative value of diagnostic study methods for dental implantation in post-menopausal osteoporosis patients has been determined;

-the regularity of the osteointegration of dental implants, depending on the degree of mineralization of the bone tissue of the jaw in post-menopausal osteoporosis has been proved;

-the quality of the primary stabilization, taking into account the conjunction of the surfaces of the bone bed and the implant of the teeth at various degree of the osteopathy of the jaws has been studied;

- a surgical protocol for dental implantation and a method for installing dental implants in patients with postmenopausal osteoporosis have been developed;

-the recommendations for the improvement of surgical stomatological aid in dental implantation in post-menopausal osteoporosis have been scientifically grounded.

Statements of the thesis to be defended:

1. Effective dental implantation in post-menopausal osteoporosis patients requires an inter-disciplinary approach (cooperation of a dental implantologist, gynaecologist, endocrinologist, orthopaedic dentist, parodontologist) and the application of modern principles for functional and aesthetic rehabilitation.

2. In the development of complications during dental implantation in patients with postmenopausal osteopathy, the induced factor is the low bone density - less than 500 HU on the Haunsfeld scale.

3. For improving the osteosynthesis process, post-menopausal osteoporosis patients should use dental implants with aggressive thread and thin stem. In this connection the creation of a 1 mm smaller bed for the implant than the dental implant itself is of importance.

Practical importance of the obtained results.

The author defines the methodical approaches to the study and justification of rational planning and implementation of dental implantation in patients with post-menopausal osteoporosis. The factors influencing the osteointegration of dental implants, depending on the degree of mineralization of bone tissue of the jaws, which is a significant contribution to the theory of dentistry were revealed.

The practical significance of the study is that the results of the study, obtained on a large clinical material, proved the necessity of developing a special surgical protocol of dental implantation and method of installing dental implants for patients with post-menopausal protocol, which is of great importance for determining the precise treatment tactics and for the timely application of modern technologies in stomatology. The factors influencing the primary stabilization and osteosynthesis of

dental implants, allowing practical dentists- implantologists to increase the efficacy of treatment and the quality of life of patients with tooth defects have been determined

Compliance with scientific development directions or State programs.

All the results presented in the dissertation work and having scientific novelty were obtained by the author personally. The author participated as an operator or assistant in operations, the results of which were then evaluated using clinical laboratory and instrumental research methods. Under the scientific guidance of consultants, he developed a method for installing dental implants and an algorithm for the diagnosis and management of patients with dental implants against the background of postmenopausal osteoporosis, which were introduced into the practice of dental clinics "Stominvest and K" (Almaty), Schools of Dentistry Asfendiyarov KazNMU, «Dental City» LLP (Almaty), Educational and Clinical Center "Dentistry" LLP (Nur-Sultan).

A PhD student's personal contribution.

All the results presented in the thesis, which have scientific novelty, were obtained by the author personally. The author participated as an operator or assistant in operations, the results of them were then evaluated with the help of clinical laboratory and instrumental study methods. Algorithm of diagnostics and management of patients with dental implants against the background of postmenopausal osteoporosis has been implemented into the practice of stomatological clinics «Stominvest and K» (Almaty city), School of Dentistry of NJSC « S.D. Asfendiyapov KazNMU », LLP «Dental City» (Almaty), LTO «Teaching Clinical Centre «Stomatology» (Nur-Sultan city).

Approbation of thesis results.

The main materials of the thesis were presented at the International Scientific and Practical Conference on Current Medical and Pharmaceutical Problems, dedicated to the 40th Anniversary of the South Kazakhstan Medical Academy, in Shymkent, Kazakhstan, from 11 to 12 October 2019; at the International online conference «Modern Dentistry: from Science to Practice», December 10, 2020, Turkestan, Republic of Kazakhstan; at the International scientific-practical online conference «Trends in dental implantology and aesthetic dentistry: experience of mentors and perspectives of young specialists» November 21, 2020, Tashkent, Republic of Uzbekistan; at the International scientific-practical conference dedicated to the memory of Professor Akanov A.A., September 25, 2019, Almaty, Republic of Kazakhstan; at the meeting of the Department of Internship on Dentistry, Almaty, February 3, 2021; and at the meeting of the Scientific Commission on Dentistry of S.D. Asfendiyarov KazNMU, Almaty, June 2, 2021.

Conclusions.

1. A literature review has shown that dental care is one of the most popular and widespread types of medical activity, due to the high prevalence of major dental diseases. The conducted studies have clearly demonstrated the possibilities of an interdisciplinary approach in solving the problems of modern implantology concerning patients with concomitant pathology.

2. Based on the conducted research, there is a direct relationship between the degree of mineralization and calcium content with the processes of osseointegration

and the size of cervical osteolysis. In this regard, it can be concluded that the degree of mineralization and calcium content in the bone tissue of the jaws in the preoperative period are the criteria for the prognosis of dental implantation.

3. Our dental examination showed that the average value of the CPI index was 24.2+1.5 teeth in group I, 22.9+1.8 in group II and 15.7+1.2. Thus, in patients with osteoporosis, the intensity of caries was 1.5 times higher than in somatically healthy individuals ($p<0.05$).

4. We have developed a clinical protocol that is designed for type IV bone with weak mineralization of bone tissue. This clinical protocol describes step by step each stage of dental implant installation. In addition, a method for installing dental implants in patients with postmenopausal osteoporosis has been developed.

The results of the clinical experiment of dental implants installation showed that the use of a new surgical protocol improved the results of primary stabilization of the dental implant, which in turn improved the integration of the dental implant with the bone tissue of the jaws of patients with postmenopausal osteoporosis, thereby improving the quality of life of these categories of patients.

Practical recommendations.

1. Predicting an increased risk of complications in the surgical and postoperative period in patients with postmenopausal osteoporosis after dental implantation surgery according to the surgical protocol proposed by us allows to achieve primary stabilization of the dental implant during surgery and will improve the conditions for the integration of the dental implant into the bone tissue of the jaws.

2. In patients with postmenopausal osteoporosis, it is necessary to determine the density of bone tissue in the area of planned dental implantation.

3. The application of the proposed clinical protocol and the method of installing dental implants in dental clinics, especially in the surgical office, will contribute to the qualitative rehabilitation of patients with postmenopausal osteoporosis.

4. It is advisable to use the CBCT method for planning and determining the quality of jaw bone tissue. Planning of the final orthopedic design before the installation of dental implants. The use of the Periotest device to determine the integration of the dental implant with the bone tissue of the jaws before prosthetics.

5. For dental implantation in patients with postmenopausal osteoporosis, we propose the involvement of endocrinologists and gynecologists for the purpose of high-quality dental rehabilitation of this category of patients.

6. We recommend the curation of patients with menopausal osteoporosis who have had dental implants installed with subsequent dental rehabilitation throughout their lives.

Publications.

On the topic of the thesis research the 4 scientific papers have been published, among them one paper -in the international peer-reviewed journals included in the Scopus database (percentile 60). Methodological recommendations were developed on the topic «Analysis of dental care in Republic of Kazakhstan» and author's certificate has been got.

Volume and pattern of the thesis

The thesis is presented on 141 pages of typewritten text and includes the introduction, the chapter «Review of literature», the chapter «Material and study methods», the chapter «Results of own studies», the conclusion, findings, practical recommendations and the list of literature. The research is illustrated by 47 pictures and 29 tables. The Bibliography includes 186 sources.