The Influence of Mesodiencephalic Modulation on the Course of Postoperative Period and Osseointegration Quality in case of Intraosseus Dental Implantation

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Abstract

Objectives: A favorable character of the early postimplantation period progression largely determines the success of the ongoing orthopedic treatment. The aim of our study was to assess the effectiveness of MDM-therapy after dental implantation to prevent inflammatory complications, improve osseointegration quality and increase the installed implant stability.

Method: Despite the presence of articulated ideas about the surveillance of patients undergoing dental implantation, incidence of infectious complications, occurring after the operation, as well as the absence of full-fledged osseointegration in some cases, forced practitioners to resort to additional measures that increase the clinical results of the treatment. Our attention was drawn by mesodiencephalic modulation method and its possibilities regarding the optimization of the recovery period and stimulation of internal resources of the patient. Scientific-experimental and clinical laboratory methods are the key ones of the present study. Findings: We have compared early and late clinical and laboratory findings of dental implantation in two patient populations (with MDM-therapy and without applying additional therapy in the postoperative period); some patients have experienced an increased gag reflex, which excluded the possibility of using a removable prosthesis. The obtained data were analyzed by mathematical processing with the determined minimum, maximum and average values of the defined indicators and comparison of the results in the two samples. An idea about the factors influencing the postoperative course of dental implantation and the quality of early and late osseointegration was formed. A dynamic assessment of clinical and laboratory parameters characterizing the inflammatory response after implantation in patients who received standard postoperative therapy and the standard treatment combined with the MDM-therapy was carried out. We have measured the performance of early and late stability of the installed dental implants in patients who received various models of accompanying therapy. Application/Improvements: Conclusions have been formulated about the MDM-therapy appropriateness in early postimplantation period for preventing inflammatory complications and increasing stability of the installed dental implants.

Keywords: Complications, Dental Implantation, Gag Reflex, Immunocompetence, Implant Stability, Inflammation, MDM-therapy, Mesodiencephalic Modulation, Orthopedic Treatment with PEEK, Osseointegration, Phagocytic Activity, Stress

1. Introduction

In modern orthopedic practice intraosseous dental implantation has been used successfully for the recovery of single dentition defects, as well as for partial and complete secondary edentia as a baseline correction method. It can be said that the success of the surgical phase is largely determined by the final result of orthopedic treatment, since the functionality, reliability and durability of the selected prosthetic design depends on the quality of osseointegration and survival of the installed implants.

The main factor that directly affects the viability of
implantation, on behalf of the specialist, is an adequate choice of surgical techniques and materials, while for the patient the postoperative progression and survival rate of the implants are determined by the intensity of non-specific inflammatory response due to surgical stress and also by the immune status, level of basic metabolic and regenerative processes and other individual characteristics, including the presence of comorbidity.

Numerous clinical observations of Russian and foreign experts suggest that it is in the early postoperative period that the risk of non-specific inflammatory complications, associated with surgical trauma and stress response of the body to injury, manifested both at the local and at the system level, is the highest. This is connected with an imbalance of pro- and anti-stress activity of regulatory mechanisms of the patient’s body, which are triggered in response to the performed surgical intervention.

Thus, the main clinical task of the specialist at the postimplantation stage of treatment is to create a favorable background promoting optimal recovery of the injured tissue and preventing complications of inflammatory nature. To this end, in the early recovery postimplantation period antibacterial, anti-inflammatory, immune correction and reparants are widely used. Today, however, the incidence of a variety of inflammatory responses in the peri-implantation zone against the background of the standard accompanying treatment remains high; in this regard to prevent and delimit the above complications, in recent years management protocols of patients, who had undergone dental implantation, increasingly include various methods of physiotherapy (laser therapy, darsonvalization and ultratone therapy, etc.), which have anti-edematous, anti-inflammatory, regenerative and immune activating effects. Despite numerous attempts to standardize physiotherapy techniques, the nature of their use in current clinical practice differs by lack of consistency and standards, while details on their effectiveness significantly differ according to different researchers, which makes the urgency of further research and practical exploration in this area.

2. Own Scientific Hypothesis

Our previous studies have shown that the Mesodiencephalic Modulation (MDM-therapy) makes apparent anti-stress effect, as well as a positive influence on the trophic, hemodynamic and regenerative-reparatory mechanisms. The therapeutic effects of MDM-therapy have complex and systemic nature. They are achieved by electrical stimulation of deep diencephalic structures responsible for the regulation of pro-stressor and neurohormonal responses of systemic and local level being antagonistic to them. The range of the local curative effect includes analgesia, reducing congestion and edema, improving tissue microcirculation and oxygenation, balancing of pro- and anti-inflammatory components of cellular and humoral links of immune presenting systems, improving immunocompetence and stimulating normal reparation.

Achievable in the MDM-therapy activation of central opioid anti-nociceptive mechanisms that are involved in pain management regulation of immune and inflammatory processes, inhibition of pro-stressor reactions of the central and vegetative nervous system with simultaneous potentiation of stress-stabilizing mechanisms creates an overall favorable background for the rehabilitation period after implantation. General relaxing and sedative effect allows for improvement of psychoemotional state of the patient undergoing complex and lengthy dental treatment. Harmonizing effect on the tone of the various neurohormonal regulatory systems of the body also helps to overcome the surgery-induced stress with inherent phenomena of aseptic inflammation and “host-implant” reaction. The balance of content of hormones and biologically active substances of sympathoadrenal complex is carried out by stimulating concerned diencephalic structures and promotes immune stabilization, increase in tissue reparative capacity while maintaining high resistance to the action of microbial agents. Furthermore, these neurohormonal mechanisms along with NO systems, prostaglandins and kallikrein-kinins are involved in activating platelet factors, reducing the inflammatory response after the intervention, restoring adequate blood and lymph flow, which plays an important role in the restoration of soft tissues and paraimplant bone. Stimulation of the production of antioxidants helps to prevent excessive cell alteration and stabilize mechanisms of stress-induced cell death. Currently, there is an experience of successful application of mesodiencorthal modulation in combustiologic, general surgical, neurological, endocrinological, rheumatological, general somatic and dental practice.

The operating principle of this method of physical therapy allows considering it as an effective means
of adjunctive therapy in combination with standard medication accompaniment of the early postimplantation period, enabling to achieve the speedy elimination of non-specific inflammatory response to surgery, to reduce edema and congestion, to decrease sensation of pain, thus preventing the development of an unfavorable background that promotes the accession of secondary infection, abnormal healing and implant rejection and creates optimal conditions for normal healing and osseointegration.

This study was aimed at evaluating the effectiveness of MDM-therapy in the early postoperative period after dental implantation to prevent inflammatory complications to improve the osseointegration quality and to increase the installed implant stability.

Research problems, whose solution helped to achieve this aim, were as follows:

- Carrying out a comparative analysis of the clinical course of the early postoperative period in patients who had undergone dental implantation, using MDM-therapy along with and without the standard postoperative treatment;
- Evaluating dynamically clinical and laboratory parameters characterizing the course of inflammatory response after implantation in patients who had received a standard postoperative therapy and standard treatment combined with MDM-therapy;
- Identifying the indicators of early and late stability of the installed dental implants in patients, with the traditional early postoperative care and with applied method of mesodiencephalic modulation;
- Comparing the obtained data of clinical and laboratory research and formulating the conclusions about the appropriateness of the MDM-therapy in the early postimplantation period to prevent inflammatory complications and to improve the quality of osseointegration and stability of the installed dental implants.

3. Materials and Methods

3.1 Characterization of Cohorts and Clinical Conditions

The study included two groups of male and female patients aged from 27 to 62 who had undergone dental intraosseous implantation. The average age of examined participants was 42 years. The 1st group (a comparison group) consisted of 24 patients who had 34 implants installed in total. The 2nd group (a control group) also included 24 patients with 30 implantations performed in total. The selection of participants for the study provided for approximately equal initial clinical situation available. Patients with severe comorbid pathologies (e.g. diabetes, osteoporosis, decompensated forms of cardiovascular disorder, etc.) were excluded from the study. In both study groups the classic two-stage intraosseous implantation was carried out without bone augmentation using BioHorizons systems (BioHorizons Implant Systems, Inc., manufactured in the U.S.).

Later, in accordance with the prepared treatment plan orthopedic structures using PEEK (Poly-Ether-Ether-Ketone) implants will be installed. This material belongs to the group of thermoplastics, the positive properties of which are high strength, biocompatibility, lightness, resistance to chemical and thermal agents, good aesthetic qualities; they do not form a galvanic couple with other materials.

All patients in both groups received adequate accompanying medication (pain relievers, anti-bacterial, glucocorticosteroid, nonsteroidal anti-inflammatory, antiseptic preparations) in the preoperative and early postoperative period to the extent necessary. Additionally, all patients in group 1 were prescribed a course MDM-therapy starting from the 2nd day of the postimplantation period.

3.2 Description of the MDM-therapy Procedure

A course of supporting physiotherapy by the mesodiencephalic modulation method consisted of 13 sessions lasting 30 minutes each. Procedures were delivered daily for 10 days, during the first 3 days two sessions were conducted with a minimum interval of 6 hours and in all subsequent days one session was performed.

The procedure was carried out in the patient’s sitting position. For this purpose, two copper nickel-plated electrodes connected with a headband were fixed on the patient’s head according to the fronto-occipital technique: The anode was placed at the center of the forehead and the cathode was attached at center of the back of the head. A disposable 16-layered flannel lining, well moistened
with water, was placed between the skin and the electrode plate.

Individual selection of the current strength was increased gradually by the introduction of its value from the computer keyboard with simultaneous continuous monitoring of the ‘pins and needles’ sensations, a slight burning or vibration sensation, the individual strokes, a slight pressure in the patient. During the device operation, the electrode resistance was automatically measured and displayed as a flashing message of the relevant content on the monitor display. If necessary, the procedure was interrupted for individual adjustment of parameters through the use of functions ‘Execute’, ‘Cancel’, ‘Pause’, ‘Set current’ and then the session was resumed. The time countdown from the beginning to the end of the procedure was carried out with a special timer and after 30 minutes, the apparatus automatically switched off. Then the patient’s was disconnected from the device and the electrode part was removed from his head. After the session for consolidation of the effect, the patients were recommended to have a sleep or a rest.

To achieve clinical results based on the previous experience of applying the MDM-therapy in dentistry, the following mode of exposure on the subcortical and stem brain regions was designed: Stimulation in the pulsed mode; 10,000 Hz current carrier frequency; low-frequency range with modulation from 20 to 100 Hz changing in a single session. The strength of the supplied current ranged from 0.5 to 4 mA during the session and was selected individually depending on the patient’s tolerability of exposure (sensations, comfort).

Physiotherapy was performed using Federation MDM-2000/1 apparatus certified in the Russian Federation manufactured at ZAT a.d., the Czech Republic, designed for pulsed current exposure on the subcortical-stem (with mesodiencephalic) region of the brain.

All the patients of the first group demonstrated high tolerability of the procedures; no complications and any adverse reactions in response to the MDM-therapy were recorded throughout the course of treatment.

### 3.3 Treatment Efficiency Control

In addition to careful clinical observation of the patient’s state in the postoperative period (including visual identification of the edema and hyperemia severity, epithelialization process and the presence of pain sensations), the idea of intensity and balance of non-specific inflammatory response that accompanies the early postoperative period, may be made on the basis of objective data reflecting the state of the various links of immunity, involved in the inflammatory response. The importance of such protection is explained by the conditions of naturally growing influence the microbial factors after surgery (complicated hygiene, formation of a hotbed for the pathogenic flora development, change in natural microbiocenosis in view of administration of topical and systemic antibacterial drugs).

In this study, we aimed to use the laboratory assessment methods that are highly indicative, targeted and acceptable for implementation.

Thus, a state of humoral immunity and immune competence of the oral mucosa was assessed by the concentration of IgA in saliva determined by enzyme immunoassay.

Cellular immunity was assessed on the basis of laboratory calculation of the phagocytic activity of saliva neutrophils. We also determined the Phagocytic Index (PI) – the percentage of immune cells which have entered phagocytosis, relative to their total number, the Phagocytic Number (PN) – an average number of bacteria located intracellularly (the result of dividing the total number of absorbed bacteria on the number of cells entered in phagocytosis) and the Index of Phagocytosis Completeness (IPC) in 30 and 120 minutes of exposure, which reflects the digestive capacity of phagocytes.

Determination of the content and level of lysozyme activity in saliva gave the idea of a local non-specific resistance.

Complex clinical and laboratory testing of all patients in both groups was performed twice: In the first day after implantation (for patients of the first group - before the start of MDM-therapy) and on the 12th day after the implantation (which corresponded to the end of the complete course of the MDM-therapy conducted among group 1 patients).

Osseointegration was controlled by determining dental implant stability using the Osstell (ISQ) meter which operates based on an indirect determination of the rigidity of the implant anchorage in the jaw bone by means of resonant frequency analysis of forced oscillations that occur in the implant under the influence of an alternating magnetic field emitted from the device emitter. The Osstell ISQ system uses SmartPeg, a special magnetic rod, attached to the dental implant or abutment by screwing.
The rod is excited by a magnetic pulse from the measuring probe. Upon receipt of the response, the signal resonance frequency is calculated, which represents a measure of stiffness of the dental implant fixed in the bone tissue. The results are displayed on the device display in the form of ISQ value (Implant Stability Quotient) ranging from 1 to 100. Higher ISQ values correspond to higher implant stability. The minimum allowable value is 55.

Implant Stability Quotient was measured in all patients participating in the study, immediately after implant placement (early stability) and repeatedly – 3 months after the intervention (late stability).

4. Results

4.1 Description of the Obtained Clinical Findings

An objective examination of the patients in the dynamics throughout the entire postimplantation period is an integral part of the work of the expert, in the course of which both the general condition of the patient, who had undergone surgery and the local status of the postoperative area are assessed. Among the most informative criteria amenable to a clear description with regards to the local status, the presence and degree of congestion and edema, quality and timing of postoperative wound epithelialization, as well as the presence and severity of pain syndrome can be distinguished.

The analysis of the clinical data showed that in the majority of patients in the comparison group the recovery postimplantation period proceeded more easily than in the control group, differing in more rapid regression of the nonspecific inflammation phenomena (congestion and edema) in the post-operative area with a relatively early onset of epithelialization and speedy regression of the pain syndrome, which significantly reduced the need to use nonsteroidal antiinflammatory drugs.

Thus, the majority of participants in the 1st group (91%) significant decrease in congestion and limitation of edema were observed already since the second day after the surgery. Among the patients of the 2nd group these processes yielded regression only on the fourth day of the postimplantation period in 79% of cases. Signs of initial epithelialization of the surgical wound were revealed during the examination of the comparison group patients on the third day after the implantation in 83% of cases, whereas signs of healing in the control group were determined not earlier than on the fifth day in 71% of patients. The complete absence of pain in the postoperative wound was observed already on the second day after the intervention among 87.5% of patients included in the 1st group (with the possible retaining of some discomfort or hypersensitivity). In contrast, in the 2nd group removing local pain was recorded only on the fourth post-operative day in 66.6% of patients, in the other cases pain and discomfort persisted longer.

4.2 Laboratory Parameters Characterizing the Severity of the Inflammatory Response

The analysis of the dynamics in the saliva lysozyme concentrations of 1st study group found that after the MDM-therapy its average gain was 3.5±0.3 mkg/mg compared to the initial value (10.6-11.9 mkg/mg), with the re-examination parameters ranging within 13.91-15.6 mkg/mg. Lysozyme activity in this group of patients ranged within 68-76 % immediately after the surgery; while being determined on the 12th day after the implantation its activity increased on average by 7.2±0.8 % and its values were in the range of 79-88 %.

Study of saliva PA changes as an indicator characterizing the cellular immune link, revealed the following picture among the first group patients before and after the MDM-therapy. The average value of PI, determined at the end of physiotherapy course (92.4-96.3 %) was by 3.6±0.5 % higher than the initial one (88.2-91.6 %). The PN increased, on average, by 1.9±0.1 units with the initial values of the index ranging within 9.2-10.4 and the final values – within 11.8-13.1. The IPC values, determined in the first group patients immediately after the intervention, ranged from 58.7 to 62.3% and after the MDM course on the 12th postoperative day its value increased on average, by 12.8±1.2 % and ranged from 70.1 to 81.5 %.

Humoral immune component was assessed by determining the IgA concentrations in saliva. On the second day after the implantation its value was in the range of 0.11-0.17 g/l and after the MDM-therapy it increased to 0.19-0.28 g/l, showing average gain of the index by 0.115±0.01 g/l.

These findings indicate a stimulatory effect of mesodiencephalic modulation with respect to the cellular,
humoral immunity as well as local factors of nonspecific protection (Table 1).

In the control group the dynamics of the above indicators from the 2nd to the 12th day of the postimplantation period was not characterized by similar intensity (Table 2). Thus, on the 2nd postoperative day the average saliva lysozyme concentration was 10.5-11.7 mkg/mg and on the 12th day its value ranged from 11.3 mkg/mg to 12.8 mkg/mg, therefore, the average gain achieved 1.2±0.3 mkg/mg. At the same time the lysozyme activity determined in the patients of the 2nd group on the 2nd day after the implantation ranged within 69-77 % and by the 12th day it grew up to 72-80 %, increasing on average by 4.1±0.5 %.

The PI value in patients of the 2nd group in the primary study of PA was 87.9-91.4 % and slightly increased by the time of re-evaluating the parameter, the value of which was determined in the range from 89.7% to 93.4%. Thus, PI increase made 1.8±0.4 %. During the first measurement of the PN in the 2nd group it was equal to 9.3-10.5 and on 12th day of the recovery period it rose to 10.2-12.0. Accordingly, the index dynamic varied in the range of 1.3±0.2 units. Initial value of the IPC for this group was found to be 58.4-63.1 % while the final index values reached 62.5-69.8 % making the average gain 7.4±1.2 %.

On the 2nd day after the implantation analysis of the IgA content in saliva of patients treated with conventional postoperative therapy showed a range of values from 0.10 g/l to 0.16 g/l, during re-evaluation it was characterized by a minimum value of 0.13 g/l and maximum value of 0.19 g/l. The average increase in the IgA concentration was 0.05±0.01 g/l in the 2nd group (see Table 2).

As can be seen from the obtained data, in the early postoperative period immunocompetence of the patients’ bodies was characterized by the state of depression or minimum normal activity at both at the cellular and humoral level when applying the standard postimplantation therapy model. Reactivity of local protective mechanisms was also within the subliminal

### Table 1. Dynamics of indicators of immune activity in patients of the 1st group

| Indicator                              | Range of the parameter values in the 1st group, determined on the 2nd day after implantation | Range of the parameter values in the 1st group, determined on the 12th day after implantation | Average gain of the index in the 1st group |
|----------------------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------------------------------|
| Lysozyme concentration in saliva       | 10.6-11.9 mkg/mg                                                                                | 13.91-15.6 mkg/mg                                                                              | 3.5±0.3 mkg/mg                          |
| Saliva lysozyme activity               | 68-76 %                                                                                         | 79-88 %                                                                                        | 7.2±0.8 %                              |
| PI                                     | 88.2-91.6 %                                                                                    | 92.4-96.3 %                                                                                    | 3.6±0.5 %                              |
| PN                                     | 9.2-10.4                                                                                       | 11.8-13.1                                                                                     | 1.9±0.1                                |
| IPC                                    | 58.7-62.3 %                                                                                    | 70.1-81.5 %                                                                                    | 12.8±1.2 %                             |
| IgA concentration in saliva            | 0.11-0.17 g/l                                                                                  | 0.19-0.28 g/l                                                                                 | 0.115±0.01 g/l                         |

### Table 2. Dynamics of indicators of immune activity in patients of the 2nd group

| Indicator                              | Range of the parameter values in the 2nd group, determined on the 2nd day after implantation | Range of the parameter values in the 2nd group, determined on the 12th day after implantation | Average gain of the index in the 2nd group |
|----------------------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------------------------------|
| Lysozyme concentration in the saliva   | 10.5-11.7 mkg/mg                                                                                | 11.3-12.8 mkg/mg                                                                              | 1.2±0.3 mkg/mg                          |
| Saliva lysozyme activity               | 69-77 %                                                                                         | 72-80 %                                                                                        | 4.1±0.6 %                              |
| PI                                     | 87.9-91.4 %                                                                                    | 89.7-93.4 %                                                                                    | 1.8±0.4 %                              |
| PN                                     | 9.3-10.5                                                                                       | 10.2-12.0                                                                                     | 1.3±0.2                                |
| IPC                                    | 58.4-63.1 %                                                                                    | 62.5-69.8 %                                                                                    | 7.4±1.2 %                              |
| IgA concentration in saliva            | 0.10-0.16 g/l                                                                                  | 0.13-0.19 g/l                                                                                 | 0.05±0.01 g/l                          |
and the lowest normal values. In the conditions caused by surgical trauma, as well as in the presence of a foreign body (implant) in the bone tissue, which is an additional irritant, along with the increased risk of secondary bacterial flora added after the conducted intervention, anti-inflammatory and immune activity of the patient’s body can be insufficiently effective with a high probability to provide favorable and uncomplicated progression of the early postimplantation period, which can lead to delays in the healing process and adversely affect the osseointegration process.

4.3 Assessment of the Dental Implant Stability

Determination of stability quotient in the first study group immediately after implant placement showed variation of ISQ values in the range of 62-66 units. In 3 months after the intervention the results of the repeated measurements ranged within 68-72 ISQ units. For the control study group the primary stability parameter was in the same range as in the 1st group (62-66 ISQ units), while the late stability of implants, installed to the 2nd group of patients, was slightly inferior in its performance than the values obtained in the comparison group and ranged from 64 to 67 ISQ units.

5. Conclusion

Comparative analysis of the clinical course of the early postimplantation period in patients, who had undergone dental implantation, showed earlier regression of the inflammatory symptoms (pain, edema, congestion), along with the increased intensity of the regenerative-reparatory processes and accelerated epithelialization of the post-operative wounds in patients who received the MDM-therapy course in addition to the standard therapy, compared to postimplantation clinical picture of patients who received only traditional treatment in the early recovery period.

Determined in the present study early and late stability of the installed dental implants in patients undergoing the traditional early postoperative care, as well as treatment combined with the mesodiencephalic modulation method showed significant difference in the form of osseointegration among patients of the experimental and control study groups confirming our hypothesis about the positive impact of mesodiencephalic modulation on the processes of post-operative recovery of the jawbone and implant clinical survival rate.

Evaluation of clinical and laboratory parameters characterizing the dynamical progression of the inflammatory response after implantation in the patients treated with standard postoperative therapy and the standard treatment combined with mesodiencephalic modulation, indicated earlier and more complete recovery of immunological reactivity in patients who had received a MDM-therapy course after dental implantation.

The technical results achieved through the use of the MDM-therapy in the early postimplantation period include pain and discomfort management, restoration of normal sensitivity and functional viability of tissues, improvement of microcirculation and oxygenation, reduced edema, localization and prevention of excessive postoperative inflammatory response, early epithelialization, increased stability of the installed implants.

Thus, the present study proves the existence of a positive effect from the MDM-therapy applied after dental implantation for prevention of inflammatory complications, osseointegration quality improvement, contributing to a more favorable course of the recovery period and achievement of a better final result of the conducted orthopedic treatment as compared to the traditional postoperative care without using auxiliary physiotherapy methods.

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