PERIÓDICO TCHÊ QUÍMICA
ARTIGO ORIGINAL

APLICAÇÃO TERAPÊUTICA E PROFILÁTICA DA MODULAÇÃO MESODIENCEFÁLICA DURANTE IMPLANTES DENTÀRIOS EM PACIENTES COM DIABETES MELLITUS DO TIPO 2

THERAPEUTIC AND PROPHYLACTIC APPLICATION OF MESODIENCEPHALIC MODULATION DURING DENTAL IMPLANTATION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

ТЕРАПЕВТИЧЕСКОЕ И ПРОФИЛАКТИЧЕСКОЕ ПРИМЕНЕНИЕ МЕЗОДИЭНЦЕФАЛЬНОЙ МОДУЛЯЦИИ ПРИ ЗУБНОЙ ИМПЛАТНАЦИИ У ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ 2-ГО ТИПА

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RESUMO

O implante dentário é estressante e pode aumentar os níveis de açúcar no sangue, colocando em risco pacientes com diabetes mellitus. Há necessidade de tratamentos alternativos que possam prevenir manifestações de estresse mental e somático durante o implante dentário nesses pacientes. Examinamos a eficácia terapêutica e profilática da modulação mesodientefálica (MDM) em pacientes com diabetes mellitus tipo 2 leve que foram submetidos a implante dentário. Este estudo clínico randomizado controlado incluiu 67 pacientes com diabetes mellitus tipo 2 leve e uma patologia dentária compreendendo um único defeito em uma arcada dentária. O grupo G-1 (n = 22) recebeu implantes dentários e terapia MDM durante o período pós-implantação inicial. O grupo TG-2 (n = 22) recebeu implantes dentários e terapia MDM durante os períodos pré-implantação e pós-implantação precoce. O grupo RG (n = 23) recebeu implantes dentários sem terapia com MDM. Os níveis de glicose no sangue, frequência cardíaca e estado emocional dos pacientes nos períodos pré e pós-implantação foram comparados. Em todos os grupos, os níveis de açúcar no sangue e a freqüência cardíaca atingiram o pico 5 minutos após a conclusão do procedimento odontológico. O aumento de 5 minutos antes do início para 5 minutos após a conclusão dos procedimentos odontológicos foi significativo nos grupos TG-1 e RG, mas não no grupo TG-2. Após 10 dias do procedimento, a qualidade de vida foi significativamente maior nos dois grupos de tratamento do que no grupo RG. O MDM tem valor terapêutico e profilático para pacientes com diabetes mellitus tipo 2 submetidos a implante dentário durante os períodos pré e pós-implante, bem como sobre a qualidade de vida no período de recuperação pós-operatória precoce

Palavras-chave: *Gliicose no sangue; implantação dentária; modulação mesodiencefálica; profilaxia; diabetes mellitus tipo 2*.

ABSTRACT

Dental implantation is stressful and can increase blood sugar levels, placing patients with diabetes mellitus at risk. There is a need for alternative treatments that can prevent mental and somatic stress manifestations during dental implantation in such patients. We investigated the therapeutic and prophylactic efficacy of mesodiencephalic modulation (MDM) in patients with mild type 2 diabetes mellitus who underwent dental implantation. This clinical randomized controlled study included 67 patients with mild type 2 diabetes mellitus and a dental pathology comprising a single defect in a dental arch. Group G-1 (n = 22) received dental implants and MDM therapy during the early post-implantation period. Group TG-2 (n = 22) received dental implants and MDM therapy during pre-implantation and early post-implantation periods. Group RG (n = 23) received dental implants without MDM therapy. Patients' blood glucose levels, heart rate, and emotional state in

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pre-and post-implantation periods were compared. In all groups, blood sugar levels and heart rate peaked at 5 minutes after dental procedure completion. An increase from 5 minutes before starting to 5 minutes after completing the dental procedures was significant in TG-1 and RG groups but not in the TG-2 group. Quality of life was significantly higher in both the treatment groups than in the RG group at 10 days after the procedure. MDM has therapeutic and prophylactic value for patients with mild type 2 diabetes mellitus undergoing dental implantation during pre- and post-implantation periods as well as on the quality of life in the early post-surgery recovery period.

Keywords: *blood glucose; dental implantation; mesodiencephalic modulation; prophylaxis; type 2 diabetes* mellitus

АННОТАЦИЯ

Имплантация зубов вызывает стресс и может повышать уровень сахара в крови, подвергая риску больных сахарным диабетом. Существует потребность в альтернативных методах лечения, которые помогут предотвратить проявления психического и соматического стресса во время имплантации зубов у таких пациентов. Мы исследовали терапевтическую и профилактическую эффективность мезодиэнцефальной модуляции (МДМ) у пациентов с легкой формой сахарного диабета 2-го типа, которые перенесли имплантацию зубов. Данная работа представляет собой клиническое контролируемое исследование методом случайной выборки и охватывает 67 пациентов с легкой формой сахарного диабета 2-го типа. У всех пациентов наблюдалась стоматологическая патология, включающая единственный дефект зубного ряда. Группа G-1 (n = 22) получала зубные имплантаты и МДМ-терапию в раннем постимплантационном периоде. Группа TG-2 (n = 22) получала зубные имплантаты и МДМ-терапию во время предимплантационного и раннего постимплантационного периодов. Группа RG (n = 23) получала зубные имплантаты без МДМ-терапии. У пациентов сравнивали уровень глюкозы в крови, частоту сердечных сокращений и эмоциональное состояние в период до и после имплантации. Во всех группах уровень сахара в крови и частота сердечных сокращений достигли пика через 5 минут после завершения стоматологической процедуры. Увеличение от 5 минут до начала до 5 минут после завершения стоматологических процедур было значительным в группах TG-1 и RG, но не в группе TG-2. Качество жизни было значительно выше в обеих группах лечения, чем в группе RG, через 10 дней после процедуры. МДМ имеет терапевтическое и профилактическое значение для пациентов с легким сахарным диабетом 2 типа, перенесших дентальную имплантацию в период до и после имплантации, а также для качества жизни в раннем послеоперационном периоде восстановления.

Ключевые слова: глюкоза; имплантация зубов; мезодиэнцефальная модуляция; профилактика; сахарный диабет 2-го типа

1. INTRODUCTION

Dental procedures, particularly invasive interventions like dental implantation, are stressful for patients (Bracha *et al*., 2006; Kvale *et al*., 2004; Enkling *et al*., 2013; Lalabonova, 2015). In patients with type 2 diabetes mellitus, stress may trigger hyperglycemia (Chang *et al*., 2018; Kampling *et al*., 2018; Davis *et al*., 2017; Moradi *et al*., 2015; Renna *et al*., 2016). Since type 2 diabetes mellitus is related to endocrine diseases, which have a psychosomatic component, stress resistance in this patient population is already reduced, and dental treatment in these patients may lead to a sharp increase in blood glucose levels (Rau *et al*., 2017; Whitworth, 2016; van Dooren *et al*., 2016). Dentists thus often face the challenge of planning safe invasive interventions in patients with type 2 diabetes mellitus. In patients with type 2 diabetes, blood glucose levels can increase above acceptable values during dental procedures, creating an adverse complication for both dental care and type 2 diabetes mellitus. In addition, hyperglycemia may negatively affect the patient's local dental status after dental implantation surgery, impacting the regenerative ability of the weakened tissues. These difficulties may lead to a prolonged post-surgery recovery period and post-implantation complications that reduce the patient's quality of life and negatively affect the survival and stability of the implant (Lacigova *et al*., 2013; Jumashev *et al*., 2016a, Jumashev *et al*., 2016b). Therefore, there is a need for the development of techniques that can address the problem of increased blood glucose levels in patients with type 2 diabetes mellitus who require dental prosthesis involving dental implants (Ershov *et al*., 2018; Timoshin *et al*., 2018).

Patients with mild type 2 diabetes mellitus

are often treated exclusively with diet therapy and graduated physical exercises; it would be inappropriate to administer hypoglycemic medicinal products to this patient group prophylactically before commencing invasive dental procedures (Lalabonova, 2015). Other prophylactic approaches are required for moderating increases in blood glucose levels caused by invasive dental procedures. Physiotherapy offers a promising solution.

Among the available physiotherapeutic methods (such as low-level laser therapy, photodynamic therapy, ultrasonic decontamination, and photobiomodulation), mesodiencephalic modulation (MDM) therapy most closely meets the needs of dental patients with type 2 diabetes mellitus (Torkzaban *et al*., 2018; Alasqah *et al*., 2019; Stein *et al*., 2007; Tang and Arany, 2013). MDM therapy has been proven to reduce stress, increase insulin secretion, and reduce insulin resistance (Lacigova *et al*., 2013; Jumashev *et al*., 2016a; Jumashev *et al*., 2016b). MDM therapy focuses on impulse currents on the mesencephalic structures of the brain through electrodes that are attached using the fronto-occipital technique (Karev, 2005). MDM therapy activates and normalizes the body's anti-stress system complex, and its effects are clinically reflected at both general and local levels (Karev, 2005).

The purpose of this study was to evaluate the efficacy of MDM therapy as a prophylactic and therapeutic treatment in patients with type 2 diabetes mellitus receiving prosthetic dental implants.

2. MATERIALS AND METHODS

The study was approved by the Commission on Bioethics I. M. Sechenov First Moscow State Medical University. This clinical randomized controlled study was conducted at the Prosthetic Dentistry Department of I. M. Sechenov First Moscow State Medical University and included 67 patients who were diagnosed with mild type 2 diabetes mellitus (E11 according to the International Classification of Diseases-10 code (ISCDRHP, 2016) and a dental pathology comprising a single defect of the dental arch (in either the upper or lower jaw). The included patients were scheduled to receive intraosseous screw dental implants (Astra Tech Dental Implants System, Dentsply Sirona, Mölndal, Sweden).

The mean age in the study group was 53.82 ± 0.69 years. The time from diagnosis of type 2 diabetes mellitus to the beginning of the study was 6.21 ± 0.54 years. The following inclusion criteria were applied: treatment of type 2 diabetes mellitus exclusively with diet therapy and graduated physical exercises, no use of hypoglycemic medicinal products, and presence of appropriate bone architecture (D2–D3) for implant placement. The following exclusion criteria were applied: the presence of micro- or macrovascular complications of type 2 diabetes mellitus, tumor, epilepsy, tuberculosis, HIV, endogenous mental pathologies, diseases associated with impaired blood clotting, acute and chronic infectious diseases, active forms of periodontal pathologies, and skin diseases in the location of electrode application. All patients gave informed consent to participate in the study. The patients were randomized to the groups using a random number table.

All study patients received standard oral cavity prophylaxis before implant placement and concomitant anesthesia during the placement of the dental implant, according to standard protocols. Patients in all the groups were recommended to refrain from taking food for 2 hours before and for 4 hours after the dental procedures. All the patients were subjected to classical two-stage intraosseous implantation without bone augmentation by using the Astra Tech Implant System (Figure 1).

The patients were randomly divided into three groups based on the type of treatment to be administered. The first treatment group (TG-1) comprised 22 patients who received dental implants in conjunction with MDM therapy during the early post-implantation period, according to an in-house developed algorithm. The second treatment group (TG-2) comprised 22 patients who received dental implants in conjunction with MDM therapy during the pre-implantation and the early post-implantation periods, according to an in-house developed algorithm. The reference group (RG) comprised 23 patients who received dental implants without MDM therapy. MDM therapy is a modification of the physiotherapeutic method of transcranial stimulation, which is a targeted effect of calibrated electric currents on the median cerebral structures. MDM therapy was performed using an MDM-2000/1 device (ZAT ad, Czech Republic), designed for pulsed exposure to currents on the subcortical-stem (mesodiencephalic) region of the brain (Figure 2). During the MDM therapy session, the patient sits. Two nickel-plated copper electrodes were fixed on the patient's head: the anode - in the middle of

the forehead, the cathode - in the middle of the nape (Figure 3).

To achieve clinical effects with MDM therapy, impulse currents had a carrier frequency of 10,000 Hz and were modulated from 20 to 100 Hz, and the patients were prepared accordin to Figure 1. The power of the current applied during an MDM therapy session varied from 0.5 to 4 mA and was set individually, depending on the patient's subjective sensations (Yur'evna *et al.*, 2018). In the pre-implantation period, TG-2 patients received five MDM therapy sessions in total per day, with the last session. Patients received one MDM therapy session per day. The last session of MDM therapy in the pre-implantation period was carried out one day before the dental procedures. In the post-implantation period, TG-1 and TG-2 patients received 10 MDM therapy sessions in all, one MDM therapy session per day, from the first day of the post-implantation period. The first MDM therapy was performed 30 minutes after the procedure of dental implant placement. The duration of each MDM therapy session was 30 minutes.

Blood glucose levels were measured in all patients by using One Touch blood glucose meter (LifeScan, Wayne, PA, USA) four times, i.e., during the first consultation (usually 1 week before the prosthetic procedure), 5 minutes before the start of dental procedures, and 5 minutes and 1 hour after the termination of dental procedures. Concomitantly with the blood glucose level measurement, the pulse rate was measured using a Contec K-80B pulsometer. Immediately before dental procedures and 5 minutes and 1 hour thereafter, the patients self-identified their own psycho-emotional state. They rated their emotional discomfort level (fear, anxiety, and emotional tension) on a four-point score, where 0 means no symptoms, 1 means weak symptoms, 2 means moderate symptoms, and 3 means severe symptoms. Fear, anxiety, and emotional tension were quantified separately (Yumashev, 2017; Utyuzh, 2018).

In order to determine the treatment efficacy and rehabilitation of patients, the MOS 36-Item Short-Form Health Survey (MOS SF-36, https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form.html) was used to evaluate the quality of life of patients. Scores for each of the eight indicators addressed in the questionnaire vary between 0 and 100 points, where 0 points mean complete lack of well-being and 100 points mean complete well-being in the context of the indicator under consideration. Patients were evaluated with the MOS SF-36 10 days after dental implant placement.

For statistical analysis, descriptive and mathematical statistics were used. These include calculation of the arithmetic mean values and standard deviations, standard error of the mean. The student's t-test was used for pair-wise comparison of values between groups. P-values < 0.05 were considered to be significant.

3. RESULTS

We developed an algorithm for MDM therapy sessions for treatment of patients who required dental implants but who had also had a long-term diagnosis of type 2 diabetes mellitus.

During the first consultation, the mean blood glucose level and heart rate values did not differ significantly across the three groups (Table 1). Five minutes before the start of dental procedures, patients in all groups showed a significant increase in blood glucose level compared to their first measurements (tEmp = 13.7; 6.0, and 15.3, $p < 0.01$, respectively). Wherein the blood glucose levels did not significantly differ between TG-1 and RG, whereas the blood glucose levels and heart rate in TG-2 patients were significantly lower than those in the other groups who did not receive MDM therapy during the pre-implantation period (tEmp = 13.7 and 7.7, $p < 0.01$, respectively).

All the patients demonstrated peak blood glucose levels 5 minutes after terminating the dental procedures. In TG-2, blood glucose level at 5 minutes after completing the dental procedures was 2.8 mmol/L less than that in TG-1. This trend continued until 1 hour after completing the dental procedures. Although blood glucose level 5 minutes before starting and 5 minutes after completing the dental procedures did not differ significantly from that in RG, the blood glucose level in TG-1 1 hour after completing the dental procedures was 1.6 mmol/L less than that in RG (Table 1, Figure 4). Blood glucose levels in the post-implantation period (5 minutes after the dental procedures) showed a significant increase in TG-1 (9.2 ± 0.21 mmol/L) and RG (9.3 ± 0.25 mmol/L) compared to the values obtained 5 minutes before starting the dental procedures (tEmp = 7.4 and 8.1, $p < 0.01$, respectively). However, at 1 hour after completing the dental procedures, there was a significant decrease in blood glucose level in TG-1 (7.6 ± 0.12 mmol/L) and TG-2 (5.8 ± 0.22

mmol/L) compared to levels taken at 5 minutes after completing the dental procedures (tEmp = 7.8 and 6.1, $p < 0.01$, respectively). These values were significantly different from those in RG, where blood glucose levels remained at the level of the previous measurement (tEmp = 7.2 and 12.1, $p < 0.01$, respectively) (Table 1, Figure 4).

For heart rate, dynamics similar to those for blood glucose was noted (Table 2, Figure 5). There were significant differences in heart rate values in TG-2 patients, who received MDM therapy sessions in the pre-implantation period, compared to the values in TG-1 and RG. Namely, the heart rate at 1 hour after completing the dental procedure in all groups was significantly reduced compared to the previous measurement and was similar to that in the first measurement. The latter two groups showed a pronounced increase in heart rate from 5 minutes before the start to 5 minutes after the completion of dental procedures, while there was no marked difference between these second and the third measurements in TG-2 (Table 2, Figure 5).

The psycho-emotional state at all stages of the survey was significantly better in TG-2 than in TG-1 and RG (Table 3). Five minutes before commencing the dental procedures, indicators in TG-2 of a stressed state were lower than those in TG-1 (fear reduced by 1.7 points, anxiety reduced by 1.8 points, and emotional stress reduced by 1.7 points). At 5 minutes after completing the dental procedures, the fear indicators were reduced by 0.2 points, anxiety by 0.5 points, and emotional stress by 1.2 points compared to those in TG-1. At 1 hour after the dental manipulations in TG-2, there were no indications of fear and anxiety, as in TG-1. Additionally, in TG-2, the indicators of emotional stress were minimal, and there were no significant differences between TG-1 and TG-2. There was no significant difference between TG-1 and RG in any of the psycho-emotional indicators at 5 minutes before starting or at 5 minutes after completing the dental procedures; however, there were significant differences at 1 hour after completing the dental procedures in terms of anxiety and emotional stress, with anxiety being 0.3 points less and emotional stress being 3.2 points less in TG-1 than in RG (Table 3).

In terms of quality of life at 10 days after dental implantation, quality of life was significantly higher for patients in both treatment groups than in RG patients (Table 4). TG-1 and TG-2 indices were not significantly different, but TG-1 and TG-2 patients faired significantly better than RG patients. The most significant differences in TG-1 and TG-2 compared with RG patients were in terms of physical functioning (by 16 and 17 points respectively, tEmp = 7.8 and 9,5, $p < 0.01$, respectively), pain (by 26.4 and 27.2 points respectively, tEmp = 26.5 and 28.2, $p < 0.01$, respectively), general health (by 20.3 and 21.1 points respectively, tEmp = 19.8 and 20.7, $p < 0.01$, respectively), emotional functioning (by 24.4 and 24.4 points respectively, tEmp = 24.2 and 24.3, $p < 0.01$, respectively), and mental health (by 23.3 and 23.4 points respectively, tEmp = 21.3 and 21.8, $p < 0.01$, respectively) (Table 4).

4. DISCUSSION:

The results of our study allowed us to prove the effectiveness of MDM therapy in treating patients with type 2 diabetes mellitus who require dental implantation. MDM therapy improved the psycho-emotional state of patients and reduced their blood sugar levels and heart rate. These effects of MDM therapy make it a method of choice for the treatment of patients with type 2 diabetes mellitus who need to undergo dental implantation.

It is important to improve the efficacy of treating patients who require dental implant procedures, given the side effects of such procedures in these patients, which are partly due to the stressful nature of this dental procedure. Since stress is associated with increased blood sugar, patients with diabetes are at increased risk. Physiotherapeutic methods may be a useful adjunctive technique to correct blood sugar levels in patients (in addition to the main methods of treatment for type 2 diabetes mellitus). Our results demonstrate the advisability of using MDM therapy during both pre- and post-implantation periods in patients with type 2 diabetes mellitus to prevent an increase in blood glucose levels immediately before and during invasive medical procedures, to normalize blood glucose levels after invasive procedures, to improve the quality of life of patients in the early post-surgical period by promoting faster pain neutralization and function recovery, and to stabilize their psycho-emotional state.

It was found that 5 minutes before starting the dental procedures in patients, blood glucose levels rose, which can be explained by the development of psycho-emotional stress while awaiting the start of invasive dental procedures. These findings were confirmed by the increase in heart rate in patients compared to the initial

measurement as well as by patients' self-identification of their emotional discomfort level. Our study demonstrated the efficacy of MDM therapy in preventing this increase in blood glucose levels during dental implantation in patients with type 2 diabetes mellitus due to psycho-emotional and somatic stress. The increase in blood glucose levels caused by the situation could be decreased in patients who received MDM therapy after the first session. Our study results indicate an increase in resistance to stress factors in patients with type 2 diabetes mellitus due to MDM therapy. In particular, MDM therapy sessions contributed to preventing the development of pronounced anxiety, fear, and emotional stress while patients waited for the invasive dental procedures to start, as evidenced by the results of patients' self-assessment of their emotional discomfort level. In most cases, the abovementioned emotional phenomena were evaluated by the patients in TG-2 as being only weakly present, whereas the patients in TG-1 and RG evaluated these symptoms as being present to a moderate or severe degree.

Unlike awaiting the start of invasive dental procedures, which involves pure psycho-emotional stress, dental implantation involves two pathogenic types of stress: psycho-emotional and somatic stresses. The third measurement values (5 minutes after terminating the dental procedures) in TG-2 demonstrated the efficacy of MDM therapy in preventing the development of distress associated with both the pathogenic aspects of stress during dental implantation. The dynamics of emotional experiences in all groups was interesting. Before the dental procedures, the patients in all the groups showed equal dominance of such emotional phenomena as fear, anxiety, and emotional stress, whereas 5 minutes after completing the dental procedures, fear and anxiety were neutralized, while emotional stress values remained elevated. One hour after the completion of the dental procedures in TG-1 and TG-2 (after a session of MDM therapy), the emotional state of patients was stabilized, according to their self-identification of neutralization of fear, anxiety, and emotional stress, while in RG, the level of emotional discomfort remained elevated and demonstrated no significant differences from the previous measurement, which was correlated with blood glucose levels.

Use of MDM therapy demonstrated a significant improvement in the quality of life of patients with type 2 diabetes mellitus in the early post-implantation period as compared to patients who had not received MDM therapy as an adjunctive therapy and prophylaxis. High quality of life in patients in both the treatment groups was achieved mainly due to higher values (compared to RG) of physical functioning; reduced pain, swelling, and inflammation at the site of implantation; normalization of emotional and mental health; and improved general well-being. A direct relationship was noted between blood glucose levels, heart rate, and emotional discomfort in patients with type 2 diabetes mellitus, which may be evidence of a shared etiopathological factor of these conditions. We did not notice the limitations and side effects when MDM therapy is used in patients with diabetes mellitus.

There are indications that dental phobia may be a contraindication for dental procedures. Therefore, to eliminate anxiety in patients who require dental treatment, various techniques have been developed, such as adequate psychological and dental pretreatment (Enkling *et al*., 2013). This technique initially reduces patients' anxiety levels; however, anxiety recurs subsequently (Enkling *et al*., 2013). In our study, we demonstrated the effectiveness of MDM therapy, physiotherapy, for improving the quality of life and reducing blood glucose levels during dental implantation in patients with type 2 diabetes mellitus. The program developed by us makes it possible to achieve the normalization of the psycho-emotional state for a longer period (we used an observation period of 10 days). Thus, MDM therapy may be considered as an appropriate method for the prevention and relief of manifestations of psycho-emotional and somatic stress during dental implantation, which may be particularly useful in patients with type 2 diabetes mellitus. We think that it is rational to continue research on the use of MDM therapy in patients receiving dental treatment not only in diabetic patients but also in other diseases, the genesis of which is associated with psycho-emotional dysfunction and physiological dysfunction.

5. CONCLUSIONS:

Improving the provision of dental care for patients with type 2 diabetes mellitus is an urgent task of modern dentistry, and it is important that dentists should consider the impact of type 2 diabetes mellitus on the recovery period after dental interventions. This study sets out the experience of providing dental care to patients

with type 2 diabetes mellitus using MDM therapy. It was proved that the use of MDM therapy in a complex of procedures for dental implantation reduces blood glucose levels and heart rate after implantation, as well as improves the emotional state of patients.

In conclusion, MDM therapy can be considered as an additional component of the provision of dental care to patients with type 2 diabetes mellitus in order to improve the condition of patients.

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Table 1. *Mean blood glucose levels at different treatment stages*

Mean blood glucose levels (mmol/L)	Groups		
	TG-1	TG-2	RG
	(n = 20)	(n = 22)	(n = 23)
During the first consultation	5.5 ± 0.09	5.5 ± 0.08	5.5 ± 0.07
5 minutes before start of dental procedures	7.4 ± 0.11	6.1 ± 0.11	7.4 ± 0.11
5 minutes after completing dental procedures	9.2 ± 0.21	6.4 ± 0.09	9.3 ± 0.25
One hour after completing dental procedures	7.6 ± 0.12	5.8 ± 0.22	9.2 ± 0.25
p (t)	< 0.01	< 0.01	< 0.01

Table 2. *Mean heart rate values in the different groups at different treatment stages*

Mean heart rate (beats/minute)	Group		
	TG-1	TG-2	RG
	(n = 20)	(n = 22)	(n = 23)
During the first consultation	66.9 ± 0.81	66.7 ± 0.90	66.8 ± 0.76
5 minutes before start of dental procedures	76.1 ± 0.80	68.2 ± 0.82	75.9 ± 0.89
5 minutes after completing dental procedures	85.2 ± 0.45	70.1 ± 0.37	85.4 ± 0.39
One hour after completing dental procedures	67.5 ± 0.72	65.5 ± 0.80	68.2 ± 0.76
p (t)	< 0.01	< 0.01	< 0.01

Table 3. *Mean emotional discomfort values at different treatment stages on the four-point scale of emotional discomfort level (fear, anxiety, emotional tension) self-reported by patients*

Measurement	Index	Group			Comparisons		
		TG-1	TG-2	RG	TG-1 vs TG-2	TG-1 vs RG	TG-2 vs RG
		points	points	points	p(t)	p(t)	p(t)
5 minutes before starting dental procedures	fear	2.9 ± 0.16	1.2 ± 0.18	2.8 ± 0.12	< 0.01	> 0.05	< 0.01
	anxiety	2.7 ± 0.09	0.9 ± 0.18	2.8 ± 0.10	< 0.01	> 0.05	< 0.01
	emotional stress	2.8 ± 0.09	1.1 ± 0.06	2.8 ± 0.08	< 0.01	> 0.05	< 0.01
5 minutes after completing dental procedures	fear	0.2 ± 0.08	0.0 ± 0.00	0.2 ± 0.11	< 0.01	> 0.05	> 0.05
	anxiety	0.6 ± 0.18	0.1 ± 0.05	0.6 ± 0.18	< 0.05	> 0.05	< 0.05
	emotional stress	2.8 ± 0.13	1.6 ± 0.11	2.8 ± 0.12	< 0.01	> 0.05	< 0.01
One hour after completing dental procedures	fear	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	> 0.05	> 0.05	> 0.05
	anxiety	0.0 ± 0.00	0.0 ± 0.00	0.3 ± 0.12	> 0.05	< 0.05	< 0.05
	emotional stress	0.3 ± 0.10	0.2 ± 0.06	3.5 ± 0.12	> 0.05	< 0.01	< 0.01

Table 4. *Quality of life assessment in the different patient groups at 10 days after dental implant placement, based on the MOS SF-36 score*

Indicator	Group			Comparisons	
	TG-1	TG-2	RG	TG-1 vs RG	TG-2 vs RG
	points	points	points	p(t)	p(t)
Physical functioning	89.6 ± 0.68	90.6 ± 1.05	73.6 ± 1.12	< 0.01	< 0.01
Role functioning	88.3 ± 1.18	88.4 ± 1.14	88.0 ± 1.25	> 0.05	> 0.05
Pain	99.0 ± 1.02	99.8 ± 1.25	72.6 ± 1.72	< 0.01	< 0.01
General health	94.6 ± 1.30	95.4 ± 1.42	74.3 ± 1.65	< 0.01	< 0.01
Vitality	85.0 ± 1.25	85.6 ± 1.04	85.0 ± 1.14	> 0.05	> 0.05
Social functioning	83.4 ± 1.50	83.6 ± 1.49	83.401 ± 1.48	> 0.05	> 0.05
Role emotional functioning	99.0 ± 0.78	99.0 ± 1.01	74.6 ± 1.48	< 0.01	< 0.01
Mental health	98.9 ± 0.82	99. ± 1.54	75.6 ± 1.62	< 0.01	< 0.01

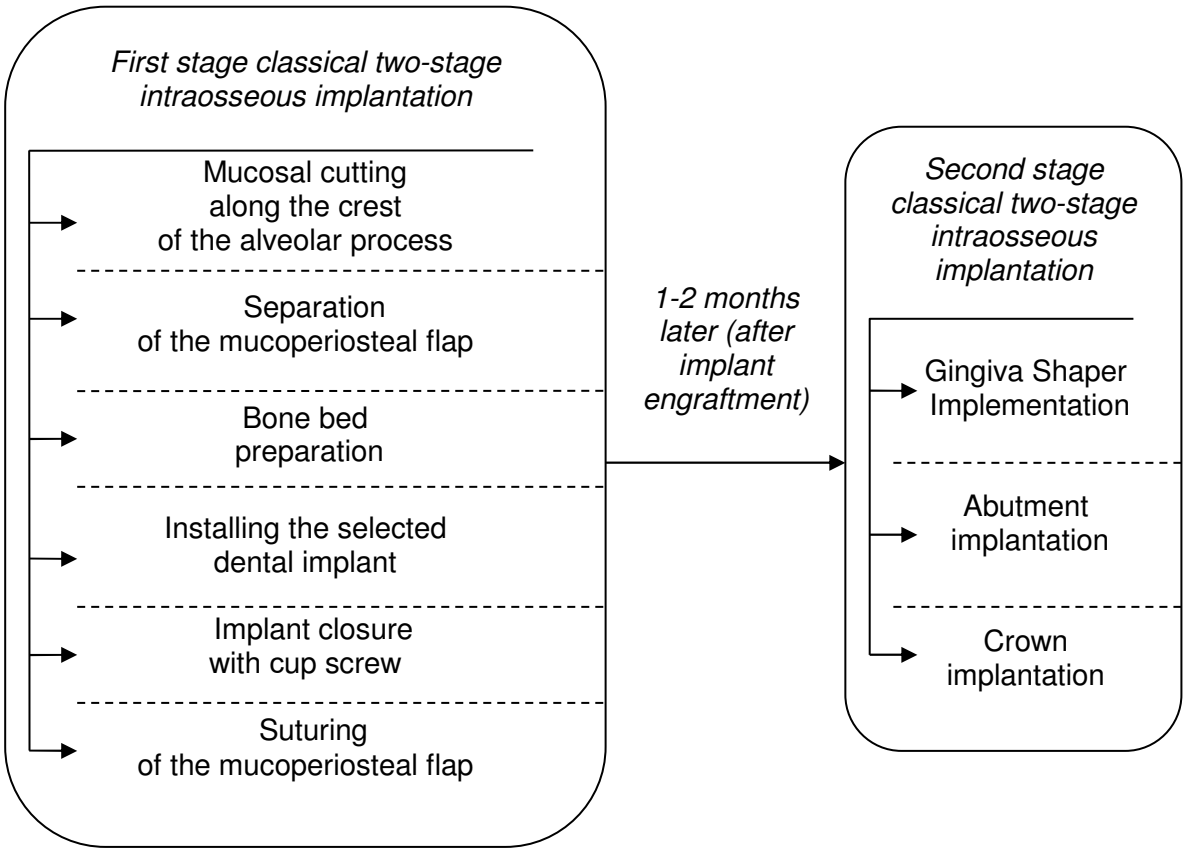

Figure 1. *Content of stage of the classical two-stage intraosseous implantation*

Figure 2. *The device "MDM-2000/1" for mesodiencephalic therapy*

Figure 3. *The MDM Therapy Procedure*

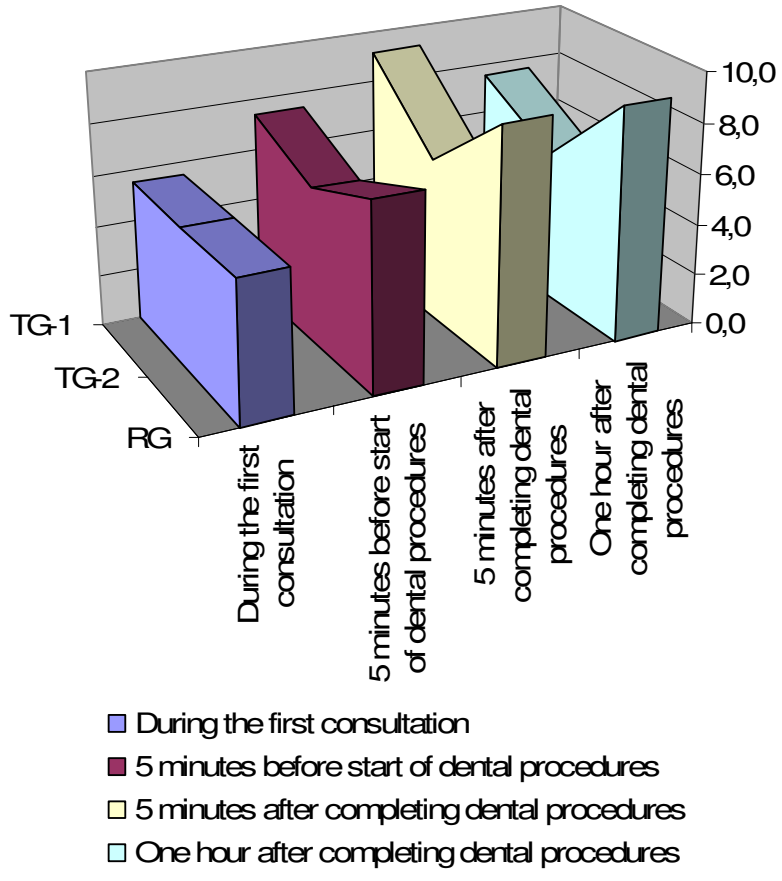

Figure 4. *Mean blood glucose levels at different treatment stages*

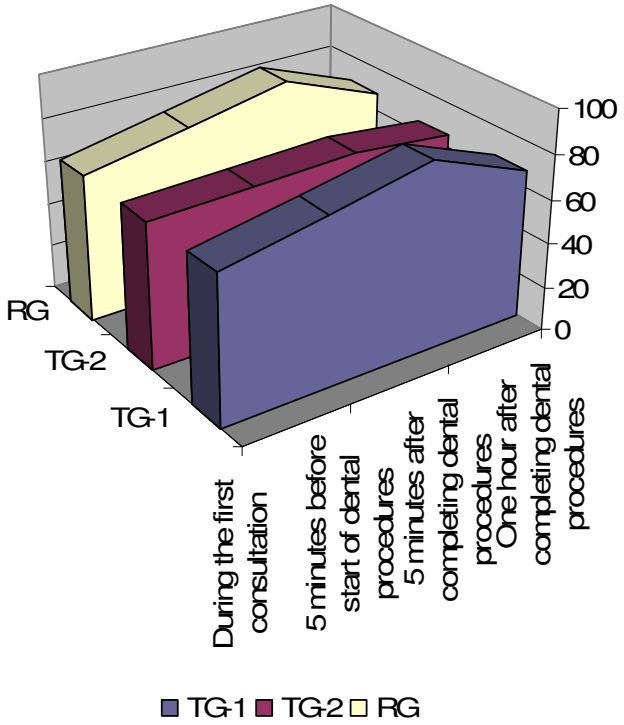

Figure 5. *Mean heart rate values in the different groups at different treatment stages*