

МЕДИЦИНСКИЕ НАУКИ

IMMUNOLOGICAL ASPECTS OF THE TEMPOROMANDIBULAR JOINT

Chikobava Sofi

PhD student

Tbilisi St. Michael Archangel Multi profile Clinical Hospital

Department of Maxillofacial Surgery

Nikolaishvili Marine

Prof. and Head of Department

I. Beritashvili Center of Experimental Biomedicine

Gogiberidze Mamuka

Professor

Tbilisi St. Michael Archangel Multi profile Clinical Hospital,

Department of Maxillofacial Surgery

ABSTRACT

The temporomandibular joint pain dysfunction syndrome (TMJPDS) is one of the most common types of facial myofascial pain syndrome. Given the above, the purpose of this work was to study the biochemical, rheological parameters of blood serum characterizing the body's response to pain and stress, by studying the content of IgA, IgM, IgG, sIg, prostaglandin E, erythrocytes aggregation, deformation of erythrocytes, plasma viscosity, Development of methods for pathogenetic treatment and secondary prevention, on the basis of the results obtained, with the use of drug and non-drug agents

Objective: to evaluate the efficiency of Biochemical Parameters of Temporomandibular Joint Pain Dysfunction Syndrome

Patients and methods: This paper presents the results of the examination and treatment of 90 patients with TMJPDS. The control group consisted of 45 people of the corresponding age and sex without signs of damage to the TMJ and myofascial pain syndrome of a different location.

Results and discussion: The full eradication of clinical manifestation was observed in the group of patients with light form of TMJPDS in 93% of cases. Two patients reported about insignificant painful sensations during chewing food and in case of hypothermia. At the end of complex treatment in a group of patients with a moderate form of TMJPDS, 69% of patients reported no pain. Six patients complained about dull pain at night. Three patients complained about the pain in the TMJ area without irradiation. Two patients reported that they did not have significant improvement. These were the patients with a ten-year-old disease record and who had severe dysfunctions of the jaw-teeth system.

Key words: Temporomandibular Joint Pain Dysfunction Syndrome (TMJPDS), biochemical and rheological parameters of blood serum.

The urgency of the problem

Temporomandibular Joint Pain Dysfunction Syndrome (TMJPDS) is one of the most common varieties of facial myofascial pain syndrome. According to the data of various authors, TMJPDS as an etiological factor of prosolalgia accounts for more than 30% of the total number of persons suffering from facial pains (Al-Belasy FA, Dolwick MF, 2007, Isong U, Gansky SA, et al 2008). Despite the more than half a century history of the study of TMJPDS, the information available in the literature about the pathogenesis of the disease is very contradictory. There are two main concepts for the development of TMJPDS: I – odonto-arthrogenic, the supporters of which believe that the main cause of the development of the disease are disorders of the dentition (Azuma T, Ito J, Kutsuki M, et al, 2009), II – myogenic, the representatives of which argue that the cause of the development of TMJPDS is the formation of trigger points in the masticatory muscles (Ikeuchi, M, Izumi, M, 2015, Serikov AA, Tolmachev 2012). There is also no consensus on the etiology of myogenic disorders among the supporters of the myogenic concept of the development of TMJPDS. The monogenic,

psychogenic, somatogenic and other causes of the formation of trigger points in the masticatory muscles are described. It is assumed that the activation of muscle trigger points occurs due to a violation of homeostasis: hypovitaminosis, disturbance of the metabolism of hormones (insulin), microelements (Sidebottom AJ. 2009, Seo, SJ, Chen, M, 2017). At the same time, there is no information in the literature about the state of the main regulatory systems that provide homeostasis: nervous, immune, and endocrine during TMJPDS and there is no description of objective criteria for diagnosing the severity of clinical manifestations of the disease.

Thus, the diversity of clinical manifestations of MNDI, the absence of generally accepted criteria for diagnosing the severity of the process, contradictions in attitudes to etiopathogenesis, and the lack of a concept of etiopathogenetic therapy, in this regard, determines the relevance of studying etiopathogenetic and therapeutic-diagnostic aspects of pain dysfunction of the temporomandibular joint.

Objectives of the study

The purpose of this study was to study the clinical features and neuro-humoral disorders in patients with pain dysfunction of the temporomandibular joint.

Research objectives include:

1. The study of the clinical features of **TMJPDS**, identifying the role of odontogenic and psychogenic factors in its development.

2. The study of the state of general and local immunity, biologically active substances to change the content of sigA, prostaglandin E in serum, in the saliva of patients with **TMJPDS** at the beginning and at the end of the course of treatment.

3. The study of blood rheological changes, as the patients with **TMJPDS** must have plasma viscosity changes due to systemic action of inflammatory processes in the parodont. Therefore, we studied the erythrocyte aggregation EAI, deformation of red blood cells EDI, hematocrit HCT, plasma viscosity.

4. Development of methods for pathogenetic treatment and secondary prevention, on the basis of the results obtained, with the use of drug and non-drug agents.

Scientific novelty

Objective criteria for the diagnosis of the severity of **TMJPDS** are proposed. For the first time, changes in the levels of sex steroid hormones in patients suffering from pain dysfunction of the temporomandibular joint were revealed. It has been shown that hyperandrogenemia occurs in individuals of reproductive age (Tlustenko VP, Kameneva LA 2013, Van Selms MK, Lobbezoo F, 2008)

It has been established that during **TMJPDS**, there is a tension of local immunity, manifested by an increase in the content of secretory immunoglobulin A in saliva and disimmunoglobulinemia 18M, at the systemic level. An increase in prostaglandin E in the blood was detected, which, in comparison with the data of psychological testing, may indicate the involvement of the central mechanisms of pain regulation during **TMJPDS**. It has been established that during **TMJPDS** immune, hormonal, and biochemical disorders have a secondary compensatory-adaptive character. A hypothetical scheme of the pathogenesis of **TMJPDS** was developed (Chen, K, Zhang, N, 2014)

For the first time the study of blood rheological changes during **TMJPDS** was conducted. Blood rheological changes are very important for regulation of inflammatory processes during the disease and detection of the risk of cardiovascular disease .

Scientific and practical value

The conducted studies expanded the understanding of the possible mechanisms for the development of **TMJPDS**, revealed the contribution of odontogenic and psychogenic factors to the etiopathogenesis of the disease.

The study of rheological changes, indicators of local and general immunity, prostaglandin E and their dynamics in the course of treatment has deepened understanding of the mechanisms of pain in **TMJPDS**.

The hypothetical scheme of the pathogenesis of the disease proposed by us allows in each case to determine the significance of its individual

components, and on this basis to develop an individual program of complex treatment.

Practical implementation

The method for diagnosing **TMJPDS** on the basis of special methods of intra-oral palpation of masticatory muscles and EMG research has been developed and introduced into practice at Tbilisi St. Michael Archangel Multi profile Clinical Hospital, Department of Maxillofacial Surgery Clinical Center. A new method of complex treatment has been proposed, including blocking of muscle trigger points, occlusion correction, relaxing therapy using a special technique, post isometric relaxation of the masticatory muscles and relaxing techniques of physical therapy (Knudsen, M, Bury, 2015)

Material and research methods

This paper presents the results of the examination and treatment of 90 patients with **TMJPDS**. The control group consisted of 45 people of the corresponding age and sex without signs of damage to the TMJ and myofascial pain syndrome of a different location tab1.

The distribution of patients by age and sex

As follows from Table 1, among the patients under the observation, women over the age of 40 prevailed, while men were 4.9 times less than women.

In accordance with the objectives of the study, patients of the main and control groups were examined, including dental, clinical-neurological and psychological, hormonal, rheological and immunological methods (Mantskava, 2014, Roitman , E.V. 2001, Sushkova M.A. 2002)

Determination of the Erythrocyte Aggregation

Index. Erythrocyte aggregation index represents the ratio of aggregated erythrocytes to the total volume of erythrocytes. We studied it using the so-called "Georgian technology".

Determination of red blood cell deformation index. The method of membrane filters (nucleopore membrane filter method), at a constant pressure (10 cm water column), determines the speed of red blood cells through a filter with the smallest 5.5 (5 microns) diameter of fibers.

Definition of viscosity. Plasma viscosity is measured at 37 C degrees with a capillary viscosimeter. Capillary diameter 1.8 mm. Plasma movement in the capillary is induced by the force of gravity, which is due to the study of plasma niveaux, about 65 mm. Any additional pressure does not play any role here. Viscosimeter calibration factor (F) is used for determining the plasma viscosity.

Dental examination

Dental examination began with a survey of patients, identifying complaints of pain in certain areas of the teeth group, other parts of the oral cavity. From the catamnesis, it was found out which factors, in the opinion of the patients, contributed to the occurrence of **TMJPDS** (traumatic tooth extraction, prosthetics, inflammatory diseases of the maxillofacial area, teeth mobility, teeth displacement due to chronic periodontitis, hypothermia).

External examination revealed asymmetry of the lower part of the face due to lateral displacement of the

lower jaw, hypertrophy of the masticatory muscles, the condition of the skin in the area of the muscles of the face and TMJ (Sembrionio S, Albiero AM, 2008).

The degree of restriction of mouth opening, the direction, the sequence and the degree of lateral displacement of the lower jaw when opening the mouth, the presence of crunch, clicking in the TMJ when opening the mouth, were evaluated. Palpation of the muscles involved in the movements of the lower jaw (superficial palpation, comparative, bimanual, revealed areas of hypertrophy, thickening of muscle tissue, he dimensions and degree of thickened areas, the pain, and areas of irradiating pain (Shimazaki Y, Saito K, 2007).

When examining the oral cavity, the state of the mucous membrane, periodontal tissues were evaluated. In case of pathological changes in the periodontium, the prevalence and the degree of gingival atrophy, bleeding, depth of the periodontal pocket by groups of teeth, mobility, and displacement of teeth were evaluated. Defects of dentition with partial secondary adentia were evaluated according to Kennedy classification. Particular attention was paid to the presence of the Popov-Godon's phenomenon, a decrease in occlusal height as a result of the pathological abrasion of hard dental tissues, the displacement of teeth in chronic generalized periodontitis. In the presence of fixed or removable prostheses, their condition and functional suitability were assessed (Talaat, W, Haider, M, 2016).

An x-ray study of the temporomandibular joints was also carried out to identify organic changes in the bone tissue and the topography of the elements of the joint on the right and left. Visual analysis of radiographs evaluated the size of the joint space, the condition of the bone tissue of the articular surfaces. The results of the dental and X-ray examination were recorded in a special map developed in the laboratory of neuro dentistry at the Research Institute based at MMSI and rheological changes.

Neurological and psychological examination

The scope of the neurological and psychological examination is determined taking into account the need to study the peripheral neuro-motor apparatus of the maxillofacial area and condition of emotional sphere of patients with **TMJPDS**. Patients in both groups were examined by a neurologist. In order to study the state of the peripheral innervation of the masticatory muscles, an electromyographic examination was carried out, which involved recording the total interference EMG of the masticatory muscles on both sides and determining the duration of the latent period of the submental reflex (Tlustenko VP, Kameneva LA, 2013). The work was performed on the electromyograph M 400 of the company "Medicor".

The pain scale of (was used to identify the features of pain syndrome during **TMJPDS** and the dynamics of its components in the course of treatment. The results were analyzed on the basis of the number of words used by patients in individual pain assessment.

Evaluation of the state of the emotional sphere was carried out with the help of psychological testing using tests of reactive and personal anxiety by C. Spilberger

(in points) and a test of differentiated self-assessment of the functional state (self-activity-mood-setting "SUN" V. A. Doskin et al., 1987). Psychological Testing of Patients with **TMJPDS** at the Beginning of Treatment Course (I). and in the End (II) tab2..

According to this table, in the process of the complex process of treatment of **TMJPDS** in groups with different degrees of severity, the positive dynamics of reactive and personal anxiety indicators are noted. In the patients with the light and moderate severity of **TMJPDS**, the levels of anxiety scales are approaching the norm and improving in the group with severe form.

Hormonal-immunological, biochemical and rheological studies.

The following study was conducted concerning blood tests. As is known from the literature (Reddy VGR, Rao CB, Krishnan G 2007) in patients with **TMJPDS**, there is an increased risk of inflammatory processes, which are very important because these processes cause the development of periodontitis and, consequently, lead to the risk of cardiovascular diseases. There is evidence that inflammatory processes and rheological changes are associated with significant atherosclerotic disorders of large-caliber arteries (Lepilin AV, Konnov VV 2010). Therefore, this topic is relevant because it was first studied in this study, so we decided to study the rheological changes in the blood of patients with mild and moderate severity of **TMJPDS**. Table N3.

As shown in the table, the aggregation of erythrocytes is statistically increased, and the deformation, on the contrary, is reduced, is statistically significant. Thus, evaluations of the data showed that rheological changes in blood occur in **TMJPDS**, which results in an increase in plasma viscosity and erythrocyte aggregation and a decrease in red blood cell deformation. Consequently, there is a change in rheology and blood coagulation on the background of vascular endothelial dysfunction, and this is a serious problem, and these patients who have the above problems can be considered in the group among patients at risk of developing cardiovascular factors. Research on rheological parameters has not yet become widespread in Georgian dental clinics. In this paper, we want to show how significant are the rheological changes in the blood, if only to determine the risk group of the disease (Knudsen, M, Bury, 2015).

The content of immunoglobulins in serum and secretory immunoglobulin sigA1 and prostaglandin E (PG) in saliva in patients with **TMJPDS** was also studied. The dynamics of immunity and data of prostaglandin E at the beginning and at the end of the course of complex treatment are shown in table No. 4.

As indicated in Table 4, before the treatment, in the patients with **TMJPDS**, the decrease in immunoglobulins A, M, G (Disimmunoglobulinemia) in blood serum and the increase in secretory immunoglobulin A in saliva and prostaglandin E in blood were noted. After conducting a complex treatment course, the level of immunoglobulins approached the level in control group. Local immunity tensions decreased (secretory immunoglobulin sigA1

in saliva), and the concentration of prostaglandin E decreased too, that corresponds to changes in rheology.

The comparison of the dynamics of clinic-immunological and biological data shows normalization of the listed parameters of the homeostasis without the use of special (hormonal, immune, etc.) correction in the treatment of a complex treatment course in patients with **TMJPDS**. This confirms the secondary, adaptive nature of the dysfunction during **MJPDS** and supposedly not only the peripheral but also the central mechanisms of forming the pain syndrome in the patients of this group (Shimazaki Y, Saito K. 2007, Sidebottom AJ. 2009).

All the patients under the observation underwent the complex pathogenetical treatment by an individual program which included:

- 1) Severe pain syndrome eradication;
- 2) Determining and elimination of the odontogenic causes (occlusion correction, prosthesis) of the disease;
- 3) Treatment course with tranquilizers and tricyclic antidepressants (taking into account the results of analyzing the components of the pain syndrome according to psychological testing and visual-analog scale);
- 4) Developing an individual program for the prevention of complications.

1. The eradication of the painful syndrome was performed by taking into consideration the possible mechanism of its formation: the balance of sensory flows from muscle trigger points (**TP**) (0,5% solution of Novocaine or the skin irrigations with chlorine ethanol in the **TP** area were administered) and activation of GABAergic blocking systems at the level of *spinal trigeminal nucleus* of trigeminal nerve (the patients received a GABAergic antagonist Baclofen 10 mg at 9 and 21 pm, according to the pharmacokinetics of the drug). In order to reduce the dystrophic process in the muscular hypertonus areas, patients underwent the therapy with a special infrared helium-neon laser that included local muscle **TP** irradiation on both sides of the upper-neck sympathetic node. This method of laserotherapy has a pain easy effect, anti-inflammatory effect that accelerates local reproductive processes. (Briskin B., Polonsky A.K. and co-authors, 1990)

2. Stomatological treatment was carried out taking into account possible etiological factors of the pathology of **TMJPDS** of the jaw-tooth system. The capacity of dental assistance was determined individually. The selective milling-polishing of the teeth to remove the occlusive disorders that prevent the contact of teeth in the central frontal and lateral dental occlusions and to avoid the Popov-Godon phenomenon. Orthopedic correction was needed for normalization of the occlusion height, for prosthesis during partial or full secondary adentia.

3. Based on the results of psychological testing and visual-analogical test and taking into account of pain syndrom analysis, the patients underwent the course of treatment with tranquilizers and tricyclic antidepressants in therapeutic doses for 3-4 weeks.

4. Individual Program for the prevention of complications was designed to create physiological

stereotypes of the lower jaw movement which included special techniques of relaxation and healing physical therapy that were undertaken at the beginning of the treatment course under the supervision of the doctor, and subsequently by patients independently.

The results of treatment of patients were as follows:

The full eradication of clinical manifestation was observed in the group of patients with light form of **TMJPDS** in 93% of cases. Two patients reported about insignificant painful sensations during chewing food and in case of hypothermia. At the end of complex treatment in a group of patients with a moderate form of **TMJPDS**, 69% of patients reported no pain. Six patients complained about dull pain at night. Three patients complained about the pain in the **TMJ** area without irradiation. Two patients reported that they did not have significant improvement. These were the patients with a ten-year-old disease record and who had severe dysfunctions of the jaw-teeth system.

Conclusions

1.1. Active Trigger Points (**ATP**) in the masticatory muscles are the main pathogenic factors ($P < 0,01$) of pain dysfunction syndrome (**PDS**) of the temporomandibular joints. Odontogenic dysfunctions cause 67% of cases of **ATP** activation, while 33% are caused by psychogenic dysfunctions.

2. In 75% of cases the odontogenic reasons for the development of **TMJPDS** ($P < 0,05$) is the occlusion disharmony and partial secondary adentia with unilateral chewing habit.

3. The most frequent localization of **TP** (in 89% of observations) during the pain dysfunction of the temporomandibular joint is the anterior part of the masticatory muscles and the posterior part pterygoid muscle ($P < 0,05$).

4. During **TMJPDS** the Immune (increased sig A amount, dysimmune globulinemia in blood serum) and hormonal (hyperandrogenia in the reproductive age and menopause - hypoandrogenia) have a secondary compensation-adaptive nature and do not needs special correction.

5. During **TMJPDS**, blood rheology, erythrocyte aggregation, deformation, blood viscosity and hematocrit are important for determining the risk of patients and, therefore, their treatment, as well as in terms of the cardiovascular system.

6. The essential condition for the effective treatment of the complex treatment during the development of osteonegenal mechanisms of **TMJPDS** is the correction of the occlusion dislocation by selective milling-polishing and prosthesis of teeth in case of secondary or full adentia ($P < 0,05$).

7. Psychological testing allows us to determine the nature of emotional disorders during the **TMJPDS** ($P < 0,05$) and can be considered as an objective criterion of adequate selection of psychotropic drugs.

References

1. Azuma T, Ito J, Kutsuki M, Nakai R, Fujita S, Tsutsumi S. (2009); Analysis of the mandibular movement by simultaneous multisection continuous ultrafast MRI. Magn Reson Imaging 27: 423-33.

2. Al-Belasy FA, Dolwick MF. (2007) Arthrocentesis for the treatment of temporomandibular joint closed lock: a review article. *Int J Oral Maxillofac Surg*;36(9):773–82.
3. Chen, K, Zhang, N, Ding, L. (2014) Early intra-articular injection of alendronate reduces cartilage changes and subchondral bone loss in rat temporomandibular joints after ovariectomy. *Int J Oral Maxillofac Surg* ; 43: 996–1004.
4. Isong U, Gansky SA, Plesh O. Temporomandibular joint and muscle disorder-type pain in U. S. adults: the National Health Interview Survey. *J Orofac Pain* 2008; 22 (4): 317–322.
5. Ikeuchi, M, Izumi, M, Aso, K. (2015); Effects of intra-articular hyaluronic acid injection on immunohistochemical characterization of joint afferents in a rat model of knee osteoarthritis. *Eur J Pain* 19: 334–340.
6. Knudsen, M, Bury, M, Holwegner, C. (2015) Effect of dexamethasone prodrug on inflamed temporomandibular joints in juvenile rats. *Arthritis Res Ther* 17: 267.
7. Lepilin AV, Konnov VV, Bagaryan EA, et al. (2010). Clinical manifestations of pathology of temporomandibular joints and masticatory muscles in patients with teeth occlusion and teeth row disturbances. *Saratov Journal of Medical Scientific Research*; 6 (2): 405–410. Russian.
8. Mantskava, M., (2014). Hemorrhagic shock and stress-cause and consequence of hemorheology disturbances on the example of the changes in erythrocyte aggregation. *Journal Stress of physiology and Biochemistry*, 10(2), 238-246.
1. Reddy VGR, Rao CB, Krishnan G. (2007) Temporomandibular joint arthrocentesis—revisited. *Int J Oral Maxillofac Surg*;36(11):1066–7.
2. Roitman, E.V. (2001). Change the rheological properties of blood and osmotic resistance of red blood cells in the activation of free radical processes /E.V.Roytman, I.I.Dementeva- *Saratov № 1 28*.
3. Sushkova M.A. (2002). Rheology of blood and physico-chemical properties of red blood cells in healthy individuals and patients with chronic allergic dermatoses before and after EHF-therapy /M.A.Sushkova//PhD. *Saratov. – № 2 23*.
4. Serikov AA, Tolmachev (2012); The methods for diagnosing and estimating the treatment effectiveness of the temporomandibular joint diseases Russian. *Medline.ru* 13 (3): 597–607
5. Sembronio S, Albiero AM, Toro C, Robiony M, Politi M. (2008). Is there a role for arthrocentesis in recapturing the displaced disc in patients with closed lock of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*;105(3):274–80.
6. Shimazaki Y, Saito K, Matsukawa S, et al. (2007) Image quality using dynamic MR imaging of the temporomandibular joint with trueFISP sequence. *Magn Reson Med Sci*; 6: 15-20.
7. Sidebottom AJ. Current thinking in temporomandibular joint management. (2009) *Br J Oral Maxillofac Surg*;47(2):91–4.
8. Seo, SJ, Chen, M, Wang, H. (2017). Extra- and intra-cellular fate of nanocarriers under dynamic interactions with biology. *Nano Today* ; 14: 84–99.
9. Talaat, W, Haider, M, Al Kawas, S. (2016); Chitosan-based thermosensitive hydrogel for controlled drug delivery to the temporomandibular joint. *J Craniofac Surg* 27: 735–740.
10. Tlustenko VP, Kameneva LA, Ponomarev AV, et al. (2013). The device for registration of vertical movements of the bottom jaw: patent Russian Federation for useful model № 133709, 27.10..
11. Van Selms MK, Lobbezoo F, Visscher CM, Naeije M. (2008) Myofascial temporomandibular Disorder pain, parafunctions and psychological stress. *J Oral Rehabil*; 35 (1): 45–52.