The Study of Biochemistry on Myorelaxation of Manducatory Muscles by Influence of Botulinic Toxine in the Context of Oral Rehabilitation in SDSS Patients

LAURA ELISABETA CHECHERITA[1], OVIDIU STAMATIN[2], AURORA CONSTANTINESCU [3], ELENA MIHAELA CARAUSU[4], BOGDAN PETRU BULANCEA[2]*, IULIAN COSTIN LUPU[4]*, DANIELA MANUC[5]

[1] Grigore T. Popa University of Medicine and Pharmacy, Department of Odontology-Periodontology and Fixed Prosthesis, 16 Universitatii Str., 700115 Iasi, Romania

[2] Grigore T. Popa University of Medicine and Pharmacy, Department of Oral Implantology, 16. Universitatii Str., 700115 Iasi, Romania

[3] Grigore T. Popa University of Medicine and Pharmacy, Department of Neurology, 16. Universitatii Str., 700115, Iasi, Romania

[4] Grigore T. Popa University of Medicine and Pharmacy, Faculty of Dental Medicine, Discipline of Management and Public Health, 16 Universitatii Str., 700115 Iasi, Romania

[5] Carol Davila University of Medicine and Pharmacy, Faculty of Dental Medicine, Discipline of Public Health, 8 Eroii Sanitari Str., 050474 Bucharest, Romania

Hypertonias, observed at stomatognatique level, pathologic expressions of striated musculature may have the opportunity of a large palette of therapeutical ways, so clasics as drugs therapy, and so well the modern therapy injection with botulinic toxin, type A Dysport. The choice upon the type of myorelaxation treatment proper to each case depends upon the severity of manifestations at muscular level, frequently a mixed therapy being the option of choice, based on the superposition of different treatment means. The use of botulinic toxin in the treatment of stomatognatic system dysfunctions is without the morphological impact quickly installed therapeutic effect and it has only short term effects.

Keywords: hypertonias, SDSS treatment, drugs, botulinic toxin, biochemistry.

The systemic approach of dental therapy implies the follow-up of multiple, complex correlations between the elements of stomatognatic system and human body in its entirety. Based on the treatment rules in time developed, muscular therapy presumes an emergence treatment, a prophylactic treatment, a curative treatment (etiologic and symptomatic), but also a maintenance treatment, with the aim of preserving the positive results obtained as a consequence of curative treatment, and secondary effect prevention at the level of other elements of stomatognatic system. In the last decade, Dysfunctional Syndrome of Stomatognathic System (SDSS) became an important problem of public health in the domain of Dental Medicinedue to the increasing trend of this pathology of prevailing once with aging (from 10% in the adults to almost 40% inpeople of 65 years old and over). Thus, SDSS representsa current and a much debated problem, with large perspectives in the research regarding incidence and\ prevalence, etiologic factors, pathophysiology, risk factorsand, not the least important, symptomatic and etiologic treatment [1].

Hypertonias represent pathologic debilitating states that impress and require a whole therapeutic arsenal for their alleviation or obviation. Muscular relaxation, integrating part of curative treatment of mandibular-cranial malrelation, offers the possibility of reconditioning or establishing of new neural-muscular engrams, the aim of our study being the establishment of action and efficiency of medicinal myorelaxation methods on short, or long, term, which are meant to conduce to the foundation of myorelaxing treatment that would finally determine the equilibration of stomatognatic system [1].

The study of experimental clinical type, which offers the highest reliability degree for the results, according to the above-mentioned aims, was developed in a 22-patient sample exhibiting the impairment of muscular activity, and were attending the Department of Neurology, Grigore T. Popa University of Medical and Pharmaceutical Sciences of Iasi, between January 1st - December 1st, 2006; the evaluation regarding the objectives pursued in our study being carried out during the neural-motor recovery treatment, but also during the hospitalization period. The results achieved constituted the source for a data base, statistical analysis of the results was accomplished by means of Microsoft Excel software package.

Gender distribution of study sample included 15 females and 7 males, ages between 36 and 79 years, which were exhibiting signs and symptoms of muscular dysfunction, with a keen interest regarding the general affectation and that of stomatognatic system, with a concern for the rehabilitation of the affected function of stomatognatic system. The selection was deliberated, in order to avoid the drop-outs in the study.

The inclusion criteria for patients taking part in our study were the following: the presence of muscular pain at the level of cephalic extremity and the presence of muscular spasms in the same region, associated or not by other spasticities.

Exclusion criteria for our patients were represented by the presence of joint affectation, of the third molar pathology (pericoronitis), osteoarthritis or neoplasms.

Myorelaxants represent a heterogeneous group of substances that act at the level of nervous system or directly at the level of the muscle, reducing muscular contraction determined by overstress, by an inflammation, by a trauma as an antalgic reaction; they are substance used in order to reduce the tonus of striated musculature [2].

We have injected botulinic toxin at the level of spastic muscles (Dysport complex), the protocol being the one established by the manufacturer: 500ui (1.0mL), divided

* email: bulanceabogdan20@yahoo.com; lupu_costin @yahoo.com

and administered on 2 or 3 of the most active muscles of the neck. We have used Dysport vials, solved in 2.5mL 0.9% sodium chlorate. We have obtained a solution with 200ui/mL Dysport per each vial. For injection we have used insulin syringe, with a-traumatic needles, with an intramuscular injection.

The following images offer a better illustration of the infiltration zones from the level of muscular insertions and mass.

For each subject, we have recorded the site of injection on an injection chart, as in the following map, on which the injection date is specified, for reasons of applied treatment precision. Post-injection effect initiated within 48 hours after the injection, with an efficiency peak at approximately 2 weeks.

The duration of the effects varied, in approximately 9-10 weeks, a new injection being required. The work protocol of the manufacturer allows a maximum of 4 injections in a year. The secondary effects were dysphagia and dysphonia; the effects were alleviated after 2-3 weeks.

Results and discussions

The degree of manducatory musculature affliction in our sample subjected to study is highlighted in the following figures 1 - 4.

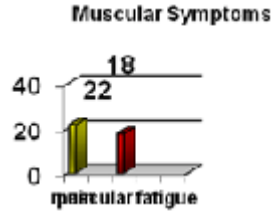

Fig. 1. Muscular symptoms affliction in our sample subjected (in ordinate)

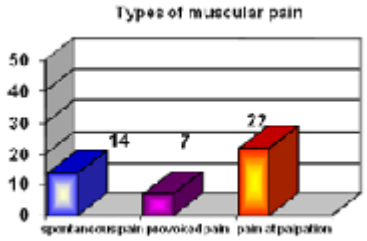

Fig. 2. Types of pain affliction in our sample subjected (in ordinate)

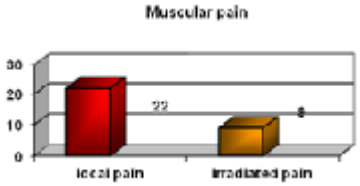

Fig. 3. Muscular pain affliction in our sample subjected (in ordinate)

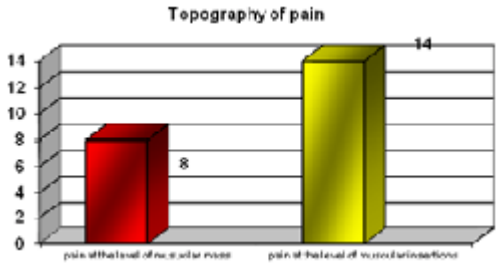

Fig. 4. Topography of pain affliction in our sample subjected (in ordinate)

As such, from the total of patient sample taking into study, 22 of these accused as primary muscular symptom the pain, 18 patients accusing muscular fatigue. From the multitude of muscular signs and symptoms, muscular pain has a higher frequency, with spontaneous manifestation, on touching or provoking.

Spontaneous manifested pain (14 cases) is difficult to be related with a specific etiological factor.

It is mandatory to examine the stomatognatic system musculature in systemic context, this fact being emphasized by the pain irradiation patterns, as Travell has established [3].

The assessment of muscular pain intensity has encountered many obstacles for each patient, pain threshold being different. The evaluation of the pain always implies a subjective side; it possesses a multidimensional character, the subjectivity being determined by the professional developing the examination, but also by the patient.

The presence of muscular pain was frequently observed at the level of muscular insertions, but for 8 patients, it has been distinguished at the level of muscular mass.

The medicinal treatment of dysfunctional syndrome is complex and implies the use of many classes of drugs (tables 1 and 2).

Table 1

DRUG CLASSES USED FOR CHRONIC MUSCULAR-SKELETAL PAIN

Drug classes used for chronic muscular-skeletal pain						
Non-narcotic analgesics	Non-narcotic analgesics	Narcotic analgesics	Muscular relaxants	Tranquilizers	Sedatives	Anti-depressives
Aspirin	Propoxifen	Codeine	Carisoprodol	Diazepam	HCl Flurazepam	Imipramine
Acetaminophen	Pentazocin	Meperidin	Baclofen	Drenzodiazepin	Meprobamat	Amitryptiline
Indometacin		Fentanyl	Methocarbamol	Meprobamat	HCl Promethazine	
Ibuprofen		Oxycodone	Diazepam		Metaqualone	
Naproxen		Morphine	Midocalm			
		Methadone				
		Hydromorphone				

Emergency treatment	Prophylactic therapy	Curative therapy
Infiltration with boicil forte	Dento-maxillary anomalies	Sedatives, hypnotics, majore and minor tranquilizers
Applicationswith ethyl clorides	Muscular junction anomalies	Centrally acting myorelaxants (mefenezina)
Administration of novocaina, xilina	Prophylaxis of tics and vicious habits	Blocking the neuro muscular junction (curtain derivates),succinylcholine)
Muscular infiltration	Ortodontics theraphy	Infiltrations with xylin at spasm muscles
	Management of odonta-lesion, parodontal ,surgical, mobile and fixed prosthetical treatment	Acupuncture
	-	Boicil forte

Table 2

TYPES OF TREATMENT AT SDSS PACIENTS IN CONTEXT OF ORAL REHABILITATION [4]

Myorelaxants with local action

Botulinic toxin represents the newest and the most modern treatment of myorelaxation, used with a cosmetic aim, but also in the treatment of stomatognatic system dysfunctions associated with muscular spasms or migraines. Today, 7 types of botulinic toxins have been discovered, and their action is being studied starting with 18th century, in its role of pathogenic agent in botulism development [5]. It was used for the first time in therapeutic aims in 1977, in order to treat a patient with strabismus. Today, cosmetics and neurology benefit equally from the temporary paralysis induced by this toxin activating by means of producing a local temporary cholinergic de-innervation [6].

A, B and E serotypes (of the seven known) are linked to the possibility of inducing botulism (fig. 5).

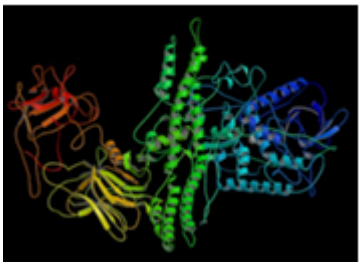

Fig. 5. 3D structure of botulinum toxin

We have used in our study the serotype A (Botox, USA, Dysport, Europe) because this type is a hemagglutinine complex, purified and stable, therapeutically used in blepharospasm treatment, and the treatment of other spasticities.

Type A exhibits an increased efficiency, has a longer term action, a specific inhibitory activity and a quick and reversible paralysing effect [7].

The actually accepted hypothesis implies a three-stage process, followed by the re-establishment of neural-muscular transmission.

Type A botulinic toxin is associated with the terminal buttons of motor plate axon (through the heavy chain, which is selective for cholinergic nervous terminations), being internalized through receptor-mediated endocytosis. Following the internalization by active transport, the light chain (which contains a domain that blocks the synaptic transmission) is released in terminal button cytoplasm [8].

The botulinic toxin does not affect the synthesis or deposing of acetylcholine, or the electric impulses along the nervous fibre. The effect (the paralysis) installs quickly and the local potentials of plate diminish within a few hours following the injection with Type A botulinic toxin. Regardless, a delay in the development of clinical effects was being noticed; this could be the result of spontaneous release of acetylcholine or the inhibition of a limited number of motor plates [9].

The affected neural-muscular joints are permanently blocked, and after a few days the *synaptic remodelling* by means of new motor plates (through new terminal buttons development) begins, so the muscular activity is gradually re-established (reaches the normal in 3-6 months) [10]

Within our study group, we have observed that 7 patients were exhibiting spasmodic torticolis; from these, 6 were women, and 1 man, mean age: 37.8 years, 7 patients were exhibiting hemifacial spasm (6 women and 1 man, mean age: 56.2 years), 5 patients were presenting blepharospasm (1 woman and 4 men - mean age: 64.8 years), and other 3 patients were presenting other spasticities (one case of infantile chronic encephalopathy, one case of multiple sclerosis paraplegic form in triple flexure and another case of paraplegic form in triple flexure following transitional cell-carcinoma (TCC) with F right haemorrhage and operated dilaceration), mean age: 40.6 years (fig. 6).

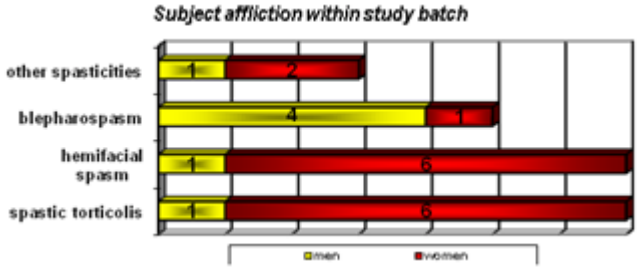

Fig. 6. Subject affection within study batch

We have recorded the presence of torticolis in a case of head distony within DHL, in 3 patients which presented post-encephalitic distony, and in 3 patients, the establishment of the cause was impossible to determine (idiopathic torticolis).

Despite the fact that studies from literature show that the malady is more frequent after the age of 50, the study conducted by the authors demonstrated a mean age of affected subjects of 37.8 years.

Hemifacial spasm of the 7 subjects was induced by *a frigore* facial paralysis. It is considered to be a tonic or clonic contracture of the interior innervated by facial nerve.

Blepharospasm is a distony located at the level of orbicularis oculi muscles [11]; we have observed this condition in 5 of our cases, due to the secondary post conjunctive effects. Involuntary contractions of eyelid muscles are taking place that determine palpebral slit between a few seconds to several minutes. This blepharospasm was singularly seen in one patient and associated with Hemifacial spasm in other four patients (table 3).

Table 3

THE RESULTS OBTAINED AT THE LEVEL OF STUDY GROUP FOLLOWING THE POST-TREATMENT EVALUATION

Number of patients	*Score (0-9 scale)*
1	8
3	7
3	6

In the evaluation of clinical results, we have used the classification based on Soulayrol et al., 1993 [12]. We have found that the best evaluation score was obtained when the dystonia had a high intensity; the duration of efficiency does not exceed three months, pain was completely suppressed, the application of Dysport injection immediately after the installation of clinical phenomena generates an assessment score better than on old manifestations, and even if the short-term dystonia is not completely suppressed, the alleviation of pain confers psychological and physical comfort.

We have recorded no secondary effect. The hemifacial spasm, affection with spontaneous aggravating tendency, more frequent on the left side, with great functional and aesthetic discomfort, and with low tolerated and of little efficiency drugs, was treated in our study batch, before the botulinic toxin treatment, with carbamazepine and benzodiazepine, their efficiency being low and associated with the recurrence tendency of the illness [13].

Applying type A Dysport botulinic toxin was accomplished in conformity with the working protocol established by the manufacturer, similar to the treatment for unilateral blepharospasm (table 4).

We have seen that all our patients have presented at least one seizure of *a frigore* paralysis, for which they have

Table 4

THE RESULTS AT THE LEVEL OF STUDY BATCH OBTAINED FOLLOWING THE AFTER-TREATMENT ASSESSMENT

Number of patients	*Score (0-7 scale)*
1	*6*
3	*5*
3	*4*

received a treatment with Carbamazepine or Clonazepam, but without efficiency; the amelioration following Dysport injection aims mostly to the upper half of the face, and in a smaller extent, the lower side, the efficiency of treatment is satisfactory and lasts for a maximum of three months. As a side effect of treatment, we have observed a grade II palpebral ptosis that occurred after two weeks and lasted around 10 days.

The score for the assessment of treatment efficiency for blepharospasm and Hemifacial spasm based on Soulayrol et al. is specific. In the treatment of bilateral blepharospasm an initial dose of 120 u per each eye is injected (fig. 7 and table 5).

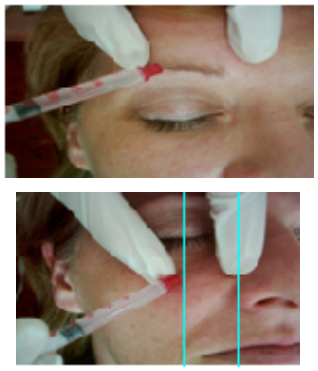

Fig. 7. The technic of administration substances in blepharospasm and hemifacial spasm

Table 5

THE RESULTS AT THE LEVEL OF STUDY BATCH OBTAINED FOLLOWING THE ASSESSMENT AFTER TREATMENT

Number of patients	*Score (0-7 scale)*
4	*5*
1	*4*

Based on the aspects presented above, we have observed the alleviation with more than 50% of the symptoms, no side effects, and the patient which presented the score 4 only, had also a psychogenic component, left untreated, aspect that has determined an amelioration on a shorter period of the symptoms.

The objective of treating other spasticities with botulinic toxin was the mediation of recovery procedures; we have observed the alleviation of the pain determined by the abnormal contracture in a long period of time, but the treatment requires large doses, because it can be applied on groups of muscles with great volume (table 6).

Table 6

THE RESULTS AT THE LEVEL OF STUDY BATCH OBTAINED AS A RESULT OF POST-TREATMENT EVALUATION

Number of patients	*Score (0-7 scale)*
3	*5*

Administration of botulinic toxin solution at the level of cephalic extremity, including the level of stomatognatic system musculature, is to be developed in specific sites.

In this type of cases in the context of oral rehabilitation the prosthetical treatment was established at 75.36% of the cases. The patients received treatment by fixed prosthetic means, conjunct in 34.78% of cases and the remaining received mixed treatments, fixed and mobile at the rate of 42.02%, the rest of removable dentures 24.64%, thus restoring the morphological and functional the dental arches, thereby restoring the homeostasis of the stomatognathic system.

Quickly installed therapeutic effect, side reactions reduced in the conditions of adequate administration, with reversible effects and diminished hepatic and renal toxicity, the absence of dependency or of cumulative phenomena, these are only a few of the objectives that a dental specialist must follow in selecting the type of medicinal substance used in muscular dysfunctions at the level of stomatognatic system. Although, the onset can be done on one element of the stomatognatic system further homeostasis disorders trigger the other elements, which can be improved in saline aerosol environments [14-19].

Conclusions

Based on the results obtained, the following conclusions can be drawn:

Hypertonias are pathologic expressions of striated musculature that determine phenomena of functional motor impotency. Based on their characteristics, hypertonias can be reversible and irreversible. Regardless their origin and manifestation, they are debilitating, so the study of the action and interaction mechanisms of myorelaxants reveals the importance of this group of drugs for the pharmacotherapy [20].

Muscular relaxation means are diverse, from myorelaxation therapy with the help of various medicinal substances, by psychotherapy, the prosthetic therapy of occlusive interception and re-equilibration, to various physical means, adjunct to the ones already listed. The choice upon the type of myorelaxation treatment proper to each case depends upon the severity of manifestations at muscular level, frequently a mixed therapy being the option of choice, based on the superposition of different treatment means [21].

Drugs that relax the striated musculature represent a heterogeneous grouping that acts at different levels through different and intricate mechanisms and it is difficult to circumscribe all of them by means of single criteria [22].

It is possible that a convenient myorelaxation to be achieved through the association of myorelaxants with various action mechanisms that could confer an additive or augmentative effect [23].

The use of botulinic toxin in the treatment of stomatognatic system dysfunctions represents a modern means for the rehabilitation of muscular functions, without the morphological impact, but, unfortunately, it has only short term effects.

Myorelaxation treatment is mandatory effected bearing in mind the stage-by-stage progress and within the rules of therapeutic diagram established and used within Department of Dental Prosthetics, but never singularly applied. Only in these conditions, can we talk about the rehabilitation of stomatognatic system musculature function. Applying of single therapeutic method acting by a single mechanism begins insufficient for muscular relaxation, the etiologic treatment being sustained and improved by means of symptomatic therapy which will create the conditions necessary for relaxation. The association of these treatments is preferred over the monotherapy [24-29].

Within the investigated patients satisfactory results were obtained: from the total remission of muscular symptoms (pain, the restriction of mouth opening, muscular spasm, muscular hypertonia, the alteration of mandible dynamics trajectories), partial remission of the symptoms up to no alteration of the symptoms. On short term, one can observe that the best results were recorded in patients on which

the relaxation therapy by means of etiologic therapy was associated with the symptomatic one [30-32].

References

1.COSTEN, J.B., Ann. Otol. Rhinol. Laryngol.,**106**, 1997, p. 805.
2.AL HAMDAN E.M., ALGHERYAFI A.M., AL-GHAREEB F.J., ASHRI N.Y., J Cosmet Laser Ther., **15,** no. 1, 2013, p. 46.
3.De BOEVER, J.A., CARLSSON, G.E., KLINEBERG, I.J., J. Oral Rehabil., **27,** no. 5, 2000, p. 367.
4.KIM J., Otol. Neurotol., **34**, no. 2. 2013, p. 319.
5.De BOEVER, J.A., CARLSSON, G.E., KLINEBERG, I.J., J. Oral Rehabil., **27**, no. 8, 2000, p. 647.
6.EBRAHIMI, M., DASHTI, H., MEHRABKHANI, M., ARGHAVANI, M., DANESHVAR-MOZAFARI, A., J. Dent. Res. Dent. Clin. Dent. Prospect. A, **5**, no. 4, 2011, p. 123.
7.GATCHEL R.J., TURK, D.C., Perspectives on pain: a historical overview, in R.J. Gatchel & D.C. Turk (Eds.), Psychosocial factors in pain: critical perspectives. Guilford Publications, Inc., New York, 1999, p. 3.
8.PARK, D.I., SHIN, H.M., LEE, S.Y., LEW, H., Acta Ophthalmol., **91**, no. 2, 2013, p. e108.
9. CONSTANTINESCU, A., POPESCU, C. Aplicaþii practice privind tratamentul cu toxina botulinica- Referat, Spitalul de Recuperare Iasi, februarie-aprilie 2007.
10.LEE, M., MONSON, M.A., LIU, M.T., REED, D., GUYURON, B., Plast Reconstr Surg., **131**, no. 4, 2013, p. 751.
11.SHEEN-OPHIR, S., ALMOG, Y., Harefuah., **152,** no. 2, 2013, p. 98.
12.PERSAUD, R., GARAS, G., SILVA, S., STAMATOGLOU, C., CHATRATH, P., PATEL, K., JRSM Short Rep., 4(2). 2013, p. 10.
13.GANCEVICIENE, R., LIAKOU, A.I., THEODORIDIS, A., MAKRANTONAKI, E., ZOUBOULIS, C.C., Dermatoendocrinol., **4**, no. 3, 2012, p. 308.
14.SANDU, I.G., VASILACHE, V., SANDU, A.V., CHIRAZI, M., HONCERIU, C., DABIJA, R.C., VLADESCU, A., COTRUT, C.M., SANDU, I., Rev. Chim. (Bucharest), **69,** no. 10, 2018, p. 2826.
15. SANDU, I., OLARIU, R.I., SANDU, I.G., STIRBU, C., PASCU, C., VASILACHE, V., VIONE, D., ARSENE, C., Journal of Aerosol Science, **81,** 2015, p. 100. DOI: 10.1016/j.jaerosci.2014.12.003
16. SANDU, I., CANACHE, M., LUPASCU, T., CHIRAZI, M., SANDU, I.G., PASCU, C., Aerosol and Air Quality Research, **13,** no. 6, 2013, p. 1731. DOI: 10.4209/aaqr.2013.01.0022
17. SANDU, I., CHIRAZI, M., CANACHE, M., SANDU, I.G., ALEXIANU, M.T., SANDU, A.V., VASILACHE, V., Environmental Engineering and Management Journal, **9,** no. 6, 2010, p. 881.
18. SANDU, I., ALEXIANU, M., CURCA, R.G., WELLER, O., PASCU, C., Environmental Engineering and Management Journal, **8,** no. 6, 2009, p. 1331.
19. CARRUTHERS, J., FOURNIER, N., KERSCHER, M., RUIZ-AVILA, J., TRINDADE DE ALMEIDA, A.R., KAEUPER, G., Dermatol Surg., **39**, no. 3 Pt 2). 2013, p. 510.
20.STEPHENS, M.L., Altern Lab Anim., **40**, no. 6, 2012, p. 346.
21.PAPAVASILIOU, A.S., NIKAINA, I., FOSKA, K., BOUROS, P., MITSOU, G., FILIOPOULOS, C., Toxins (Basel)., **5**, no. 3, 2013, p. 524.
22.GUARANY, F.C., PICON, P.D., GUARANY, N.R., DOS SANTOS, A.C., CHIELLA, B.P., BARONE, C.R., FENDT, L.C., SCHESTATSKY, P., PLoS One., 8, no.2,. 2013, p. e56479.
23.KAJI R., J Physiol., **591**, no. Pt 4, 2013, p. 749.
24.GREENE, CS (2010). American Association of Dental Research, Management of patients with TMDs: a new standard of care. Int. J. Prosthodont,, **23**, no. 3, 2010, p. 190.
25. RICHARDS, BL; WHITTLE, SL; VAN DER HEIJDE, DM; BUCHBINDER, R., J Rheumatol Suppl. Sep; 90, 2012, p.:34.
26. O'NEIL, MJ (ed.). The Merck Index- An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006.
27.SANDU, I., CANACHE, M., MIHAESCU, T., CHIRAZI, M., SANDU, A.V., TRANDAFIR, L.M., LUCA, A.C., CHECHERITA, L.E., Rev. Chim. (Bucharest), **66,** no. 1, 2015, p. 60.
28. CHECHERITA,L.,E.**,** REZUS, E., LEON ,M.,M., STAMATIN, O., CARAUSU,E.,M., Rev.Chim.(Bucharest), **68**, no. 5, 2017, p. 977
29. SANDU, I., CANACHE, M., SANDU, A.V., CHIRAZI, M., MIHAESCU, T., CHECHERITA, L.E., SANDU, I.G., Environmental Monitoring and Assessment, **187,** no. 2, 2015, Article Number: 15. DOI: 10.1007/s10661-014-4239-y
30. MANUC, D., CARAUSU, E.M. Sante Publique, Ed. Carol Davila,Bucuresti, 2015, pp. 47-54.
31. CHECHERITA,L.E., LUPU, C.I., STAMATIN, O., MANUC, D., Rev. Chim.(Bucharest), **69**, no. 7, 2018, p. 1752
32. FORNA, N.C**.,** CHECHERITA, L.E., Muscular Rehabilitation in Patients with Dysfunctional Syndrome of the Stomatognathic System, Vol. I and II, Publisher Gr.T.Popa, U.M.F.Iasi, 2018.

Manuscript received: 16.07.2018