The Effect of Antidepressant Chemical Compounds on Masticatory Muscles Activity in Depressive Patients

Electromyographic study

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Using the surface electromyography, we evaluated the effect of long- term intake of antidepressant chemical compounds on the masticatory muscles electrical activity at rest in twenty-one subjects. We compared the patient's acquired data from the masseter and temporalis muscles with the default values for the resting activity of these muscles. We found significantly higher mean rest values concerning the amplitude of signals in all sites ($p<0.05$), except the left masseter. Considering the limits of the study, it appears that long-term treatment that uses chemically compounds with antidepressant effect may influence the masticatory muscles activity, manifested by hypertonicity at rest.

Keywords: antidepressants, depression, masticatory muscles, electromyography, craniomandibular disorder

The occurrence of muscular dysfunctions in craniomandibular disorders is increased, and restoring the balance of the stomatognathic system requires complex examinations and treatments [1-4].

Comorbidity in craniomandibular disorders (CMDs) is currently unanimously recognized [5]. Within it, several psychological factors such as depression, anxiety, and somatization seem to be contributing to the onset of CMDs or perpetuating a dysfunction already present [6-9].

In the treatment of CMDs, drug therapy mainly targets the pain and muscle tension and uses different drugs. Some heterocyclic chemical structures address depression, especially tricyclic antidepressants. These have been proposed as therapeutic means in craniomandibular dysfunctions, particularly in myogenic forms, as well as in bruxism or fibromyalgia [10-12]. These compounds are three ringed (fig.1), and they act by blocking the serotonin and the norepinephrine transporter, causing a higher synaptic concentration of these neurotransmitters [13].

The new developments in the field of antidepressants are the selective serotonin reuptake inhibitors (SSRIs), and the tetracyclic antidepressants. Antidepressants are widely discussed in the literature concerning the CMDs, considering in part their association with depressive states and on the other hand, the use of antidepressant medication in the management of this disorder. There is minimal data in the literature on the effect of some chemical drug compounds on neuromuscular masticatory activity, and these are mainly related to anti-inflammatory drugs [14].

This study has as aim to assess the effect of long-term clinical administration of antidepressants on the masticatory neuromuscular activity at rest.

Experimental part

Patients

In the research were included 21 subjects, 8 males (mean age 51,8) and 13 females (mean age 51) diagnosed with different forms of depression by a psychiatrist. All the patients were under long-time (2-3 years) treatment with antidepressant medication, consisting of oral intake of a combination of drugs, including one of the following antidepressants: clomipramine (a tricyclic antidepressant), mirtazapine as a tetracyclic piperazino-azepine antidepressant (*1,2,3,4,10,14b-Hexahydro-2-methylpyrazino(2,1-a)pyrido(2,3-c)benzazepine*) and sertraline (a selective serotonin reuptake inhibitor). No patient had clinical signs and symptoms of the craniomandibular disorder. We asked each subject for informed consent regarding the electromyographic investigation.

Electromyography

The BioEMG II (BioResearch Assoc.Inc, Milwaukee, WI, USA) electromyographic device and the BioPak Software version 5.5. (fig.2) is designed to record the electrical activity from eight masticatory muscles simultaneously.

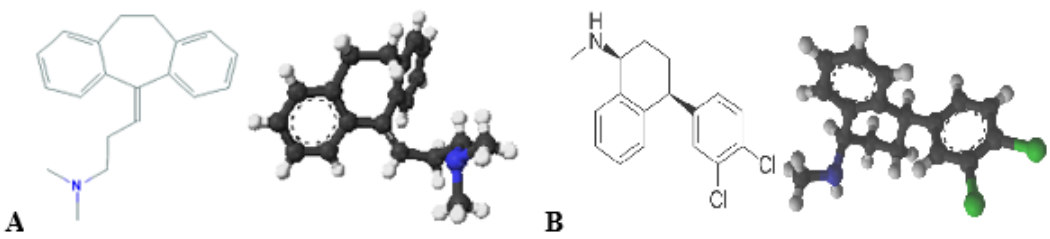

Fig. 1. General chemical structure of a tricyclic antidepressant (A) and a selective serotonin reuptake inhibitor (B)

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Fig. 2. The BioEMG III electromyographic device used in the study

Microvolt signals are amplified to 5000 times their original levels. We recorded the muscle activity of four masticatory muscles (right masseter, left masseter, right temporalis anterior and left temporalis anterior) in a resting state (the mandible is hanging loose, and there is no teeth contact). The surface BioFlex EMG adhesive electrodes are placed on the skin, and then the alligator clips of the wire are attached to the tabs. The lines created by the electrodes should run with the fibres of the muscles. An auxiliary electrode (Uni Tab TENS electrode) was also set for the ground wire connection, on the side of the patient's neck (fig. 3).

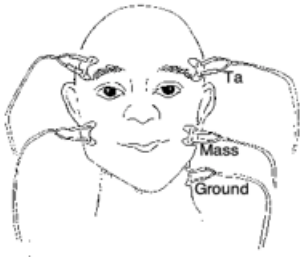

Fig. 3. The placement of the surface and the ground electrodes

During the registration, signals are displayed on a computer as original time domain waveforms and average levels. For the registrations analysis, three sections during the recording were selected at random (fig. 4).

Statistics

The collected data were statistically processed using the GraphPad InStat v 3.1. Software. We selected the unpaired Mann Whitney U nonparametric test to assess if the means between the electromyographic activity at rest in the four examined muscles differ significantly from the default values suggested for the rest-activity in these muscles (1.5-2.1 μV). A p-value under 0.05 was considered significant for this difference.

Results and discussions

The values of the resting electrical activity recorded in the investigated muscles, except for the left masseter, are much higher compared to the typical mean values for this electromyographic parameter ($p < 0.05$). Table 1 shows the average values of resting electromyographic activity for the investigated muscles in the male subjects, while in table 2, the same data are for the female patients.

Table 3 presents the statistical differences in the whole group of 21 subjects between the resting activity of the studied muscles and the mean default resting rate (1.8 μV).

The table 4 presents a series of other descriptive statistics on the levels of electromyographic activity in the study.

In the literature, scientific evidence for the use of antidepressant medication in patients with cranio-mandibular dysfunction is minimal. One single trial, the double-blind study of Rizatti-Barbosa et al., was able to demonstrate the beneficial effect of taking a low dose of amitriptyline at night for two weeks [15].

Most authors consider low-dose tricyclic antidepressants (10mg) to be beneficial in tension-type headache [16], in musculoskeletal pain in fibromyalgia [17] as well as in night bruxism [18], or to improve the quality of sleep [19]. The increased muscular activity at rest in this study seem to agree to the findings of a research conducted by Scrivani et al., that the selective serotonin reuptake inhibitors cause

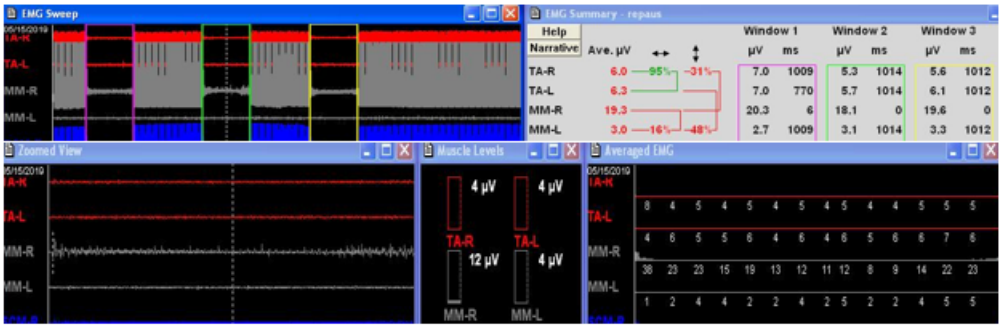

Fig. 4. The recorded data processed by the BioPack Software,v.5.5

Table 1

THE AVERAGE ELECTROMYOGRAPHIC ACTIVITY (μV) OF THE FOUR MASTICATORY MUSCLES AT REST IN MALE GROUP (n=8)

R mass	L mass	R temp.	L temp.
3.1	0.9	1	1
29	0.6	2.3	0.8
13.9	0.4	1.1	2.2
40.4	0.7	2.4	6
2.3	1.5	3.8	2.8
11	7.7	2.1	3
19.4	3	6	6.3
1.5	3.9	5.2	3.2

Table 2

THE AVERAGE ELECTROMYOGRAPHIC ACTIVITY (μV) OF THE FOUR MASTICATORY MUSCLES AT REST IN FEMALE GROUP (n=13)

R. mass	L. mass	R. temp.	L. temp
8.3	4.6	7.7	9.5
37.1	0.7	2.9	2
13.3	0.7	1.4	1.6
7	1	2	3.1
24	1	2	2
16.4	0.7	2.3	2.3
14.2	0.5	2.9	2.8
3.2	2.4	9.5	5.4
1.9	1.8	3.8	2.6
5.9	0.9	3	1.4
1.2	1.7	4.6	4.5
1.6	4.6	2.8	3.5
2.3	3.7	17.3	4.3

Table 3

THE DIFFERENCE BETWEEN THE REST ACTIVITY OF THE STUDIED MASTICATORY MUSCLES FOR THE ENTIRE GROUP (n=21) AND THE DEFAULT AVERAGE ELECTROMYOGRAPHIC ACTIVITY AT REST IN THE MENTIONED MUSCLES, IN HEALTHY SUBJECTS

Muscle	Mean rest activity (μV)	Default mean value (μV)	Two-Tailed p value
R. masseter	12.238	1.814	p < 0.0001 (extremely significant)
L masseter	2.048		p = 0.2269 (ns)
R temporalis ant.	4.100		p = 0.0011 (verry significant)
L temporalis ant.	3.348		p = 0.0018 (verry significant)

Table 4

SOME DESCRIPTIVE STATISTICAL DATA CONCERNING THE LEVEL OF THE ELECTROMYOGRAPHIC ACTIVITY AT REST (μV)

	Std.dev.	Median	Lower 95% CI	Upper 95% CI
R masseter	11.856	8.300	6.841	11.635
L masseter	1.897	1.000	1.184	2.911
R temporal	3.711	2.900	2.411	5.789
L temporal	2.078	2.800	2.402	4.293
Default	0.3071	2.1	1.675	1.954

increased masticatory muscular activity and episodes of night bruxism [20]. Haddad and Dursun described the serotonin syndrome as a side effect to antidepressants [21]. It results as an *excessive serotonergic transmission* and is manifest as neuromuscular hyperactivity and muscle spasms.

Depression may play an essential role in some dysfunctions by the neuromuscular side effects of antidepressant medication [22]. Regardless of the cause-effect relationship, when dysfunctional and depressive symptoms coexist, the therapeutic solution addressing both problems is the recommended solution [23,24]. Tversky et al. suggest that patients with masticatory muscles dysfunction who do not respond to conventional therapies should be included as having chronic depression and treated accordingly [23]. Some other authors have described the adverse effects that long-term use of antidepressants can induce, including muscle hyperactivity [25-28].

We used as an electromyographic parameter the activity at rest to remove the influence that other factors, such as the occlusal ones, might have on the recordings. The default average value of resting muscle activity (1,5 - 2,1μV) used for comparison with the recorded data in subjects is suggested by numerous studies [29-31].

Conclusions

Considering the limits of the study, it appears that long-term treatment that uses chemically compounds with antidepressant effect may influence the masticatory muscles activity.

The activity of the masticatory muscles was manifested by hypertonicity at rest .

The values of the resting electrical activity recorded in the investigated muscles, except for the left masseter, are much higher compared to the typical mean values for this electromyographic parameter

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