Chlorzoxazone and vibrator induced jaw muscle tension

GUSTAF HELLSING & GLENN HAEGERSTAM

Department of Stomatognathic Physiology, Karolinska Institute, Huddinge, Sweden and Medical Department, Astra Läkemedel AB, Södertälje, Sweden

Hellsing, G. & Haegerstam, G. Chlorzoxazone and vibrator induced jaw muscle tension. *Acta Odontol. Scand.* 1981, 39, 321 – 327

The objective of the study was to clarify some mechanisms behind the relaxing effects of chlorzoxazone. Motor effects induced by vibration of the masseter and digastricus muscles were studied in seven subjects. The response was measured by means of simultaneous recordings of EMG of masseter and digastricus as well as bite force. The measurements were performed before as well as after oral administration of 250, 500 and 1000 mg chlorzoxazone. Since no effect of the medication was seen, it was concluded that the muscle relaxing influences of chlorzoxazone are not effective on segmental levels. Large interindividual differences in responses to vibrations were observed.

Key-words: Muscle relaxants; drug evaluation; reflex; therapeutics

Glenn Haegerstam, Med. Dept., Astra Läkemedel AB, S-151 85 Södertälje, Sweden

The therapeutic efficacy of centrally acting, nonsedating muscle relaxant drugs in man has been achieved almost entirely through clinical evalutation. Clinical studies (e.g. 12, 13, 14, 15, 16) indicate that chlorzoxazone (Paraflex) is efficient in decreasing the severity of spasm, pain and other symptoms from a variety of musculoskeletal disorders. Chlorzoxazone is considered to be centrally acting. In contrast to e.g. diazepam it exhibits no tranquilizing action, nor does it to addiction. It is therefore often the drug of choice in pharmacological treatment of spastic patients. The neurophysiological background of the muscle relaxing effect of chlorzoxazone has not yet been clarified.

The tonic vibration reflex (TVR) (1, 5, 6) is considered to imitate the tonic stretch reflex (TSR) in normal muscle function. By continued application of a vibrator to a muscle belly contraction slowly develops. During the vibration phasic reflexes are progressively supressed as the TVR mainly activates the tonic motoneurones. These cells are smaller than the phasic motoneurones and more easily activated. In contrast to the phasic motoneurones they are capable of continuous discharge during a plateau of stretch (4). The TVR can be evoked in jaw elevator as well as jaw opening muscles (3, 7, 9) with the same classical features as seen in limb muscles. This means a slowly progressing activation of the vibrated muscle and a

Received for publication, July 14, 1980

corresponding inhibition of its antagonists. Primary afferent discharge evoked by vibration is mediated onto the motoneurones mainly through polysynaptic pathways. Thus, functionally, there are many differences between the monosynaptic, phasic myotatic reflexes and the tonic ones.

Pain and tenderness in the jaw musculature as a consequence of nonfunctional activities like jaw clenching and nocturnal tooth grinding is a common phenomenon (8). Chlorzoxazone is often given to patients with these symptoms because of its limited side effects. There are many reasons to believe that the tonic motoneurones are responsible for such sustained jaw muscle contractions of nonfunctional character (bruxism). Effects of chlorzoxazone administration on vibration induced jaw muscle tension may therefore be a model of clinical relevance.

The aim of the present study was to clarify some mechanisms behind the relaxing effects of chlorzoxazone on the jaw musculature.

MATERIALS AND METHODS

Seven healthy subjects, three males and four females ranging in age from 20 to 30 years, participated in the study. During the experiments they were seated in a comfortable chair provided with a head rest.

EMG activity was recorded from the right masseter and anterior digastric muscles with surface electrodes (Band Biomedical ECG Monitoring Electrodes). After thorough cleaning of the skin the electrodes together with cables for preamplifier connection were taped approximately two cm apart over the muscle bellies. Bite force was recorded during closure with a strain gauge built into a rigid, 10 mm thick mouthpiece placed between the front teeth. Notches were provided for the upper and lower incisors. The EMG and bite force were measured using an input adapter 15 B and a universal amplifier EMT 12 B and recorded with a Mingograph M 34 Polygraph.

The vibrator was an electric motor with an eccentric load (Heiwa Hv-13D). It was manually applied on the muscle belly with a constant force of 10–20 N and had a contact area of about 2 cm^2. Sites of application were the left masseter muscle and the anterior belly of the digastric muscle. The vibration cycles were recorded with the aid of an Entrans accelerometer, attached to the vibrator. The vibration frequency was 130 Hz and the amplitude was 0.2 mm.

Chlorzoxazone effects were tested with a single dose double-blind cross over dose-response method. Tablets with 250 mg of the drug and placebo were given together with breakfast to fasting subjects in the following three proportions:

Group I: One active and three placebo tablets
Group II: two active and two placebo tablets
Group III: four active tablets.

The experiments were performed during three days and each of the doses was tested on every subject. The test procedure was as follows: The subject was instructed to bite on the strain gauge with light force (between 10 and 30 N) and not to change his effort ("constant effort" test) during 50 s: 10 s without vibration, 30 s with left masseter vibration and 10 s after withdrawal of the vibrator. The test was then repeated, this time with vibration of the left anterior digastric muscle instead of the left masseter.

This test procedure was performed immediately before the tablet intake

and repeated after 40, 80, 120, 160, 200 and 240 min.

Before the test procedures started all subjects were tested regarding TVR sensibility in the biceps and triceps muscles, according to Lance, de Gail & Neilson (11).

In order to check that known pharmacological effects could be recorded in our experimental model one subject was tested regarding TVR response in the biceps, the triceps, the left masseter and the left anterior digastric muscles after premedication of 10 mg diazepam (Valium) (c.f. 11).

Analysis of data

The obtained recordings of the EMG and the bite force recordings from the different tests were evaluated visually using the following scales.

EMG activity Index 0: No activity
Index 1: The basic activity at the start of each test.
Index 2: Presence of EMG amplitudes ⩾ twice the size of the amplitudes at the basic level.
Index 3: Presence of EMG amplitudes ⩾ three times the size of the amplitudes at the basic level.

Ethics

The study was conducted at the department of anaesthesiology, S:t Eriks Hospital in Stockholm and reviewed by an independent peer ethics committée.

RESULTS

Before the experimental runs the subjects were tested regarding TVR sensibility in some «constant effort» tests. All of them showed good responses to stimulation of the masseter, the digastric and the biceps muscles, and all but one of them to vibration of the triceps muscle (Table 1). During the first test procedure all subjects reacted with a good TVR response. Table 1 illustrates how this response in some subjects remained unaltered (e.g. subjects 4, 6 and 7) during all test series, while in some subjects the response rapidly decreased and was strongly disturbed after three tests (120 '). After these initial changes every subject developed a stable and individually characteristic response to the vibratory stimulus.

While Table 1 illustrates the consistency of the TVR-responses in every subject regardless of drug intake, Table 2 gives detailed data of the mean EMG changes caused by vibration of the masseter and the digastricus muscles. No positive or negative correlation could be found between the amount of administered chlorzoxazone and the TVR-effects. The mean EMG activity of the digastricus muscle was often not larger during vibration of the digastricus muscle than during masseter vibration. Figs. 1 and 2 illustrate two typical examples of reactions during masseter and digastricus vibration. Thus, neither the small intraindividual nor the large interindividual variation of this response was influenced by chlorzoxazone intake.

After medication with 10 mg diazepam (Valium) the initially clear TVR responses of the subject tested disappeared in all the tested muscles, the biceps, the triceps, the left masseter and the left anterior digastricus muscles.

No adverse reactions due to the medication were observed during the experiments.

Table 1. *TVR responses from the left masseter (mass) and (the left) anterior digastricus (dig) muscles of the seven subjects during the three days; initially before the test series (basic) and 120 min after tablet intake (120').*
− = no response. (+) = TVR response compensated by simultaneous antagonist contraction, + = clear response, + + = strong response. Question marks in the Control tests indicate weak TVR response

	Day one				Day two				Day three				Control test	
	basic		120'		basic		120'		basic		120'			
subject	mass	dig	mass	dig	mass	dig	mass	dig	mass	dig	mass	dig	biceps	triceps
1	+	+	+	+	−	−	−	−	−	−	−	−	+	−
2	+	+	−	−	−	−	−	−	−	−	−	−	+	+
3	+ +	+	+ +	−	+ +	−	+ +	−	+ +	−	+ +	−	+	+
4	+	+	+	+	+	+	+	+	+	+	+	+	+	+
5	+	+	+	−	−	−	+	−	−	−	−	−	+	+
6	+	+	+	(+)	+	(+)	+	+	+	(+)	+	(+)	+	+?
7	+	+	+	(+)	+	(+)	+	+	+	+	+	(+)	+	+?

Table 2. *EMG activity index recorded from the masseter muscle and the digastricus muscle by vibrating each of the muscles*

		Vibration masseter		Vibration digastricus	
		EMG mass	EMG dig	EMG mass	EMG dig
Group 1	Basic	2.0±0.82	1.4±0.53	1.0±0.58	1.1±0.69
250 mg	40'	2.3±0.76	1.1±0.38	1.3±0.95	1.4±0.79
chlorzoxazone	80'	1.9±1.07	1.1±0.69	1.3±0.76	1.1±0.69
	120'	1.7±0.49	1.0±0.58	1.0±0.58	0.7±0.82
	160'	1.9±0.90	0.7±0.76	1.1±0.90	1.1±0.69
	200'	1.9±0.90	1.1±0.38	1.3±0.52	1.4±0.53
	240'	1.9±0.90	1.0±0.58	1.4±1.13	1.4±0.79
Group 2	Basic	1.9±1.21	1.4±0.79	1.3±0.76	1.2±1.10
500 mg	40'	1.7±1.38	1.0±0.58	1.3±1.38	1.3±0.76
chlorzoxazone	80'	1.6±1.13	1.0±0.58	1.6±0.79	1.4±0.98
	120'	1.6±1.27	1.1±0.69	0.9±0.69	1.1±0.90
	160'	2.0±0.82	1.1±0.69	0.9±0.69	1.3±0.76
	200'	1.9±1.07	1.1±0.69	0.8±0.75	1.0±0.71
	240'	1.5±1.05	1.0±0.89	1.1±0.69	1.0±0.63
Group 3	Basic	1.9±1.21	0.9±0.69	1.4±1.13	1.3±0.96
1000 mg	40'	2.1±1.38	1.1±0.38	1.1±0.69	1.2±0.98
chlorzoxazone	80'	1.9±1.13	1.3±0.49	1.6±1.13	1.8±0.84
	120'	1.9±1.27	1.3±0.49	1.2±0.41	1.8±0.45
	160'	1.6±0.82	1.1±0.38	1.2±0.75	1.2±0.84
	200'	2.0±1.07	1.1±0.38	1.1±0.38	1.3±0.95
	240'	1.7±1.05	1.3±0.49	1.3±0.49	1.2±0.75

DISCUSSION

No effects of chlorzoxazone administration upon the TVR has been found in the present study. These observations seem contradictory to the findings by Herman (10). He studied the effect of chlorzoxazone on the myotatic stretch reflex of the spastic triceps surae muscle in patients with hemiplegic spasticity and spinal cord disease. The stretch reflex produced tension was significantly reduced in 11 of 15 spastic patients after chlorzoxazone intake. However, as he remarks, in healthy in-

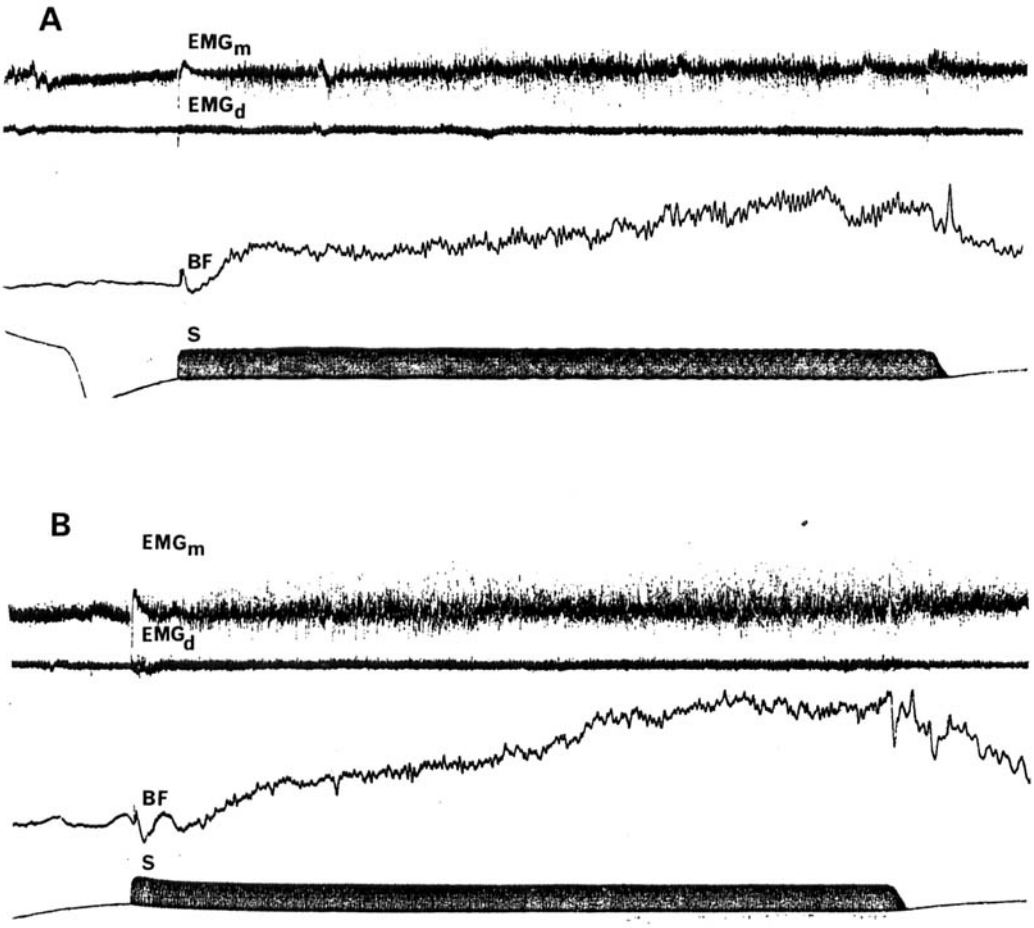

Fig. 1. Responses to masseter vibration of one of the subjects. TVR responses before medication (A) and 80 min after intake of four tablets (1000 mg Chlorzoxazone) (B) are very similar. EMG registration of masseter (EMG$_m$) and digastricus (EMG$_d$), bite force (BF) and vibration marker (S).

dividuals this effect is not seen. His hypothesis was that in spastic patients tonic motoneurones are mainly activated while in healthy patients a tendon tap causes discharge of the phasic motoneurones mainly. He argued that the polysynaptic pathway transmission utilized by the patients is more vulnerable to central-acting agents than the monosynaptic stretch reflex transmission utilized by healthy individuals.

Chlorzoxazone was shown to be capable of abolishing the crossed extensor, crossed adductor and crossed Babinsky reflex (2). Thus there exists some evidence inferring a central action at segmental or brain stem level by chlorzoxazone. Our study does not lend support to this hypothesis. The TVR is considered to utilize the same type of polysynaptic reflex arch as those causing long sustained contractions in spastic patients responding to tendon taps (11). Yet the TVR was not influenced by chlorzoxazone. It may therefore be concluded that the muscle relaxing influences of chlorzoxazone are not effected on segmental levels.

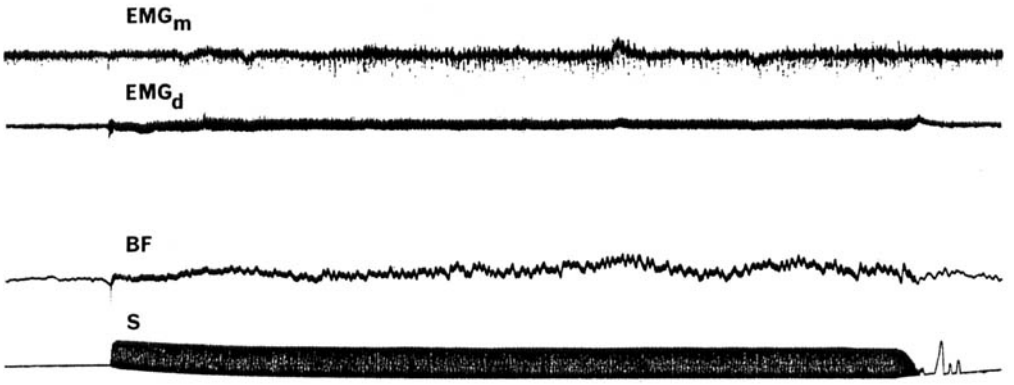

Fig. 2. Simultaneous masseter (EMG$_m$) and digastricus (EMG$_d$) activation at vibration of the digastric muscle (vibration marker s), resulting in increase of bite force (BF). The subject has evidently not been able to follow the «constant effort» instruction, but increased his masseter activity to compensate for loss of bite force during vibration of the digastric muscle.

Large interindividual differences in TVR response were observed, independent of drug intake (Table 1). Some subjects responded consistently with strong activation of the vibrated muscle. In other subjects, despite good TVR response initially, this response failed to appear after a few tests. Probably the latter group of subjects were distracted by the rather stressful experimental situation and were not able to follow the «constant effort» instructions. It has been demonstrated that the TVR is under voluntary control (6, 7). This is an example of gating effects from higher centra. In other words, descending impulses from the cortex are capable of blocking the vibrator induced primary afferent discharge. During the experiments of the present study the initially given instructions to the subjects could not be repeated due to lack of time. Initially on day one, all subjects responded with activation of both the tested muscles at vibration. Some of the subjects (Nos. 1, 2, 5, Table 1) were not able to consistently follow the «constant effort» instructions. Instead, their TVR responses soon disappeared. Other (Nos. 4, 6, 7 Table 1) followed these instructions well and consistently showed good TVR responses. Drug intake did not influence these intraindividually, rather constant characteristics.

The mean digastric EMG activity was not larger during vibration of the digastric muscle than during masseter vibration. This is probably due to compensatory activation of the antagonists when the subjects were unable to follow the «constant effort» instructions. At increase of the bite force during masseter vibration they unconsciously activated their jaw openers to counteract this effect.

The vibration-induced tonic contraction of jaw elevator and opening muscles as well as of the arm extensors and flexors was abolished by 10 mg diazepam in accordance with the findings by Lance, de Gail & Neilson (11). Chlorzoxazone and diazepam may therefore by assumed to be different in mechanism of action.

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