DETERMINATION OF INTRAMUSCULAR MOTOR ENDPOINT FOR THE EFFECTIVE ADMINISTRATION OF BOTULINUM NEUROTOXIN IN THE TREATMENT OF SPASTICITY

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Introduction

The treatment of spasticity with botulinum neurotoxin (BoNT) is effective and recognized method. BoNT blockade of transport proteins takes place in the axon terminal. Neuromuscular transmission is carried out by the axon terminals in the limited areas of muscle (~1 cm^3) – neuromuscular junctions (NMJ) or intramuscular motor endpoint (IME). Ultrasonic navigation (US) is the best way the introduction of BoNT while treating spasticity. But targeted administering to the IME can make the injection even more effective. IME were found with the help of electromyography (EMG).

In 1993 C. M. Shaari and I. Sanders experimentally showed that administering of BoNT into the IME increases the effect by 50%. J.-M. Gracies (2002, 2009) demonstrated the effectiveness of targeted administering for example, injection into m. biceps brachii. T. Rekand et all (2017) did not find a difference between targeted IME administering and the standard administering of different concentrations of BoNT (the methodology of the study was not presented).

Aims

The aim of our work was to the study the location IMEs for targeted BoNT administering in the treatment of spasticity. The objectives of the study were:

1. confirming the possibility of finding the IME injecting electrode;
2. determining the possibility of using surface electrodes to search for IMEs;
3. conducting a study of the muscles of the limb using surface monopolar stimulating electrode, finding the IMEs and making the map of IMEs of the limbs muscles for administering of BoNT;
4. testing the difference in efficiency between injection BoNT into IME and beyond IME.

Methods

1 Phase. 40 healthy volunteers of both sexes, aged from 23 to 64 years were examined. Their height ranged from 158 to 200 cm and weight - from 47 to 110 kg. .EMG scanning the front surface of the arm and forearm in the projection of the flexor muscles was made. Injecting electrode with a current of from 1 to 4 mA was used while screeing.

Then in order to develop a method of rapid diagnosis and to reduce patients' trauma, surface monopolar stimulating electrode NEUROSIGN Natus was applied, with a current ranging from 5 to 10 mA. Frequency in both cases was equal to 2 Hz.

IMEs were considered found by maximizing muscle contraction during stimulation of minimal current, and ultrasonic verification of the muscle.

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For each IME the following indicators were measured: amperage in which of muscle contraction, the distance from the midline, the distance from the elbow and wrist bend, the circumference of the limb at this level, taking into account the height, age, body weight, body mass index, thickness of fat layer, dominance of the hand. US was used to identify muscle.

2 Phase. Then patients with post-stroke spasticity (16 people) were divided into two groups and they were injected with 1000 U abobotulinumtoxinA: Group 1 (8) with US control. Group 2 (8) with US and EMG control of the injection in the IME. Checkpoint study – 2,4 weeks, Modified Ashworth Scale (MAS), Tardue sacale (TS) and GAS was used.

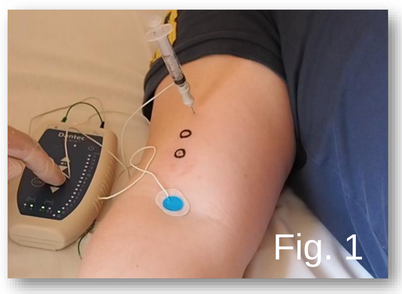


Fig. 1


Fig. 2

Results

1 Phase

1. IME search was performed in the projection m. biceps brachi (BB) from the elbow sequential injection with a step of 1.5-2 cm in the proximal direction (Fig. 1). IME BB was found 93±5 mm from the elbow, 25±4 mm from the midline of the shoulder in the medial direction (current of 1 mA). The result was confirmed in all 7 cases.
2. Surface monopolar stimulating electrode (current of 5 mA) was used to search for IME BB. IME localization was identical with the injection electrode. The result was confirmed in all 7 cases (Fig. 2.).

These results showed that using the surface electrode is correct. The difference in threshold current of 4 mA is a consequence of the impedance of the skin and fat layer.

Full examination of muscles of upper and low limbs and shoulder girdle was carried out. Therefore, IME were found and localized.

T-test (0,89) showed no significant differences in the location of IMEs muscles on the right and left arms & legs. This allowed us to combine data arrays and count the number of observations as 80.

Muscle	Amperage, mA	Distance (cm)			
		From middle line		From the elbow	From the wrist
		Medial	Lateral		
Biceps brachii dex.					
- caput longum	5	-	1,9±0,4	10±0,5	-
- caput brevis	5	2,8±0,3	-	9,3±0,4	-
Biceps brachii sin.					
- caput longum	5	-	1,9±0,4	10,1±0,5	-
- caput brevis	5	2,9±0,2	-	9,0±0,3	-
Brachialis dex.	6,9±0,9	-	4,1±0,3	7,5±0,5	-
Brachialis sin.	5,6±0,9	-	4,1±0,3	7,5±0,5	-
Brachioradialis dex.	5,6±0,6	-	4,3±0,3	2,9±0,5	23,0±0,8
Brachioradialis sin.	5,7±0,6	-	4,4±0,4	2,2±0,3	23,5±1
Flexor carpi radialis dex.	6,9±0,9	2,8±0,3	-	5,7±0,5	19,4±0,8
Flexor carpi radialis sin.	6,7±0,9	2,7±0,5	-	6,2±0,5	20,1±0,8
Pronator teres dex.	5	0	-	-	-
Pronator teres sin.	5	0	-	-	-
Flexor digitorum superfacialis dex.					
- II finger	7±0,9	1,7±0,1	-	17,5±0,6	6,8±0,7
- III finger	7,5±0,9	0,7±0,3	-	13,6±0,5	10,9±0,7
- IV finger	7,5±0,9	4,5±0,3	-	9,1±0,3	16,2±0,7
- V finger	9,2±0,7	3,0±0,2	-	19,7±0,6	5,5±0,4
Flexor digitorum superfacialis sin.					
- II finger	7,5±0,9	1,9±0,4	-	17,9±0,8	7,4±0,4
- III finger	8,6±0,8	0,6±0,2	-	15,4±0,6	10,6±0,4
- IV finger	7,9±0,9	4,8±0,5	-	9,6±0,4	16,5±0,8
- V finger	9,2±0,7	2,9±0,3	-	19,9±0,5	5,9±0,5
Flexor pollicis longus dex.	10	-	2,4±0,2	17,8±0,7	6,0±0,5
Flexor pollicis longus sin.	10	-	2,4±0,2	17,7±0,8	7,0±0,4

Note: the results obtained for the IME of the muscles of the lower limbs, the shoulder girdle extensors and arm.

EMG-scanning of FDS showed four IMEs, each one was the trigger for the corresponding finger (II-V). IME and the bundles of fibers FDS III finger brush are located more laterally than the bundles of FDS and IME of II finger.

Thus, the order of the IMEs and muscle bundles in FDS is not ascendant and is in the following order: III, II, IV, V. In the literature we have not found these facts (Fig. 3).

The existence of four IMEs FDS proves that the number of motor points does not depend on the size of the muscle, and on the complexity of its movements.

Analysis of variance (0.33) and the exact method of Fisher (0,38) showed no effect of length of the limb on the IME coordinates when measured from a specified reference lines. 22 IMEs were in the same distribution area (valuation range of extremes) and did not differ in the density of the dispersion (measured by variation index of 0,095) in all 80 cases.

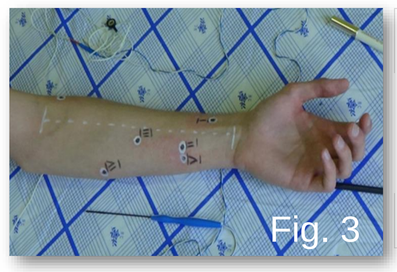
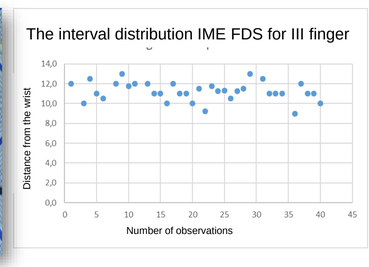


Fig. 3



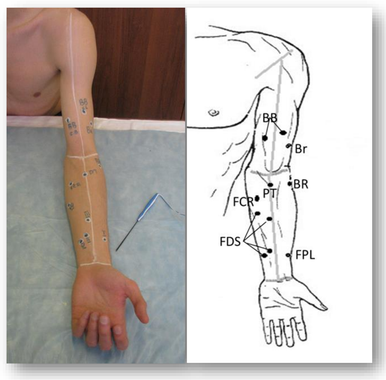
2 Phase

Patients were assessed at 2 and 4 weeks after injection of 1,000 U Dysport using of MAS and GAS, group 1 (8 patients) with US control, group 2 (8 patients) with US and EMG control of the injection in the IME.

Scale	Group 1 (8 patients)	Group 2 (8 patients) Injection in IME
MAS base date	2,33±0,52	2,29±0,49
MAS 2 week	2±0,5*	1,64±0,38*
GAS 2 week	-1,67±0,47**	-0,43±0,53**
MAS 4 week	1,33±0,37	1,29±0,39
GAS 4 week	-0,17±0,69	-0,29±0,49

Indicators MAS and TS are significantly different (P<0.05) 2 weeks after BoNT injection; the difference in group 1 and 2 in the evaluation of MS and TS decreases (0.83) 4 weeks after BoNT injection; the significant differences in the values of GAS 2 weeks after the injection of BoNT (0.001) and the accuracy is reduced to 4 weeks (0.39).

The results of GAS was significantly better in group 2. The effect was almost equal in both groups after 4 weeks. Thus, we may need a study involving a larger number of patients.



Conclusions

1. The use of a unipolar surface electrode is an effective way to search for IMEs superficial muscles
2. The location of the IMEs is identical and does not depend on gender, age and dominant limb of the subject, allowing you to create a map of the location and the metric table.
3. This study showed IME of the upper and low limb and shoulder girdle and allows us to create a surface map with IME location.
4. M. flexor digitorum superficialis has four motor points located in the order III, II, IV, V.
5. The effect of BoNT injection in IME develops faster than in the usual way, but is compared with it in 4 weeks.
6. This data might improve the clinical efficacy and the feasibility of IME targeting, when injecting BoNT in spasticity.

Further research is required.

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