

NEUROPHYSIOLOGICAL ANALYSIS OF THE FUNCTIONAL STATE OF NEUROMOTOR APPARATUS IN THE CHILDREN WITH CEREBRAL PALSY DURING TREATMENT WITH BOTULOTOXIN-A

63 children with cerebral palsy were under medical surveillance in the Republican Children's Psychoneurological Hospital (Tashkent, Uzbekistan). The age was fluctuated from two to 14 years, mean age was 8 ± 6 years. The children with spastic forms of cerebral palsy and dyskinetic cerebral palsy with rigid muscles were selected for treatment with local injections of Botulotoxin-A. Injection of Botulotoxin was administered in those muscle agonists that were significant in the formation of pathological muscular synergia. The results of electroneuromyography (EMG) on the background of treatment with botulotoxin testify to the reliable decrease of tonus not only in injected muscles, but also in muscles of antagonists and agonists.

FARKHOD KHAMRAEV,
SHOIRA NURMATOVA

*U. Kurbanov Republican Pediatric
Psychoneurological Hospital
Uzbekistan*

Keywords: Botulinum toxin type A, electromyography, infantile cerebral paralysis, muscular tonicity, rehabilitation.

UDC: 616.8+616-053.2+616-036.82/.85

Background

A number of key clinical manifestations of infantile cerebral paralysis significantly affecting the diseases outcome can be specified. First of all, this is the time of formation of static locomotor habits reflecting "maturation" of antigravitation functional system that should be mentioned. Then the spasticity follows, significantly limiting development of voluntary motility, decreasing not only the patients' locomotor capacity but also their vital activity and resulting in transformation of reflex contractures into the non-reflex ones, due to secondary fibro-trophic changes in muscles and capsular ligamentous complex. Spasticity triggers development of contractures. Pareses and palsies in ICP patients are less pronounced than the muscular tonicity pathology. These are contractures that serve as a leading mechanism limiting further evolution of motor sphere and significantly reducing quality of life in this category of patients (Bronnikov and Kravtsov, 2007).

Though not an end in itself, muscular hypertonicity reduction in patients with spastic ICP forms is important since elimination and considerable reduction of its effect as a key factor of development of contractures would allow achieving functional improvement in the patients (Kojevnikova, 2005; Doris Valencia Valencia, 2009). Despite sufficient number of methods for the muscular tonicity reduction in ICP, they all have disadvantages, side and adverse effects and contraindications. Most modalities require prolonged management, the effect being short. Search for novel, more efficient non-invasive methods for the muscular tonicity correction with long-lasting effect, minimum side effects and contraindications is under way. In this respect local injections of botulotoxin-A seem attractive (Carla Rito et al., 2009; Doris Valencia Valencia, 2009; Isolda Ferreira de Araujo et al., 2009). Our experience in the field, high efficiency and, ultimately, good promises of the method for rehabilitation and subsequent social adaptation of the incapacitated children were among the motives to study the aspect in detail and more profoundly.

The work was initiated to study effect of botulotoxin-A injections on parameters of neuromotor apparatus's functional condition in patients with ICP spastic forms by means of global and stimulation electromyography.

Materials and methods

We examined 63 patients, 32 boys and 31 girls among them, aged from 2 to 14 years (mean age 8 ± 6 years) with infantile cerebral paralysis hospitalized at U.K. Kurbanov Republican Pediatric Psychoneurological Hospital, Tashkent, Uzbekistan. Botulotoxin-A injections were prescribed to

patients with spastic forms of infantile cerebral paralysis (ICP) and dyskinetic cerebral paralysis with muscular stiffness.

Given late formation of motor habits in ICP patients with inevitable subsequent restriction of information area, primarily the treatment aimed at early rehabilitation of the patients' motor sphere. As an upright posture and walking constitute the most significant stage, to master them was the purpose to achieve in the 1st group of patients (n=16). As rehabilitation seemed impossible to contribute to mastering an upright posture and walking due to overt psychomotor development retardation in children included in the 2nd group (n=17), they were administered with botulotoxin-A to help master other loco-motor acts, such as, rolling over, sitting and crawling. Thirty children receiving botulotoxin-A for elimination of a cosmetic defect and walking correction were included into the 3rd group.

Botulotoxin-A was selectively injected into the agonistic muscles, which are known to be the key ones in formation of pathological muscular synergisms. Upon simultaneous blockade of several muscles both the dose distributed and the total dosage varied. Patients receiving botulotoxin-A were scrutinized more carefully. Scheduled measurement of body temperature and skin examination was performed. One-week interval was made in administration of all medications, except anticonvulsants. Movement therapy and massage were prescribed starting from the 2nd day, instrumental physiotherapy being prescribed in the absence of contraindications.

PC-based four-channel electroneuromyograph (NEURO-MVP4, Neurosoft, Russian Federation) with global lead of potential oscillations from the motor point of a muscle was used to assess electrobiological activity (EBA) of the crural muscles, such as, *musculus gastrocnemius* (calf muscle) and *musculus tibialis anterior* (anterior tibial muscle). Electrobiological activity of the medial head of calf muscle and anterior tibial muscle was measured at rest and upon both dorsal and plantar flexion of the foot with registration of nerve conduction velocity in the tibial and the peroneal nerves. Surface electromyography (EMG) was used to register EBA of the bicep and tricep muscles at rest and upon the elbow joint flexion with nerve conduction velocity measured in the median and radial nerves of the upper extremities.

To assess severity of motor disorders in ICP patients and to compare EBA values of synergistic and antagonistic muscles, adequacy and reciprocity coefficients were calculated (Carla Rito et al., 2009). Adequacy coefficient (AC) was derived from division of calf muscle medial head EBA upon dorsal foot flexion by anterior tibial muscle medial head EBA upon plantar foot flexion. Reciprocity coefficient (RC) was the quotient from division of calf muscle medial head EBA upon dorsal foot flexion by anterior tibial muscle EBA upon dorsal foot flexion.

In addition, to assess spinal motoneurons we used monosynaptic testing of N-reflex as a response of the soleus muscle to electrical excitation of the medial popliteal nerve and M-response, Nmax/Mmax ratio being determined (Carla Rito et al., 2009). Stimulation electroneuromyography (ENMG) was performed prior to botulotoxin-A injections (pre-treatment) and 15 days after (post-treatment).

Results and discussion

Pre- and post treatment parameters of global ENMG in the crural muscles and N-reflex testing can be seen in Table 1. Pre-treatment spastic tonicity can be seen both in the calf muscle and the anterior tibial muscle. At rest the highest and the lowest EBA in the calf muscles was registered in the 1st and 3rd group patients, respectively (144.8 ± 5.1 versus 127.0 ± 4.6 mV). Similarly, the highest and lowest EBA in the anterior tibial muscles at rest could be observed in the groups above (199.2 ± 6.9 versus 115.0 ± 4.4 mV).

The RC value turned out too high in all groups as compared with the normal one (0.2) to be the evidence for significant abnormalities in reciprocal relationships between the crural muscles and enhancement of co-contraction in the antagonist muscles. The highest RC value (0.83 ± 0.03) can be seen in the 2nd group patients, that is, those with severe abnormalities. Similar too high AC value (0.94 ± 0.04) was found as compared with the normal one (0.2) and directly proportional to severity of the disorder.

Full-scale examination of the patients administered with botulotoxin-A performed in 15 days demonstrated evident improvement in condition of neuromuscular apparatus, confident positive dynamics in the ENMG parameters being observed. EBA amplitude of the calf muscle and the anterior tibial muscle at rest was found reduced by 34.4% and 46.9%, respectively, clinically manifesting in reduction of the crural muscular tonicity.

TABLE 1. PARAMETERS OF GLOBAL ENMG IN THE CRURAL MUSCLES AND N-REFLEX TESTING BEFORE BOTULOTOXIN-A THERAPY AND IN 15 DAYS

Groups of patients		Group 1		Group 2		Group 3	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Anterior tibial muscle	EBA at rest, mV	199.2± 6.9	76.8±2.9***	154.1±5.9	91.5±3.5***	115.0±4.4	80.3±3.1***
	EBA upon muscle contraction, mV	539.0±20.5	663.4±25.9**	504.0±19.7	742.5±29.5***	546.5±19.8	826.6±32.2***
Calf muscle	EBA at rest, mV	144.8±5.1	76.4±2.9***	133.5±5.3	113.0±4.1**	127.0±4.6	74.8±2.8***
	EBA upon muscle contraction, mV	333.6±12.3	469.8±16.9***	448.3±17.8	500.7±19.1*	380.1±14.8	596.5±24.5***
Reciprocity coefficient		0.52±0.02	0.36±0.01***	0.83±0.03	0.64±0.02***	0.69±0.02	0.40±0.01***
Adequacy coefficient		0.92±0.03	0.53±0.02***	0.94±0.04	0.63±0.002***	0.81±0.03	0.52±0.02***
N/M, %		33.6±1.3	38.4±1.4*	12.6±0.5	22.4±0.9***	10.1±0.4	13.9±0.5***

Note: * - confident in relation to pre-treatment data (*P<0.05; ** P<0.01, ***P<0.001).

FIGURE 1 PRE- AND POST-TREATMENT EBA OF THE CALF MUSCLE AT REST

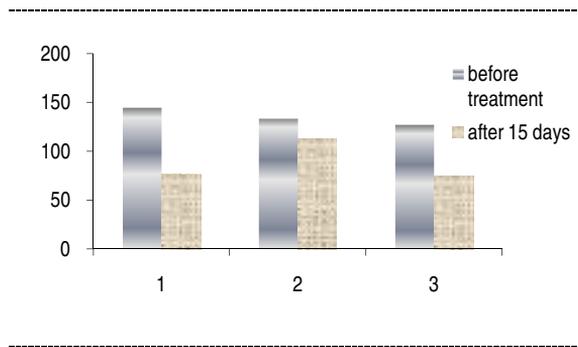
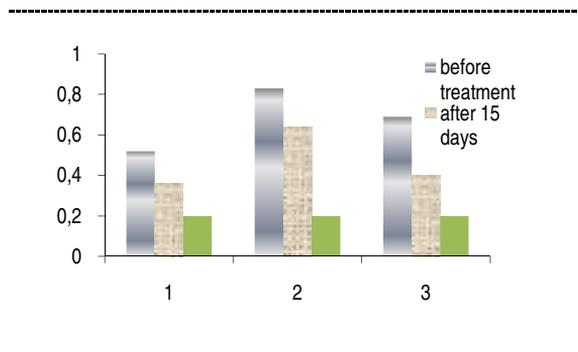


FIGURE 2. PRE- AND POST-TREATMENT CR VALUES IN COMPARISON WITH THE NORMAL ONE



The most pronounced dynamics in EBA at rest can be seen in the 1st group patients with high rehabilitative potential and in the 3rd group patients mastering habits of independent walking. The least pronounced changes can be seen in the 2nd group patients with the severe disorder (Fig. 1).

More significant positive changes were registered in the antagonistic muscles not in the injected ones, probably, owing to normalization in reciprocal relationships confirmed by positive RC and AC dynamics (mean reduction by 30.9% and 30.3%, respectively) (Fig.2).

Significant EBA increase is registered upon maximum tension both in the calf muscle (34.86%) and the anterior tibial muscle (40.46%) to be the evidence for enhancement of voluntary muscular activity clinically manifesting in formation of novel motor habits.

Pre-treatment monosynaptic testing demonstrated that Nmax/Mmax ratios specific for excitability of spinal neurons prior to botulotoxin-A injections varied from 2.31 to 64.7% in the patients. This parameter is considered a measure for excitability of spinal motoneurons that can be divided into large (physical) and small (tonic). In healthy subjects its mean variation is 45-60% (Carla Rito et al., 2009). Tendency to reduction in patients with initially high Nmax/Mmax ratios and increase of the parameter in those with basally low values was observed in post-treatment period. Mean values of the parameter is registered increasing in all groups to be the evidence for multiplication of motor units of the motoneuron pool involved in the reflex response.

Post-treatment ENMG parameters can serve as a confirmation of positive changes in functional condition of the ICP patients' neuromuscular apparatus. These parameters change in parallel to those in clinical picture. Reduction of EBA at rest in the spastic muscles, increase of its amplitude in the antagonist muscle upon voluntary motion, decrease of reciprocity and adequacy coefficients reflecting improvements in coordination muscular relationships as well as changes in functional condition of spinal cord motoneurons demonstrated by monosynaptic test findings establish favorable conditions for normalization of motor program in the process of the treatment. Reduction in tonicity of muscles responsible for pathological posture breaks down the tonic reflex links significantly decreasing their effect on the formation of motor stereotype. Positive changes in peripheral neuromuscular apparatus are impossible without those in suprasegmental structures. Changes in muscular tonicity and inter-muscular relationships are known to normalize flow of afferent impulses to the central control structures resulting in reconstructions of motor-kinesthetic analyzer subsequently to contribute to preservation of the clinical results achieved.

Conclusion

EMG findings after treatment of ICP patients with botulotoxin-A are the evidence for confident reduction of tonicity not only in the injected muscles, but also in antagonistic muscles and agonists. The voluntary activity of crural muscles is found to increase due to mean EBA enhancement by 40.6%, clinically manifesting in mastering novel motor habits. Reciprocal relationship between antagonists is found to improve by the 15th day of treatment reflecting in mean reduction of both reciprocity and adequacy coefficients by 30.6%. Monosynaptic test findings are the evidence for increase in total number of motor units in motoneuron pool involved in the reflex response. Positive changes in peripheral neuromuscular apparatus result in reconstruction of the central control structures. Changes in EMG parameters parallel positive dynamics observed in clinical picture.

References

- Bronnikov, V., Kravtsov, Yu., 2007. Substantiation of adaption-regulatory approach to complex rehabilitation of patients with infantile cerebral paralysis [Obosnovanie adaptatsionno-regulyatornogo podkhoda k kompleksnoy reabilitatsii detey s cerebralnymi paralichami], in Russian, Novgorod.
- Carla Rito, Isabel Batalha, Maria Vasconcelos. 2009. "Treatment of spasticity in cerebral palsy," Abstract, 5th World Congress of the International Society of Physical and Rehabilitation Medicine. Istanbul, p.1254
- Doris Valencia Valencia, 2009. "Colombian experiences with botulinum toxin type A in children with cerebral palsy," Abstract, 5th World Congress of the International Society of Physical and Rehabilitation Medicine. Istanbul, p.1252
- Isolda Ferreira De Araujo, Simone Carazzato Maciel, Solange Sumire Aoki, 2009. "Comparison between peripheral nerve block with phenol 5% and with botulinum toxin type A on hip adductor muscles in patients with cerebral palsy," 5th World Congress of the International Society of Physical and Rehabilitation Medicine, Istanbul, p.1253
- Kojevnikova, V., 2005. Today technology in complex physical rehabilitation of patients with infantile cerebral paralysis, [Sovremennye tekhnologii v kompleksnoy fizicheskoy reabilitatsii bolnykh detskim cerebralnym paralychom], in Russian, Moscow.