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Botulinum toxin A injection precision control at spastic forms of cerebral palsy: choosing methodology

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The article provides general information on botulinum therapy in treating spastic forms of cerebral palsy; a review of modern botulinum toxin A drugs' injection precision control methods at spasticity and other pathologic states is given; advantages and disadvantages of each injection control method are analyzed in detail. Special attention is paid to the substantiated choice of the injection control method in pediatric practice; muscles of the highest degree of complexity for botulinum therapy at spastic forms of cerebral palsy are described. The authors' observations and results of applying ultrasound botulinum toxin A drugs' injection control at different spasticity patterns in children are given.

Key words: *botulinum toxin A, botulinum therapy, cerebral palsy, rehabilitation, spasticity, hand, ultrasound, electromyography, posterior tibial muscle, ulnar flexor muscle of wrist, round pronator muscle, long palmar muscle, iliopsoas muscle.*

Botulinum toxin A (BTA) was for the first time approved for application according to medical indications by the American Food and Drug Administration (FDA) in 1989 to treat strabismus and blepharospasm [1]. Since then the range of registered and used off-label indications for BTA injections has continuously been broadening and has included pathological conditions caused by hyperactivity of skeletal and nonstriated muscles, glands, and pain syndromes of various etiology. Use of BTA to reduce spasticity at cerebral palsy (CP) was first described ca. 20 years ago [2, 3]. Numerous prospective and retrospective CP botulinum therapy effectiveness trials have been conducted since then, reviews and meta-analyses have been compiled, national and international recommendations on the use of BTA for treating spasticity and rehabilitation of CP patients have been suggested [4-13]. It has been admitted that "the use

of BTA to treat local/segmental spasticity is effective and, in whole, safe method with A level of evidence, according to the evidence-based medicine criteria" [10].

However, acknowledgment of BTA application effectiveness in reducing spasticity and improving medical-social rehabilitation of CP patients has not resolved a range of issues concerning the selection of optimal dosages, drug's dilution proportions and time of repeated injections. It has mainly been connected with the precision of administering BTA drugs into target muscles. Many authors noted that advantages achieved by BTA application at spasticity may be nullified by hitting not a target muscle, but a different one, or irrational spread of the drug over the muscle's periphery. Unfavorable BTA diffusion may cause side effects associated with the developing weakness of adjacent muscles; this is especially relevant for pediatric practice due to small size and superficial arrangement of muscles [14]. It is partly connected with the drug's natural diffusion, which, according to the experimental data, is in proportion to BTA concentration and injection volume [15-17], number of injections into the muscle and needle thickness [18]. Moreover, it has been proven that botulinum toxin may diffuse through muscular fasciae [19].

BTA diffusion capability may play a positive role, e.g., when treating palmar hyperhidrosis, as it allows reducing the number of painful injections, or when reducing spasticity of large muscles in children, when drug's dosage is limited by a child's weight and number of injections – by a patient's pain threshold. Several authors suggested potentiating BTA diffusion in large spastic muscles by increasing drug's dilution in certain cases [20, 21]. However, unfavorable BTA diffusion when administered to neck and shoulder girdle muscles may lead to dysphagia, respiratory disorders, difficulties in control of head, and thus, of all body in children with CP, to weakness of hand muscles and deterioration of their function. Thus, correct choice of injection method at spastic CP forms allows not only reaching optimal expected result, but also minimizing risk of side effects and complications.

The following techniques are used in order to increase precision of BTA injections: anatomic orientation/palpation, electromyography (EMG), electric stimulation, ultrasound control, computed tomography (CT), fluoroscopy, endoscopy.

It is necessary to take into account the following specificity when selecting methods of controlling BTA injections in children with spastic CP forms: children are very pain-sensitive, are alert about complicated medical manipulations and devices, big number of medical personnel, poorly tolerate prolonged immobility and are not always open to cooperation; this is aggravated by patients' age and main disease's severity aggravation. That is why special approach to methods of controlling BTA injections (which have proved themselves effective in adult patients) is necessary in pediatric practice.

Palpation/anatomic control

Traditional and the most widespread method of controlling BTA injection at spasticity is the use of anatomic landmarks and palpation of tense muscles together with visual control of the needle injected into the muscle at voluntary or passive movement in the corresponding joint.

The doctor conducting injection must have a perfect knowledge of both normal topographic anatomy of skeletomuscular system and neurovascular fascicles and possible variations of thickness, density and positional relationship of anatomic structures altered by disease course and spasticity [22]. Naturally, one and the same muscle may be different in size, form and occurrence depth in patients of different age and sex (pic. 1 a, b).

Prolonged spastic muscle tension leads to atrophy and connective-tissue degeneration of a part of fibers (pic. 1 c); this disturbs regular anatomic landmarks and reduces effectiveness of BTA injections when the drug hits the altered muscular tissue area [23]. Palpatory/anatomic method does not allow precisely determining the needle's position in the target muscle and controlling drug's spread.

Anatomic method's advantages are procedure's quickness, no need in special equipment and additional consumables (costs), possibility of using thinner and less traumatic needles than those used for EMG-control. When it is necessary to administer BTA into a superficial, large, well-contouring muscle, palpation and visual control are usually enough to achieve optimal drug's spread [24]. However, T.Y. Chin et al. [25] compared precision of manual needle injection control and target muscle electric stimulation control in 1,372 BTA injections in 226 children with muscular spasticity of upper and lower extremities. First, Teflon EMG-needle for BTA injection was injected into the target muscle according to the anatomic parameters, palpation and needle's relocation at passive movements in the corresponding joint, then electric stimulation was conducted to specify the needle's real position. Precision of injections into target muscles without additional control (electric stimulation) was 78% for gastrocnemius/soleus muscles, 68% for long and short adductor muscles of thigh, 62% for biceps muscle of arm, 46% for semimembranosus and semitendinosus muscles, 32% for adductor muscle of the first finger, 22% for round pronator muscle, 16% for ulnar flexor muscle of wrist and only 12% for radial flexor muscle of wrist and posterior tibial muscle, i.e. relatively satisfactory results were achieved only at injections in large muscles of calf. It is necessary to employ an additional method of controlling precision of injection for small and deeply located muscles.

EMG and electric stimulation

There are 2 types of electrophysiological methods of controlling BTA injections: electromyography and electric stimulation [26]. Special needle electrode is introduced into the muscle and pathological tonic activity at rest and activity EMG at voluntary tension are recorded to register bioelectric activity. The registered signal's character helps specifying correctness of muscle choice and electrode's position in relation to neuromuscular synapse endplates. Electric stimulation applies additional electric impulse to the EMG-needle injected into the muscle; it causes contraction of the target muscle. In case the EMN-needle is positioned correctly, the drug is administered through it. This method of controlling BTA injections is widely used to treat cervical dystonia and graphospasm; this allows achieving significantly better results than by palpatory-anatomic needle orientation [27-29].

Patients with spastic motor disturbances, especially children with CP, are often unable or refuse to make precise, isolated motions in certain muscle groups and relax the electrode-injected extremity; this complicates the use of EMG-control in this group of patients or leads to erroneous interpretation of the received EMG-signal [30]. Moreover, EMG-control often requires repeated needle injection in order to find its optimal position in the muscle; together with the increased needle's diameter, it aggravates the procedure's painfulness and its unacceptance by children. Use of anesthesia leads to the general reduction in muscular tone and EMG-signal amplitude; this makes it indistinguishable from EMG-signal of the adjacent muscles. In these cases it is necessary to employ additional electric stimulation.

Thus, method of EMG-controlling BTA injections at spastic CP forms has certain informativity, but it requires not only adequate sedation and anesthesia, but also additional equipment, consumables and doctor's (who conducts injections) knowledge of basics of electrophysiological techniques.

Endoscopic and radiographic methods of controlling BTA injections

Endoscopy is used for direct visualization of BTA injections into muscles of gastrointestinal tract (in case of esophageal achalasia, sphincter of Oddi dysfunction, gastroparesis), urogenital system (in case of hyperactive urinary bladder, Hinman syndrome, benign prostate hyperplasia), larynx and vocal cords (at spastic dysphonia) [31-36].

CT and fluoroscopy are methods of controlling BTA injections used primarily to specify needle's position in the deeply located neck, back and pelvis muscles adjacent to anatomically important structures – at certain forms of cervical dystonia [37], piriformis syndrome [38], spasticity of iliopsoas muscle.

BTA injections at spastic forms of cerebral palsy using CT and radiographic control increase patient's radiation exposure, require anesthesia, proper diagnostic equipment,

participation of an anesthesiologist and roentgen diagnostician; this restricts the use of this technique to a narrow range of clinical indications and well-equipped medical institutions.

BTA injections controlled by ultrasound (US-control)

Ultrasound has successfully been used for several decades at various medical manipulations and minimally invasive interventions. Ultrasound provides not only good informativity, but also high reiteration of study results at the visualization of muscles, tendons, neurovascular fascicles and soft-tissue masses [39]. Relatively low cost, quickness, non-invasiveness of the trial and lack of radiation exposure allow using this method for repeated control before, during and after medical manipulation.

The first work dedicated to the US-control of BTA injections at esophageal achalasia was published in 1996 [40]. By 2002 there had been data on the effectiveness of using US-control at BTA administration into spastic muscles at CP [41-44]. As experience of using US-control in botulinum therapy at spasticity accumulated, more authors started giving preference to this method, which became the most widespread in pediatric practice [30, 45, 46].

Standard linear US measuring devices (7-18MHz) are used for US-control of BTA injections; they are used to visualize musculoskeletal and superficially positioned soft-tissue structures. Injections are conducted by needles (thickness – 25-27G). The required needle length can be calculated during the preliminary US-trial of the target muscle, by measuring its thickness and occurrence depth.

Main advantages of ultrasound over other methods of controlling BTA injections at spasticity in children is the possibility of quick, painless and safe on-line visualization not only of target muscles, but also of adjacent muscles and structures, possibility of controlling the needle injection and its passing by vessels, nerves, bones and ligaments, optimal needle position in the injectable muscle. Use of ultrasound control allows determining position and structure of the spastic muscle, which is different from anatomic norm in size and density, before the injection; this allows avoiding repeated needle injections and ineffective use of the drug.

Another important advantage of US-control of BTA injections in pediatrics is the procedure's quickness and lack of need in active patient-doctor cooperation. S. Berweck et al. [47] showed that average time spent on finding the target muscle and BTA injection is from 5 seconds for superficially located muscles (gastrocnemius muscle, biceps muscle of arm) to 30 seconds for deep muscles (posterior tibial muscle, iliopsoas muscle) by example of 350 children (more than 6,000 injections into 70 different muscles). Moreover, US-devices are available a every medical institution conducting BTA injections, while the US-control procedure requires almost no additional consumables.

Recently there have been accumulating clinical data confirming that the use of US-control increases not only precision, but also effectiveness of BTA injections in children with spastic CP forms [48, 49]. The data that have been published are only preliminary. There are further clinical studies, comparison of effectiveness of different methods of controlling BTA injections in children, including injections into muscles of upper extremities.

Authors' experience of US-control of BTA injections in children with spastic CP forms

Unfortunately, the most widespread method of controlling BTA injections in children with spastic CP forms in Russia remain palpation/anatomic control. We have not found national works on using botulinum therapy US-control in pediatric practice in medical literature. At the same time, preliminary results obtained by implementing US-control of botulinum toxin injections at the FSBI "Scientific Center of Children's Health" allow speaking of good effectiveness, safety and convenience of using this method in national medical practice.

We have been conducting US-control of botulinum toxin injection since September 2012. Specialized botulinum therapy office started operating in November 2012; it is equipped with modern equipment for anesthesia, which is important when injection BTA to infants and patients with severe CP forms.

Before a BTA injection, patients with spastic CP forms undergo preliminary examination and, according to indications, laboratory and instrumental examination, specification of the general condition. In case there are no contraindications against injections, patients are examined by a neurologist (able to conduct botulinum therapy), orthopedist, exercise therapy doctor, physiotherapist and, if anesthesia is required, anesthesiologist together. Together with parents and patients, doctors choose priority objectives of BTA injections and subsequent rehabilitation; then they choose target muscles for injection, determined dosage and necessity of anesthesia.

During the procedure the doctor conducting injection using US-control preliminarily visualizes the target muscle and adjacent structures, chooses the safest way for the needle; this is especially important for injection into posterior tibial muscle, iliopsoas muscle and forearm muscle. US also helps determining the most altered and the most preserved parts of muscles in case of intense prolonged spasticity. US-device is positioned perpendicularly to muscular length. The needle is injected at a small angle to the device's axis, away from its edge to avoid damaging the device's membrane. Needle's tip progress is usually clearly seen on the device's screen; several authors recommend making slight oscillatory motions with a needle without its significant displacement [41, 45]. After the needle has been optimally positioned, the BTA drug is administered, its spread – controlled (using the device's screen). US-control shows the drug

spreading in the muscle as a widening cloud, echo-density of which is different from echo-density of the adjacent tissues.

Muscles, which pose difficulties for palpatory control of BTA injections and, thus, require US-visualization more often, are iliopsoas, piriform, posterior tibial muscles, gracilis muscle of thigh, almost all muscles of forearm, including the most subject to spasticity at CP superficial and deep flexor muscles of fingers, ulnar and radial flexor muscles of wrist, round pronator muscle (see pic. 1 a-c) [45].

When conducting injection into an iliopsoas or posterior tibial muscle, not only the deep position of muscles poses difficulty, but also their close contact with neurovascular fascicles (pic. 2, 3). That is why BTA injections with US-control require child's still position or sedation/anesthesia in certain cases. When conducting injections into muscles of forearm, it is necessary to remember about the complex topographic relationship of anatomic structures in this area, big number of vessels and nerves, which, if damaged, may lead to the extremity's malfunction, and small size of the injectable muscles, especially in children. Thus, e.g., long palmar muscle may lead to flexion contracture in wrist joint in case of spastic tension. However, this muscle is naturally present not in all people, is small in diameter and superficial (pic. 4), which makes reliable hit almost impossible employing palpatory control of BTA injections. US-control helps to resolve this issue.

In conclusion we give preliminary results of authors' use of US-control at BTA injections. Throughout 4 months, BTA injections with US-control were made into 41 muscles of 7 patients with spastic CP forms with the age range of 3 years 1 months to 15 years 4 months (4 boys, 3 girls), who had not received BTA drugs before (tb.). US-control was necessary in all cases due to muscular spasticity in patients, which is why muscles could only poorly be identified by standard palpatory-anatomic methods. Before, 1 and 3 months (in 5 patients) after administering BTA and providing a 2-week-long standard rehabilitation course (massage, exercise therapy, physiotherapy, orthostatics) we assessed tone and strength of injectable muscles according to the modified Ashworth scale and 6-point muscle strength evaluation scale. Gradual reduction in muscular tone was noted on the 4th post-injection day; it reached its lowest level by the end of the first month (spasticity reduction by 1-3 points off the initial level by Ashworth scale without significant muscle strength loss). Neither weakness in adjacent muscles nor complications associated with injury of adjacent structures developed in all cases. Spasticity in injectable muscles started increasing in 3 out 5 patients 3 months after the injection; the conducted treatment's effect remained on the prior level in 2 patients. Muscular tone increased in all cases, most prominently in muscles of lower extremities; in muscles of arm the conducted treatment's effect remained for longer periods.

It should be noted that it is precise, measured reduction of pathological tone in muscles of upper extremities that not only reduces dynamic deformities and visual defect, but also increases amplitude of active movements and improves arm function. Timely pathological tone correction in upper extremities allows both avoiding further orthopedic complications and optimally using the damaged brain plasticity reserves and extensive compensatory nervous system's capabilities associated with arm function, which certainly reflects on the psychoverbal development of CP patients, on possibility of their future social and labor adaptation [50].

Conclusions

Use of palpatory and anatomic orientation at botulinum toxin A injections is insufficiently effective and reliable for deeply occurring or small muscles, which is especially relevant in pediatric neurologic practice. Precision control of BTA injections at spastic CP forms requires a quick, minimally traumatic and painful, reliable and reproducible, economically sound method. Ultrasound visualization optimally meets all these requirements. US-control of BTA injections in children with spastic CP forms is a method of choice in many foreign medical and rehabilitation centers, however, it does not rule out using other control methods.

Use of ultrasound visualization of BTA injection in authors' own practice allowed achieving high clinical botulinum therapy effectiveness in all the described patients. The data obtained during the trial confirm good effectiveness, clearness and convenience of using US-control method for injections in pediatric neurologic practice. Further study of possibilities this method gives, comparison of its effectiveness with other approaches to localization of target muscles will allow choosing an optimal method of conducting botulinum therapy in each clinical case and improving treatment and rehabilitation results for patients with cerebral palsy in whole.

REFERENCES

1. Scott A. B. Botulinum toxin injection into extraocular muscles as an alternative to strabismus surgery. *Ophthalmology*. 1980; 87 (10): 1044–9.
2. Koman L. A., Mooney J. F., Smith B., Goodman A., Mulvaney T. Management of cerebral palsy with botulinum-A toxin: preliminary investigation. *J Pediatr Orthop*. 1993; 13 (4): 489–95.
3. Cosgrove A. P., Corry I. S., Graham H. K. Botulinum toxin in the management of the lower limb in cerebral palsy. *Dev Med Child Neurol*. 1994; 36 (5): 386–96.
4. Dutikova E.M., Lil'in E.T. *Farmateka - Pharmateca*. 2007; 7 (142): 37–42.
5. Zmanovskaya V.A. *Klinicheskie varianty spasticheskikh form detskogo tserebral'nogo paralicha i otsenka effektivnosti botulinoterapii. Avtoref. dis. … kand. med. nauk* [Clinical Types of Spastic Form of Cerebral Palsy and Evaluation of Botulinum Toxin Therapy. Author's abstract]. Ekaterinburg, 2011. 22 p.
6. Kurenkov A.L., Batysheva T.T., Vinogradov A.V., Zyuzyaeva E.K. *Zhurnal nevrologii i psikhiatrii – Journal of neuropathology and psychiatry*. 2012; 7 (2): 24–28.

7. Graham H. K., Aoki K. R., Autti-Ramo I., Boyd R. N., Delgado M. R., Gaebler-Spira D. J., Gormley M. E., Guyer B. M., Heinen F., Holton A. F., Matthews D., Molenaers G., Motta F., Garcia Ruiz P. J., Wissel J. Recommendations for the use of botulinum toxin type A in the management of cerebral palsy. *Gait Posture*. 2000; 11 (1): 67–79.

8. Aldosari M. S., Bohlega S. A., Al-Jadid M. A., El-Tamawy M. S., Ramadan M. A., Mousali Y. K., Yaghmour A. T., Kurdi A. M., Koussa S. H., Khamis S. N., Zeljic V. E., Shacfe H. D., Molteni F. G. Pan-Arab consensus statement on the use of botulinum toxin type A in spasticity management. *Neurosciences (Riyadh)*. 2007; 12 (4): 279–81.

9. Heinen F., Desloovere K., Schroeder A. S., Berweck S., Borggraefe I., van Campenhout A., Andersen G. L., Aydin R., Becher J. G., Bernert G., Caballero I. M., Carr L., Valayer E. C., Desiato M. T., Fairhurst C., Filipetti P., Hassink R. I., Hustedt U., Jozwiak M., Kocer S. I., Kolanowski E., Krageloh-Mann I., Kutlay S., Maenpaa H., Mall V., McArthur P., Morel E., Papavassiliou A., Pascual-Pascual I., Pedersen S. A., Plasschaert F. S., van der Ploeg I., Remy-Neris O., Renders A., Di Rosa G., Steinlin M., Tedroff K., Valls J. V., Viehweger E., Molenaers G. The updated European Consensus 2009 on the use of Botulinum toxin for children with cerebral palsy. *Eur J Paediatr Neurol*. 2010; 14 (1): 45–66.

10. Delgado M. R., Hirtz D., Aisen M., Ashwal S., Fehlings D. L., McLaughlin J., Morrison L. A., Shrader M. W., Tilton A., Vargus-Adams J. Practice parameter: pharmacologic treatment of spasticity in children and adolescents with cerebral palsy (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology*. 2010; 74 (4): 336–43.

11. Fehlings D., Novak I., Berweck S., Hoare B., Stott N. S., Russo R. N. Botulinum toxin assessment, intervention and followup for paediatric upper limb hypertonicity: international consensus statement. *Eur J Neurol*. 2010; 17 (Suppl. 2): 38–56.

12. Hoare B. J., Wallen M. A., Imms C., Villanueva E., Rawicki H. B., Carey L. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy (UPDATE). *Cochrane Database Syst Rev*. 2010; 1.

13. Love S. C., Novak I., Kentish M., Desloovere K., Heinen F., Molenaers G., O'Flaherty S., Graham H. K. Botulinum toxin assessment, intervention and after-care for lower limb spasticity in children with cerebral palsy: international consensus statement. *Eur J Neurol*. 2010; 17 (Suppl. 2): 9–37.

14. Lim E. C., Quek A. M., Seet R. C. Accurate targeting of botulinum toxin injections: how to and why. *Parkinsonism Relat Disord*. 2011; 17 (Suppl. 1): 34–9.

15. Shaari C. M., Sanders I. Quantifying how location and dose of botulinum toxin injections affect muscle paralysis. *Muscle Nerve*. 1993; 16 (9): 964–9.

16. Borodic G. E., Ferrante R., Pearce L. B., Smith K. Histologic assessment of dose-related diffusion and muscle fiber response after therapeutic botulinum A toxin injections. *Mov Disord*. 1994; 9 (1): 31–9.

17. Hsu T. S., Dover J. S., Arndt K. A. Effect of volume and concentration on the diffusion of botulinum exotoxin A. *Arch Dermatol*. 2004; 140 (11): 1351–4.

18. Kinnett D. Botulinum toxin A injections in children: technique and dosing issues. *Am J Phys Med Rehabil*. 2004; 83 (10 Suppl.): 59–64.

19. Shaari C. M., George E., Wu B. L., Biller H. F., Sanders I. Quantifying the spread of botulinum toxin through muscle fascia. *Laryngoscope*. 1991; 101 (9): 960–4.

20. Gracies J. M., Hefter H., Simpson D. M., Moore P. Spasticity in adults. In: Moore P., Naumann M., eds. Handbook of botulinum toxin treatment. *Oxford: Blackwell Science*. 2003. P. 219–71.

21. Pathak M. S., Nguyen H. T., Graham H. K., Moore A. P. Management of spasticity in adults: practical application of botulinum toxin. *Eur J Neurol*. 2006; 13 (Suppl. 1): 42–50.

22. Shortland A. P., Harris C. A., Gough M., Robinson R. O. Architecture of the medial gastrocnemius in children with spastic diplegia. *Dev Med Child Neurol*. 2002; 44 (3): 158–63.

23. Vasilescu D., Vasilescu D., Dudea S., Botar-Jid C., Sfrangeu S., Cosma D. Sonoelastography contribution in cerebral palsy spasticity treatment assessment, preliminary report: a systematic review of the literature apropos of seven patients. *Med Ultrason*. 2010; 12 (4): 306–10.

24. Childers M. K. The importance of electromyographic guidance and electrical stimulation for injection of botulinum toxin. *Phys Med Rehabil Clin N Am*. 2003; 14 (4): 781–92.

25. Chin T. Y., Nattrass G. R., Selber P., Graham H. K. Accuracy of intramuscular injection of botulinum toxin A in juvenile cerebral palsy: a comparison between manual needle placement and placement guided by electrical stimulation. *J Pediatr Orthop*. 2005; 25 (3): 286–91.

26. Wissel J., Poewe W. EMG for identification of dystonic, tremulous and spastic muscles and techniques for guidance of injections in Handbook of Botulinum Toxin Treatment, 2nd Edition (Moore N. M., ed.) *Blackwell Science: Oxford*. 2003. P. 76–98.

27. Comella C. L., Buchman A. S., Tanner C. M., Brown-Toms N. C., Goetz C. G. Botulinum toxin injection for spasmodic torticollis: increased magnitude of benefit with electromyographic assistance. *Neurology*. 1992; 42 (4): 878–82.

28. Dressler D. Electromyographic evaluation of cervical dystonia for planning of botulinum toxin therapy. *Eur J Neurol*. 2000; 7 (6): 713–8.

29. Traba Lopez A., Esteban A. Botulinum toxin in motor disorders: practical considerations with emphasis on interventional neurophysiology. *Neurophysiol Clin*. 2001; 31 (4): 220–9.

30. Schroeder A. S., Berweck S., Lee S. H., Heinen F. Botulinum toxin treatment of children with cerebral palsy — a short review of different injection techniques. *Neurotox Res*. 2006; 9 (2–3): 189–96.

31. Kalloo A. N., Pasricha P. J. Therapy of sphincter of Oddi dysfunction. *Gastrointest Endosc Clin N Am*. 1996; 6 (1): 117–25.

32. Lake J. M., Wong R. K. Review article: the management of achalasia — a comparison of different treatment modalities. *Aliment Pharmacol Ther*. 2006; 24 (6): 909–18.

33. Game X., Castel-Lacanal E., Bentaleb Y., Thiry-Escudie I., De Boissezon X., Malavaud B., Marque P., Rischmann P. Botulinum toxin A detrusor injections in patients with neurogenic detrusor overactivity significantly decrease the incidence of symptomatic urinary tract infections. *Eur Urol*. 2008; 53 (3): 613–8.

34. Lim E. C., Seet R. C. Botulinum toxin: description of injection techniques and examination of controversies surrounding toxin diffusion. *Acta Neurol Scand*. 2008; 117 (2): 73–84.

35. Reddymasu S. C., Singh S., Sankula R., Lavenbarg T. A., Olyaee M., McCallum R. W. Endoscopic pyloric injection of botulinum toxin-A for the treatment of postvagotomy gastroparesis. *Am J Med Sci*. 2009; 337 (3): 161–4.

36. Blitzer A. Spasmodic dysphonia and botulinum toxin: experience from the largest treatment series. *Eur J Neurol*. 2010; 17 (Suppl. 1): 28–30.

37. Glass G. A., Ku S., Ostrem J. L., Heath S., Larson P. S. Fluoroscopic, EMG-guided injection of botulinum toxin into the longus colli for the treatment of anterocollis. *Parkinsonism Relat Disord*. 2009 Sep; 15 (8): 610–3.

38. Yoon S. J., Ho J., Kang H. Y., Lee S. H., Kim K. I., Shin W. G., Oh J. M. Low-dose botulinum toxin type A for the treatment of refractory piriformis syndrome. *Pharmacotherapy*. 2007; 27 (5): 657–65.

39. Fischer A. Q., Carpenter D. W., Hartlage P. L., Carroll J. E., Stephens S. Muscle imaging in neuromuscular disease using computerized real-time sonography. *Muscle Nerve*. 1988; 11 (3): 270–5.

40. Schiano T. D., Fisher R. S., Parkman H. P., Cohen S., Dabezies M., Miller L. S. Use of high-resolution endoscopic ultrasonography to assess esophageal wall damage after pneumatic dilation and botulinum toxin injection to treat achalasia. *Gastrointest Endosc*. 1996; 44 (2): 151–7.

41. Berweck S., Feldkamp A., Francke A., Nehles J., Schwerin A., Heinen F. Sonography-guided injection of botulinum toxin A in children with cerebral palsy. *Neuropediatrics*. 2002; 33 (4): 221–3.

42. Berweck S., Heinen F. Use of botulinum toxin in pediatric spasticity (cerebral palsy). *Mov Disord*. 2004; 19 (Suppl. 8): 162–7.

43. Willenborg M. J., Shilt J. S., Smith B. P., Estrada R. L., Castle J. A., Koman L. A. Technique for iliopsoas ultrasound-guided active electromyography-directed botulinum a toxin injection in cerebral palsy. *J Pediatr Orthop*. 2002; 22 (2): 165–8.

44. Westhoff B., Seller K., Wild A., Jaeger M., Krauspe R. Ultrasoundguided botulinum toxin injection technique for the iliopsoas muscle. *Dev Med Child Neurol.* 2003; 45 (12): 829–32.

45. Alter K. E. High-frequency ultrasound guidance for neurotoxin injections. *Phys Med Rehabil Clin N Am*. 2010; 21 (3): 607–30.

46. Hustedt U. Botulinumtoxin bei spastischen Bewegungsstorungen. Ultraschallgestutzte Technik und Anwendung. *KVM*. 2010. P. 13–15.

47. Berweck S., Schroeder A. S., Fietzek U. M., Heinen F. Sonography- guided injection of botulinum toxin in children with cerebral palsy. *Lancet*. 2004; 363 (9404): 249–50.

48. Py A. G., Zein Addeen G., Perrier Y., Carlier R. Y., Picard A. Evaluation of the effectiveness of botulinum toxin injections in the lower limb muscles of children with cerebral palsy. Preliminary prospective study of the advantages of ultrasound guidance. *Ann Phys Rehabil Med.* 2009; 52 (3): 215–23.

49. Kwon J. Y., Hwang J. H., Kim J. S. Botulinum toxin a injection into calf muscles for treatment of spastic equinus in cerebral palsy: a controlled trial comparing sonography and electric stimulationguided injection techniques: a preliminary report. *Am J Phys Med Rehabil*. 2010; 89 (4): 279–86.

50. Baranov A.A., Klochkova O.A., Kurenkov A.L., Namazova-Baranova L. S., Nikitin S.S., Artemenko A.R., Mamed"yarov A.M. *Pediatricheskaya farmakologiya – Pediatric pharmacology*. 2012; 9 (6): 24–32.
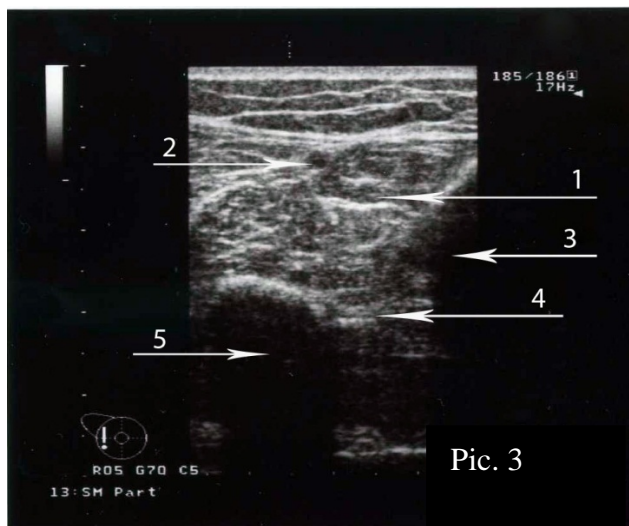
Pic. 1. Ultrasound imaging of round pronator muscle (arrow-pointed) in (a) a healthy 12-year-old boy, (b) a healthy 27-year-old woman and (c) a 12-year-old patient with spastic tetraparesis (approximate muscle contour is highlighted by dots)
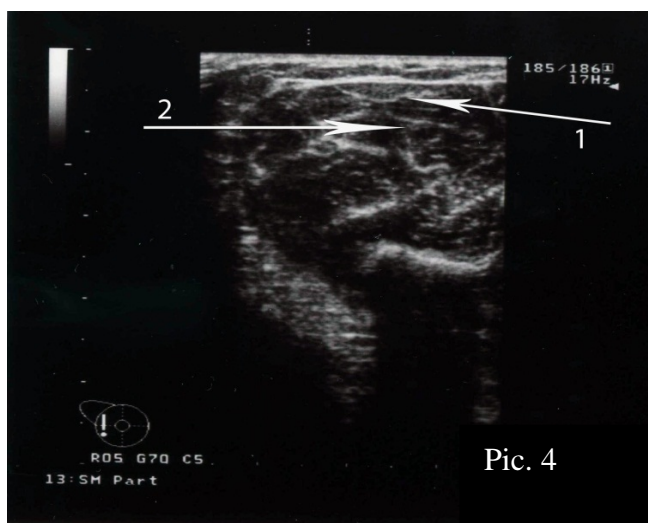
Pic. 1a

Pic. 1b

Pic. 1c
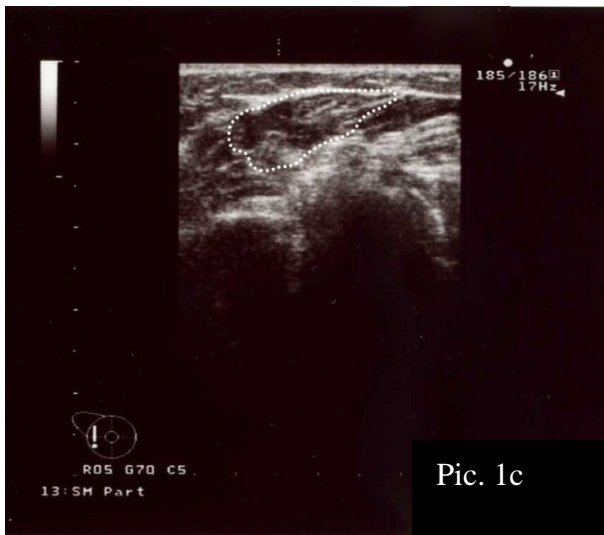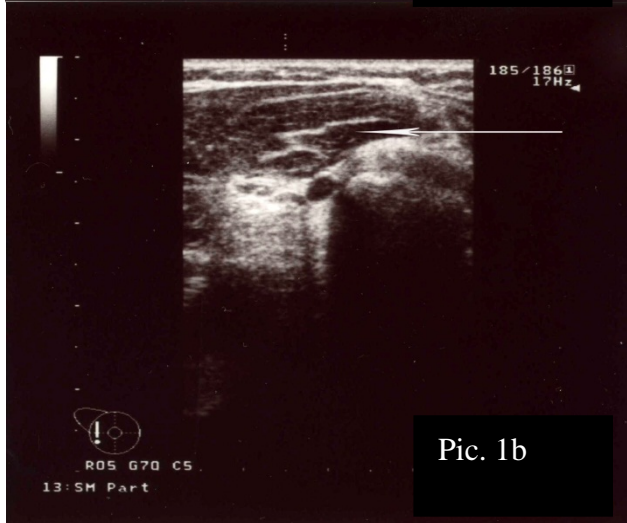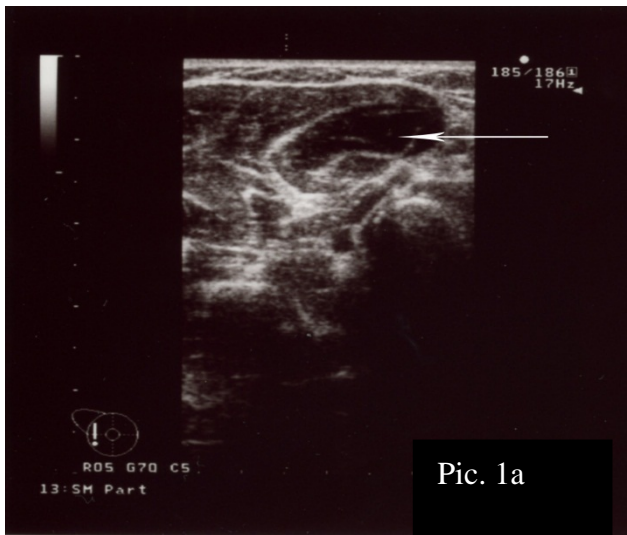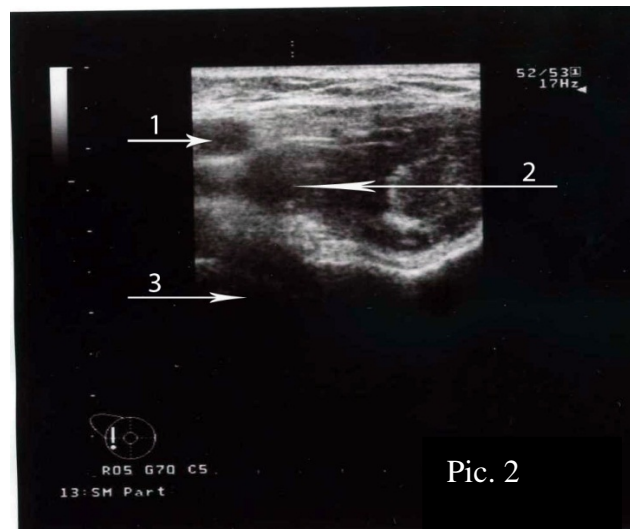
Pic. 2. Ultrasound imaging of iliopsoas muscle (2) and adjacent structures – femoral artery (1) and hip joint (3)

Pic. 3. Ultrasound imaging of a posterior tibial muscle (1) and adjacent structures: peroneal artery (2), shin bone (3), interosseous membrane (4) and fibular bone (5)

Pic. 4. Ultrasound imaging of a long palmar muscle (1) and adjacent superficial flexor muscle of fingers (2)

Table 1. Choice of target muscles for BTA injections with US-control in 7 patients with spastic CP forms

Patient (age, diagnosis/code according to the ICD-10) Muscles	G., 12 years 1 month G82.4	L., 5 years 5 months G80.1	L., 3 years 7 months G80.2	S., 14 years 11 months G82.4	S., 11 years 2 months G80.1	S., 3 years 1 month G82.4	Y., 15 years 4 months G80.2	Total muscles
M. brachialis	+		+					2
M. biceps brachii			+	+	++	+		5
M. brachioradialis				+				1
M. flexor digitorum superficialis				+				1
M. flexor digitorum profundus				+				1
M. flexor carpi ulnaris	+		+	+				3
M. pronator teres	+	++	+		++	+		7
M. palmaris longus				+	+			2
M. adductor pollicis	+			+				2
M. gastrocnemius		++	+			+		4
M. semimembranosus		++			++			4
M. semitendinosus		++			++			4
M. gracilis		++						2
M. adductor magnus et longus					++			2
M. extensor hallucis longus							+	1
Total muscles								41

Note. + - BTA was injected in muscle of one extremity; ++ - BTA was injected in muscles of both extremities; G80.1 – spastic diplegia; G80.2 – infantile hemiplegia; G82.4 – spastic tetraplegia.