J Rehabil Med 2020; 52: jrm00014



## LETTER TO THE EDITOR

# BOTULINUM TOXIN TYPE A FOR SPASTIC CEREBRAL PALSY: IS IT TIME TO CHANGE PRAXIS?

We read the articles by Schasfoort et al. (1, 2) with great interest, since the use of botulinum toxin type A (BoNT-A) in children with spastic cerebral palsy (SCP) has been the subject of our research. The great congruence in study design, subjects/patients and methods with one of our papers prompts us to describe our observations, comparisons and conclusions, and to publish certain data from our study (3) for the first time here.

In designing our study, based on our previous experience we decided to apply BoNT-A with the aim of correcting dynamic spastic equinus, if the following inclusion criterion was fulfilled: dynamic contracture of the ankle joint with inadequate response (no reduction in spasticity over a period of 2 months of continuous physical therapy (CPT)) (3). The design of CPT is identical to intensive physiotherapy alone and, if necessary, it can be combined with ankle-foot orthoses to achieve full comprehensive rehabilitation (CR), as described by Schasfoort et al. (1, 2).

BoNT-A treatment adhered to international consensus recommendations related to preparations, cautions, dose modifiers, localization techniques and safety aspects (4).

By fulfilling the aforementioned criterion, a total of 17 children were excluded from our study. We publish this data for the first time here, since it was not the aim of our study. Twelve of the children had motor functional status level II, determined by Gross Motor Function Classification System (GMFCS) and 10 children had gastrocnemius muscle spasticity degree 2, estimated by the Modified Ashworth Scale (MAS).

Six months after the application of BoNT-A into the spastic gastrocnemius muscle, when BoNT-A is no longer pharmacologically effective, the results showed statistically significant benefit in the following parameters: ankle joint range of movement (active and passive) and motor functional status estimated by Gross Motor Function Measure (GMFM) dimension D (standing), while the tendency towards lower spasticity values has no statistical significance.

CPT was applied for a period of 16 weeks after application of BoNT-A. Six months after application of BoNT-A the parents completed a questionnaire. This revealed an important piece of information; that 75% of parents continued to perform physical exercises with their children at home, based on the exercise programme they attended 2–3 times a week during the research. We have not published this information previously, as it was not sufficiently significant (questions arise as to the parents' competence, the duration of exercise, etc.).

The results and data from our study (3) can be viewed in correlation with the results reported by Schasfoort et al. (1, 2). We support their conclusions, that the role and therapeutic efficacy of BoNT-A, CR, and orthoses, alone and in combination, should be defined in spasticity treatment in children with SCP.

In favour of these data we refer to the paper by Dai & Demiryürek (5), who compared 2 groups of children with SCP after BoNT-A injection in the lower extremities, with or without orthoses. The results suggested that, in children with orthoses, spasticity was statistically significantly lower, as measured by MAS. The conclusion is that the reduction in spasticity cannot be attributed to BoNT-A, since the orthosis was applied at the time of maximum effect of BoNT-A, when there was no active movement to the functional position (5).

There has been great enthusiasm in recent decades about the results of BoNT-A application in the treatment of lower limb spasticity in ambulatory children with SCP, but new studies have pointed out some adverse effects. A study by Caroline et al. revealed that atrophy of the injected muscle after first application of BoNT-A in the gastrocnemius muscle in children with SCP is greater in comparison with further applications, and hypertrophy is evident in the soleus after exposure of the gastrocnemius to BoNT-A (6).

It has been proven that the second identical injection of BoNT-A 3 months after the first causes an intense and permanent loss of muscle function and alternations in muscle structure. Structural abnormalities include fibre type transition, fibre type grouping, and lipid accumulation. The precise mechanisms of these changes remain unclear (7).

Available published data show that, after application of BoNT-A injection for lower limb spasticity in children with spasticity levels 2 and 3 based on MAS, sleep disorders were reduced, sleep quality improved, and maternal depression decreased. The results of the study revealed that the rate of night-time orthoses was as high as 83.3%, but this information was ignored in the discussion and conclusion, and there are no data related to the use of physical therapy (8). It should be noted that we have not found any current papers in the research literature dealing with these problems after exercising CR. Thus, it can be concluded that BoNT-A treatment is preferred and is most important with regards to the benefits of multimodal treatment of spasticity in children with SCP and in the mental health domain.

We fully agree with Schasfoort et al.'s points of view, as mentioned above, but we would also like to make the following suggestions.

 ISSN 1650-1977 doi: 10.2340/16501977-2641

Firstly, instrumented assessment of the neural and non-neural contribution to hyper-resistance has been a huge step in achieving an adequate treatment approach (9). The non-neural component intensifies in children with SCP as a consequence of maladaptation to growth, implying that, in the reported subgroup of children with CP, the non-neural component was undoubtedly significantly present. Thus, we believe that utilization of CR, as a treatment for dynamic contractures in ambulatory children with SCP up to the age of 12 years and spasticity based on MAS up to degree 2, should be evaluated, along with determination of an optimal timeframe. We believe that the aforementioned approach to the subgroup of children with SCP, along with a positive therapeutic effect, would make this method available, and cost-effective, without causing discomfort in children while undergoing electromyography.

Secondly, utilization of CR during the growing years in children with SCP should be considered in relation to the protocol, since there is also an ethical question as to whether to expose children to stress (e.g. injections of toxin, not necessarily under anaesthesia), if identical results can be achieved by using non-invasive methods.

## REFERENCES


1. Schasfoort F, Dallmeijer A, Pangalila R, Catsman C, Stam H, Becher J, et al. Value of botulinum toxin injections preceding a comprehensive rehabilitation period for children with spastic cerebral palsy: a cost-effectiveness study. J Rehabil Med 2018; 50: 22–29.
2. Schasfoort F, Pangalila R, Sneekes E, Catsman C, Becher J, Horemans H et al. Intramuscular botulinum toxin prior to comprehensive rehabilitation has no added value for improving motor impairments, gait kinematics and goal attainment in walking children with spastic cerebral palsy. J Rehabil Med 2018; 50: 732–742.
3. Colovic H, Dimitrijevic L, Stankovic I, Nikolic D, Radovic-Janosevic D, Zivanovic D. The effects of botulinum toxin type A on improvement and dynamic spastic equinus correction in children with cerebral palsy – preliminary results. Arch Med Sci 2014; 10: 979–984.
4. Love SC, Novak I, Kentish M, Desloovere K, Heinen F, Molenaers G et al; Cerebral Palsy Institute. Botulin 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.
5. Dai AI, Demiryürek AT. Serial casting as an adjunct to botulinum toxin type a treatment in children with cerebral palsy and spastic paraparesis with scissoring of the lower extremities. J Child Neurol 2017; 32: 671–675.
6. Alexander C, Elliott C, Valentine J, Stannage K, Bear N, Donnelly CJ et al. Muscle volume alterations after first botulinum neurotoxin A treatment in children with cerebral palsy: a 6-month prospective cohort study. Dev Med Child Neurol 2018; 60: 1165–1171.
7. Minamoto VB, Suzuki KP, Bremner SN, Lieber RL, Ward SR. Dramatic changes in muscle contractile and structural properties after 2 botulinum toxin injections. Muscle Nerve 2015; 52: 649–657.
8. Binay Safer V, Ozbudak Demir S, Ozkan E, Demircioglu Guneri F. Effects of botulinum toxin serotype A on sleep problems in children with cerebral palsy and on mothers sleep quality and depression. Neurosciences 2016; 21: 331–337.
9. van den Noort JC, Bar-On L, Aertbeliën E, Bonikowski M, Braendvik SM, Broström EW, et al. European consensus on the concepts and measurement of the pathophysiological neuromuscular responses to passive muscle stretch. Eur J Neurol 2017; 24: 981–e38.


Accepted Dec 19, 2019; Epub ahead of print Jan 8, 2020

*Hristina Colovic,MD, PhD[1,2], Lidija Dimitrijevic, MD, PhD[1,2], Ivona Stankovic, MD, PhD[1,2], Dragana Radovic-Janosevic, MD, PhD[3,4] and Dragan Zlatanovic, MD, PhD[1,2]*

From the [1]Department for Physical Medicine and Rehabilitation, Faculty of Medicine, University of Nis, [2]Clinic for Physical Therapy and Rehabilitation, Clinical Centre of Nis, [3]Department for Gynecology and Obstetrics, Faculty of Medicine, University of Nis and [4]Clinic for Gynecology and Obstetrics, Clinical Centre of Nis, Nis, Serbia.

E-mail: hristina.colovic@medfak.ni.ac.rs

---

The authors of the original articles (Schasfoort et al.) were given the opportunity to comment in response to this Letter, but chose not to do so.