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Original Article

Effect of combined rehabilitation program with botulinum toxin type A injections on gross motor function scores in children with spastic cerebral palsy

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Abstract. [Purpose] To examine whether combining botulinum toxin type A with physiotherapy is better than botulinum toxin type A alone in reducing muscle tone and improving gross motor function in spastic diplegia. [Subjects and Methods] Forty-six ambulatory children with spastic diplegia (age: 25–154 months) were recruited. Patients were assigned to Groups 1 (n=18) and 2 (n=28). After baseline assessment, all children received botulinum toxin type A injections (6 units/kg) into the lower limb muscles. A second botulinum toxin type A injection was given 6 months later. The ankles were placed in plaster casts for 2 weeks after the first injection and an orthosis was prescribed after cast removal. Group 2 received 2 weeks of intensive physiotherapy. The gross motor function scores for the 2 groups were recorded at baseline, 4, 6, and 52 weeks. [Results] The improvement in gross motor function scores was significant for Group 2 and non-significant for Group 1. After 4, 6, and 52 weeks, Groups 1 and 2 showed 2.6% and 6.3% improvement, 4.8% and 12% improvement, and 5.5% and 19.4% improvement, respectively. [Conclusion] The addition of a 2-week physiotherapy programme after the initial botulinum toxin type A injections produced significantly greater improvements in gross motor function scores.
Key words: Botulinum toxin type A, Physiotherapy, Cerebral palsy

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INTRODUCTION

Spasticity is a common feature of cerebral palsy (CP). It often interferes with motor function, causes painful muscle spasms, and predisposes individuals to the development of fixed contractures. Successful treatment of spasticity usually improves selective motor control and motor function and delays or prevents the occurrence of contractures[1)]. Several assessment scales are used to assist in the diagnosis of spasticity and to measure its severity. These include the Ashworth scale, pendulum tests, spasm scores, Tardieu scales, and electrogoniometer. These clinical rating scales all have a subjective component for the assessment of spasticity.

Many treatment modalities, either individually or in combination with each other, are used for the treatment of spasticity. Botulinum toxin type A (BTX-A) has been shown to be a very safe and effective treatment for spasticity in children with CP. It reduces muscle tone, relieves muscle pain, and improves motor function[2–10)]. Few studies have evaluated the efficacy of treatment programs after BTX-A injection[11)]. The combination of treatment modalities has been shown to be more effective than the use of one treatment in the management of muscle spasticity. For example, Bottos et al. reported significant improve-

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ment in gross motor function (GMF) scores measured in children treated with BTX-A and plaster casts[8]. Empirical clinical observations suggest that physical activity enhances the beneficial effect of BTX-A. For example, Koman et al. observed that children with CP who were more physically active had better improvement in the tone of the injected muscle and a longer duration of effect after BTX-A injections than those who were less active[3]. However, the superiority of BTX-A and physiotherapy over BTX-A alone has not been conclusively demonstrated. Some authors have found the combined use of BTX-A and physiotherapy to be more effective than BTX-A alone[12], but this observation was not confirmed by other investigators[13]. Furthermore, one study that reported better clinical improvement with the combined use of BTX-A and physiotherapy (PT) over PT alone did not control for the content of the PT programme or the number of hours of treatment[14]. In this study, patients in the BTX-A and PT group received an average of 27.8 hours of treatment compared to those who received BTX-A alone. The purpose of the current investigation was to examine whether the combination of BTX-A and physiotherapy is more effective than BTX-A alone in reducing muscle tone and improving motor function in children with spastic diplegia.

SUBJECTS AND METHODS

Ambulatory children with CP were recruited for the study if they had spastic diplegia with predominantly spasticity of the ankle planter flexors causing significant gait abnormality. Those with clinical evidence of fixed contracture of the gastrocnemius/soleus muscle-tendon unit, significant leg length discrepancy resulting in gait asymmetry, history of lower limb surgery, or severe co-morbidity were excluded. Forty-six children (25 boys and 21 girls) were recruited for the study. All patients had spastic diplegia and dynamic equinus foot deformity. Their age ranged between 25 and 154 months at the start of the study.

This was a prospective, longitudinal study. The study was carried out at two rehabilitation centres. The same protocol was followed at each centre. The project was approved by the local research ethics committee. The patients' parents gave written informed consent for their children to take part in the study. The guidelines of the Declaration of Helsinki were followed. The children were assigned to one of two groups: Group 1 received BTX-A (Botox, Allergan Pharmaceuticals, USA) injections into the lower limb muscles on study entry and six months later. The number of muscles injected depended on the clinical indications, and included the gastrocnemius, soleus, hamstrings, or hip adductor muscles. The ankles were placed in plaster casts for 2 weeks after the first injection and the children were fitted with medical shoes after removal of the casts. Group 2 received the same treatment with the addition of intensive physical therapy for 2 weeks after the removal of the casts. The BTX-A injections were applied by an experienced clinician without electromyographic guidance, but using anatomical surface landmarks[14]. Local anaesthetics were not used before administering the injections. The injections were prepared by following the standard procedure recommended by the drug manufacturer. The dose administered was 6 units/kg of body weight per injection site. When a child received multiple injections, the total dosage of BTX-A did not exceed 200 units of Botox. The physiotherapy programme was delivered daily for 2 weeks and each treatment session lasted approximately one hour. It consisted of muscle stretching and a graded programme of exercises including non-weight bearing exercises, exercises against the therapist's resistance, and weight bearing motor functional activities.

Gross Motor Function Measure (GMFM) was the primary outcome measure. GMFM is a standardised observational instrument designed and validated in children with cerebral palsy[15]. The test includes 88 items grouped in five dimensions: Lying and Rolling; Sitting; Crawling and Kneeling; Standing; Walking, Running, and Jumping. The total score is obtained by calculating the mean of the five dimension scores. Assessments were carried out on study entry (baseline), and 4, 6, and 52 weeks after the BTX-A injections.

GMFM scores were analysed on a personal computer using the Gross Motor Ability Estimator (GMAE) software program[16]. Between groups comparison was performed with Mann-Whitney tests and one-way analysis of variance (ANOVA) was used for within group comparisons. The results were considered to be significant at $p<0.05$.

RESULTS

A total of 46 children were recruited for the study. Eighteen children received BTX-A alone (Group 1) and 28 had BTX-A and intensive physiotherapy for 2 weeks (Group 2). The allocation to the two groups was not balanced and randomised because of the hospital catchment areas. However, post-hoc statistical analysis revealed that no corrections were required. Before treatment began, there were no statistically significant differences between the initial GMFM scores of the two groups ($p=0.950$). There was an improvement from baseline in the mean GMFM scores in both groups at the subsequent points of assessment (Table 1). The magnitude of improvement in mean GMFM was greater in Group 2. Within group comparisons were performed using ANOVAs. In Group 1, the GMFM scores did not change significantly from baseline at any point of assessment ($p=0.358$). However, in Group 2, there was a statistically significant increase in the GMFM score above baseline values within the group after initial treatment ($p=0.001$).

Between groups comparison performed using the Mann-Whitney test showed that the improvement in GMFM scores was significantly greater in Group 2 than in Group 1 at each point of assessment ($p\leq0.001$). It is noted that, the GMFM scores at week 4 showed that Group 2 scored higher than Group 1. In addition, the GMFM scores after 52 weeks for children in Group 2 were higher than those in Group 1. No adverse effects were observed or reported during the study.

Table 1. Mean and standard deviations of the GMFM scores of the two groups before treatment and at intervals of 4, 6, and 52 weeks after initial treatment

Assessment week	Group 1 (n=18)	Group 2 (n=28)
	Mean ± SD	Mean ± SD
Baseline	58.3 (9.3)	58.1 (10.9)
Week 4	59.8 (9.6)	61.8 (11.0)
Week 6	61.1 (10.9)	65.1 (11.0)
Week 52	61.5 (10.3)	69.4 (13.0)

GMFM: Gross Motor Function Measure; SD: standard deviation.

DISCUSSION

BTX-A has been used in the management of spasticity in children with cerebral palsy to reduce muscle tone[3, 4, 15], improve motor function[1, 5, 17], and facilitate the use of orthoses. It may also delay the need for corrective orthopaedic surgery[1, 5, 18]. The current work supported that, the effectiveness of BTX-A appears to be enhanced when it is combined with an intensive rehabilitation program used in the current study.

The present study showed a significantly greater improvement in GMFM scores when BTX-A treatment was combined with a two-week physiotherapy programme compared to the use of BTX-A alone. Before BTX-A injection the mean GMFM scores were 58.3 ± 9.4 in group 1 and 58.1 ± 10.9 in group 2. At 4 weeks after the injection the mean scores were 59.8 ± 9.6 in Group 1 and 61.8 ± 11 in Group 2. By 6 weeks the mean score for Group 1 was 61.1 ± 10.1 and 65.2 ± 1 in Group 2. Finally, after 52 weeks it was 61.5 ± 10.3 in Group 1 and 69.4 ± 13 in Group 2. The GMFM scoring system has been recommended by several authors[1, 5, 16, 19] because it is a valid measure of motor function in children with cerebral palsy and it is sensitive to changes over time. This technique gives strength to the observations because it does not rely on subjective assessments. Few comparable studies are available. In agreement with the current work, a previous report supported the presence of functional improvement when administering plaster cast combined with BTX-A[8]. Another study supported the superiority of comprehensive rehabilitation together with BTX-A rather than BTX-A alone on mobility improvement[12].

In disagreement with the current work, a previous study by Reddihough et al. compared the effect of treatment of children with spastic CP with either BTX-A and physiotherapy (n=22) or physiotherapy alone. They measured the GMFM scores of both groups at 3 and 6 months. They found no statistically significant differences in the GMFM scores of the two groups, i.e. neither group improved[14]. This could be attributed to the timing of the assessments. Previous studies showed that the effect of BTX-A was strongest at 8 weeks and that, on average, it wore off 12 weeks after the injection[2]. In the present study, serial measurements were taken to allow a more complete comparison of the study treatment arms. The improvement in GMFM scores in Group 2 is clear and statistically significant at week 4 (6.3%) and week 6 (12%) of the study. It was also significant at week 52 (19.4%). However, the improvement in Group 1 was 2.6% at week 4, 4.8% at week 6, and 5.5% at week 52. These assessments showed that BTX-A alone is ineffective in improving GMFM scores at these times.

The present study examined the effect of the interventions on functional activities rather than changes in muscle tone. The GMFM is commonly used to establish the level of motor function at baseline and to detect change after therapeutic interventions, and it is sensitive except in patients with the mildest form of disability[16, 18]. The GMFM technique is known to have a reduced sensitivity in very severely affected cases where the scores are below 25. The children in this study scored above 35, and thus insensitivity of the assessment method does not apply to our sample.

One limitation of this study is the method of allocation of the children to the study and control groups. This was ultimately determined based on which hospital the children regularly attended. Strict randomisation could not be performed because of family circumstances. It is unlikely that significant bias was introduced into the study since the two study groups were closely matched for their demographic and clinical variables, including their baseline GMFM scores.

In conclusion, this study provides support for the use of combination therapies employing BTX-A and intensive physical therapy. There is evidence for its effect being greatest when used in children with mild to moderate spasticity.

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Presentation at a conference

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Conflict of interest

None.

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