SHORT COMMUNICATION

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The effect of physical therapy in the treatment of patients with cervical dystonia with or without concomitant use of botulinum toxin

Efekat fizikalne terapije u lečenju obolelih od cervikalne distonije sa ili bez istovremene primene botulinskog toksina

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Abstract

Background/Aim. Botulinum toxin is a basic, recommended method of treatment in controlling cervical dystonia (CD). Physical therapy has limited effect due to the nature of the disease that is a result of a disorder in structures and relationships of the basal ganglia. The aim of this study was to analyze the effect of physical therapy applied as monotherapy, or with parallel application of botulinum toxin in patients with CD. **Methods.** Randomized controlled clinical pilot study included 14 patients diagnosed with idiopathic CD. All patients were initially assessed by using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and Torticollis Rating Scale (Tsui scale). In the control group, composed of 5 patients, the treatment included only physical therapy. The experimental group (9 patients) was first given botulinum toxin, and physical therapy was applied after five days. Physical therapy was conducted five times a week in the period of two weeks at the Clinic. Patients of both groups were instructed to continue with the physical therapy at home. The effects of treatment were analyzed after 1, 3 and 6 months using TWSTRS and Tsui scale. **Results.** At the beginning of the investigation, the differences in TWSTRS and Tsui scale between the groups were not significant. In the control group, after 1 month, significant improvement was achieved in all three parts of the TWSTRS. After 3 and 6 months, the effects of physical therapy were reduced to control levels. In the experimental group, highly significant increase of all parameters of TWSTRS was noted after 1, 3 and 6 months. In the control group, highly significant decrease of changes in Tsui scale was noticed only after one month while in the experimental group, it was maintained after 3 and 6 months. **Conclusion.** Application of physical therapy provides a significant improvement in disease severity, but the effect is better and of longer duration when combined with the botulinum toxin.

Key words:
cervical dystonia, primary; physical therapy modalities; botulinum toxins; classification.

Apstrakt

Uvod/Cilj. Primena botulinskog toksina predstavlja osnovnu, preporučenu metodu lečenja u kontroli cervikalne distonije (CD). Fizikalna terapija ima ograničene domete s obzirom na prirodu bolesti koja je posledica poremećaja u strukturama i vezama bazalnih ganglija. Cilj ovog rada bio je analiza efekta fizikalne terapije primenjene u smislu jedinog terapijskog modaliteta ili uz paralelnu primenu botulinskog toksina kod bolesnika sa CD. **Metode.** Randomno, kontrolisano kliničko istraživanje po tipu pilot studije obuhvatilo je 14 bolesnika kod kojih je postavljena dijagnoza idiopatske CD. Kod svih bolesnika inicijalno je procenjena težina bolesti korišćenjem *Toronto Western Spasmodic Torticollis Rating Scale* (TWSTRS) i *Torticollis Rating Scale* (Tsui skala). U kontrolnoj grupi, sastavljenoj od 5 ispitanika, lečenje je podrazumevalo fizikalnu terapiju, a u eksperimentalnoj, sastavljenoj od 9 bolesnika, prvo je dat botulinski toksin, a posle pet dana je primenjena fizikalna terapija. Fizikalna terapija je primenjivana 5 dana nedeljno tokom 10 dana na Klinici. Bolesnicima obe grupe je receno da nastave sa fizikalnom terapijom u kućnim uslovima. Efekti terapije analizirani su nakon 1, 3 i 6 meseci korišćenjem TWSTRS i Tsui skale. **Rezultati.** Na početku istraživanja, razlike u TWSTRS i Tsui skali između grupa nisu bile značajne. U kontrolnoj grupi, nakon 1 meseca, postignuto je značajno poboljšanje u sva 3 dela TWSTRS. Nakon 3 i 6 meseci, efekat fizikalne terapije smanjen je do početnog nivoa. U eksperimentalnog grupi, postignuto je značajno poboljšanje svih praćenih parametara TWSTRS

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nakon 1, 3 i 6 meseci. U kontrolnoj grupi, značajno smanjenje parametara u Tsui skali primećeno je samo nakon 1 meseca, dok se u eksperimentalnoj grupi održavalo i nakon 3 i 6 meseci. **Zaključak.** Primena fizikalne terapije daje značajno poboljšanje težine bolesti, ali je efekat bolji i dugotrajniji ako se primenjuje uz botulinski toksin.

Ključne reči:
cervikalna distonija, primarna; fizikalna terapija, metodi; botulin, toksini; klasifikacioni indeksi.

Introduction

Cervical dystonia (CD) is the most frequent form of focal dystonia in adults, with typical repeated spastic (clonic) or prolonged (tonic) muscle contractions which cause non-physiologic movements, or positions of the head, neck and shoulder. Torticollis, lateral shift, and oscillatory movements can follow as a consequence of CD. This disease is more frequent in females, with the incidence of 1: 10, 000 [1].

Certain activities and stress can increase positional changes in CD. Temporary amelioration of the disease can be seen in the morning after rest, after antagonistic movements, or particular positions. CD typically worsens during the first five years of illness, with stabilization of the changes. Pain accompanies CD in 75% of patients, and its intensity sometimes correlates with the stage of CD. The disease can have spontaneous recovery, especially in younger patients, but it is usually short-term [1–4].

Treatment of CD includes physical procedures such as stretching, range of motion exercises, muscle relaxation, and cervical orthoses. Different medicaments are used for therapy, mainly anticholinergics, dopamine antagonists, benzodiazepines, and gamma-aminobutyric acid (GABA) agonists. The effect of medication is various, with average 40% of success [5]. Surgical therapy of CD includes dorsal ramisectomy, bilateral pallidotomy, or stimulation of globus pallidus, and it is advised in advanced forms of disease [6].

Botulinum toxin (BT) was successfully applied in the therapy of CD. Its high efficiency was proven, with few side effects. Both forms of BT are used, type A (Botox®, Dysport®), and B (Myobloc®). The mechanism of action is based not only on denervational relaxation, but also on the influence on muscle fibers, basal ganglia, thalamus, and cortex [7–10].

However, the duration of the effect of BTA in CD has not been sufficiently studied.

The aim of this paper was to analyze the effect of physical therapy applied as monotherapy or in combination with botulinum toxin type A in patients with CD.

Methods

This randomized controlled clinical pilot study included 14 patients with CD. The diagnosis of CD was based on criteria proposed by Albanese et al. [11] in 2013. The study was approved by the Institutional Ethic Committee. All the patients gave written informed consent.

The patients were randomly divided into two groups. The first, control one, enrolled five patients who underwent physical therapy treatment without BT application. Physical therapy included exercises to increase range of motion, muscle stretching, occupational and functional therapy. It was planned individually (according to the patient's clinical findings), and conducted five times a week in the period of two weeks.

The second, experimental group, included 9 patients treated with BT A (Dysport®, Ipsen Biopharm Ltd, UK). One ampule of BT, 500 IU, diluted with 2.5 mL sterile 0.9% NaCl just before the application, was used for application in few places of the neck muscles according to the level of spasticity. Ipsilateral *m. sternocleidomastoideus* was the predominant site. *M. splenius*, *m. scalenus*, *m. semispinalis*, and *m. levator scapulae* were addionally injected. Five days after the BT application, the patients in this group received the same physical therapy, as in the control group, five times a week in the period of two weeks.

One, three and six months after the therapy, the effects were analyzed using the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) and the Torticollis Rating Scale (Tsui scale) [12–14].

TWSTRS consists of three parts. The first part is the torticollis scale (maximum score amounts 35 and represents the biggest changes) and includes rotation (range 0–4), *laterocollis* (range 0–3), *antero* and *retrocollis* (range 0–3), lateral shift (range 0–1), sagittal shift (range 0–1), duration (range 0–5 multiplied by 2), sensory ticks (range 0–29), elevation/shift in shoulder (range 0–3), range of motion (range 0–4), and time (0–4). The second part is the disability scale (maximum 30) which includes: work, activities of daily life, driving, reading, watching television and activities outside home (range for each of them 0–5). The third part is the pain scale (maximum 20) which consists of severity of pain (range 0–10), duration of pain (0–5), and disability caused by pain (range 0–5).

The Torticollis Rating Scale (Tsui scale) has four parts. The first one is amplitude of sustained movements (range 0–9) with rotation, shift, and antero or retrocollis (for each range 0–3). The next part is duration of sustained movements (range 0–2), as well as elevation of shoulder (range 0–2). Finally, there is head tremor (range 1–4, intensity x duration). Total torticollis is obtained by multiplying the first and the second part, and adding the third and fourth part of the scale.

The tests were filled in by professionals who were unaware of the treatment groups. Obtained data were processed using standard statistical methods (Students' *t*-test, Mann-Whitney test, and Kruskal–Wallis one-way analysis of variance).

Results

Fourteen patients aged 32–52 years, average age 42.3 ± 5.6 years, were included in the study. Females predominated

(females : males = 11 : 3), and CD lasted for 13.5 ± 6.4 months (range 9–27).

The values of TWSTRS in the control and the experimental group were without significant differences at the beginning of the study. In the control group, applied physical therapy produced significant improvement in all three parts, especially in pain subscale ($p < 0.01$), but also in torticollis and disability subscale ($p < 0.05$) after one month from the start of the treatment. Three and six months after the beginning of the treatment, the effect of physical therapy was reduced. Application of BTA and physical therapy resulted in highly significant increase of all the parameters of TWSTRS ($p < 0.01$) after one month. This effect was maintained later on. After three months, it was also highly significant, and after six months, most of the parameters were still improved ($p < 0.05$), except for anterocollis, lateral and sagittal shift, sensory ticks, and range of motion. Longer effect was noticed for disability and pain subscales (Tables 1 and 2).

At the beginning of the investigation, the differences in Tsui scale between the control and the experimental group were not significant. In the control group, highly significant decrease of changes was noticed after one month. Further follow-up demonstrated the loss of the positive effects. Contrary to this, BTA and physical therapy produced much better and longer improvement. Most of the improvements was initial ($p < 0.01$), with retaining slightly lower results after three and six months ($p < 0.05$) (Tables 3 and 4).

No side-effects of BTA treatment were noticed.

Discussion

Our study showed highly significant improvement of all the parameters of CD in the patients treated with BTA and physical therapy after one and three months, and significant improvement after six months. The results were better when compared with the patients who were treated with physical therapy only.

Our study also documented that physical therapy produced good, but short-term improvement in patients with CD. Contrary to this, BTA and physical therapy produced highly significant positive effects especially in the first three months. After six months, the effect was reduced, but still present.

Physical therapy of CD was insufficiently studied, without any randomized controlled study. However, physical treatment produced only insignificant improvement of movements in CD. Also, the impact of iontophoresis on CD was minimal [14].

Botulinum toxin type A is the most efficient medicamentous treatment of CD producing reversible denervation of neuromuscular junction by inhibition of acetylcholine release in presynaptic axons of motor plates. It is used to reduce pain, dystonic position, reduced range of motion, and tremor. Kinematic studies have confirmed that BT normalizes the speed and amplitude of neck movements in patients with CD [15].

Table 1

The values of TWSTRS scale in cervical dystonia after the treatment with physical therapy

Parameter	Before therapy	After 1 month	After 3 month	After 6 month
	mean ± SD	mean ± SD	mean ± SD	mean ± SD
Torticolis scale				
rotation	3.0 ± 0.2	2.6 ± 0.4†	2.8 ± 0.4	2.9 ± 0.2
laterocollis	2.4 ± 0.2	2.0 ± 0.2†	2.2 ± 0.3	2.3 ± 0.2
antero/retrocollis	2.3 ± 0.3	1.9 ± 0.2†	2.0 ± 0.2	2.1 ± 0.3
lateral shift	0.8 ± 0.1	0.5 ± 0.1†	0.6 ± 0.1	0.7 ± 0.2
sagittal shift	0.6 ± 0.2	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.2
duration factor	7.9 ± 1.0	6.3 ± 0.5†	6.0 ± 0.5†	6.3 ± 0.7†
sensory tricks	1.4 ± 0.2	0.9 ± 0.2†	1.3 ± 0.2	1.3 ± 0.2
shoulder elevation/shift	2.3 ± 0.3	2.1 ± 0.3†	2.1 ± 0.3†	2.1 ± 0.4†
range of movement	3.0 ± 0.6	2.7 ± 0.5†	2.7 ± 0.7	2.9 ± 0.5
time	3.0 ± 0.6	2.6 ± 0.4†	2.8 ± 0.5	2.9 ± 0.5
Disability scale				
work	3.7 ± 0.5	3.2 ± 0.5†	3.7 ± 0.4	3.6 ± 0.4
daily life activities	3.8 ± 0.5	3.2 ± 0.5†	3.5 ± 0.4	3.6 ± 0.5
driving	4.0 ± 0.7	3.4 ± 0.3†	3.5 ± 0.4	4.2 ± 0.5
reading	3.8 ± 0.4	3.0 ± 0.4†	3.7 ± 0.2	3.8 ± 0.4
watching television	3.8 ± 0.4	3.0 ± 0.4†	3.7 ± 0.2	3.5 ± 0.2
activities outside home	3.8 ± 0.6	3.2 ± 0.5†	3.5 ± 0.4	3.5 ± 0.2
Pain scale				
intensity	7.5 ± 1.0	5.6 ± 0.9*	6.4 ± 1.0†	6.5 ± 0.8†
duration	4.0 ± 0.5	3.1 ± 0.5*	3.2 ± 0.6†	3.7 ± 0.3
disability by pain	4.1 ± 0.5	3.1 ± 0.3*	3.0 ± 0.8†	3.7 ± 0.3

TWSTRS – Toronto Western Spasmodic Torticollis Rating Scale; SD – standard deviation;*$p < 0.01$; †$p < 0.05$.

Table 2

The values of TWSTRS scale in cervical dystonia after the treatment with physical therapy and botulinum toxin type A

Parameter	Before therapy	After 1 month	After 3 months	After 6 months
	mean ± SD	mean ± SD	mean ± SD	mean ± SD
Torticolis scale				
rotation	3.1 ± 0.4	1.9 ± 0.5*	2.1 ± 0.6*	2.6 ± 0.7†
laterocollis	2.5 ± 0.3	1.6 ± 0.4*	1.7 ± 0.4*	2.0 ± 0.6†
antero/retrocollis	2.2 ± 0.5	1.3 ± 0.5*	1.2 ± 0.4*	2.0 ± 0.7
lateral shift	0.7 ± 0.2	0.2 ± 0.1*	0.3 ± 0.1*	0.6 ± 0.2
sagittal shift	0.6 ± 0.3	0.3 ± 0.1*	0.3 ± 0.2*	0.4 ± 0.3
duration factor	8.0 ± 1.4	5.2 ± 1.6*	5.0 ± 1.8*	5.8 ± 2.2†
sensory tricks	1.3 ± 0.4	0.8 ± 0.6*	1.1 ± 0.3	1.0 ± 0.5
shoulder elevation/shift	2.4 ± 0.3	1.9 ± 0.6*	1.9 ± 0.8	2.1 ± 0.7†
range of movement	3.2 ± 0.9	2.1 ± 1.1*	2.3 ± 0.7*	2.7 ± 1.2
time	3.1 ± 0.6	2.0 ± 0.8*	2.1 ± 0.7*	2.4 ± 1.5†
Disability scale				
work	3.8 ± 0.9	2.3 ± 0.7*	2.4 ± 0.8*	3.1 ± 0.9†
daily life activities	3.9 ± 0.7	2.1 ± 0.5*	2.3 ± 1.2*	2.9 ± 1.1†
driving	4.2 ± 0.8	2.2 ± 0.8*	2.2 ± 1.0*	2.7 ± 1.1*
reading	3.6 ± 0.8	2.3 ± 0.6*	2.7 ± 1.1*	2.8 ± 0.9
watching television	3.7 ± 0.7	2.6 ± 1.0*	2.7 ± 1.0*	2.6 ± 0.9*
activities outside home	3.8 ± 0.6	2.2 ± 1.2*	2.4 ± 1.3*	2.8 ± 1.2†
Pain scale				
intensity	7.9 ± 1.5	4.7 ± 1.9*	4.6 ± 2.0*	5.8 ± 1.8†
duration	4.1 ± 0.9	2.0 ± 0.8*	2.2 ± 1.3*	2.8 ± 1.4*
disability by pain	4.2 ± 0.6	1.9 ± 0.7*	2.0 ± 1.8*	3.1 ± 0.9†

TWSTRS – Toronto Western Spasmodic Torticollis Rating Scale; SD – standard deviation; *$p < 0.01$; †$p < 0.05$.

Table 3

The values of Tsui scale in cervical dystonia after the treatment with physical therapy

Parameter	Before therapy	After 1 month	After 3 months	After 6 months
	mean ± SD	mean ± SD	mean ± SD	mean ± SD
Amplitude of movement				
rotation	2.5 ± 0.4	2.0 ± 0.3*	2.2 ± 0.4†	2.4 ± 0.3
shift	2.5 ± 0.4	2.0 ± 0.3*	2.4 ± 0.4	2.4 ± 0.3
antero/retrocollis	2.7 ± 0.3	2.2 ± 0.4*	2.2 ± 0.4†	2.4 ± 0.3
Duration of movement				
duration	2.0 ± 0.2	1.7 ± 0.2*	1.8 ± 0.3†	2.0 ± 0.2
Shoulder elevation				
elevation	2.0 ± 0.2	1.7 ± 0.2*	1.9 ± 0.3	1.9 ± 0.9
Head tremor				
intensity	1.8 ± 0.2	1.5 ± 0.2*	1.6 ± 0.3	1.7 ± 0.2
duration	1.8 ± 0.2	1.5 ± 0.2*	1.6 ± 0.3	1.7 ± 0.2

SD – standard deviation; *$p < 0.01$; †$p < 0.05$.

Table 4

The values of Tsui scale in cervical dystonia after the treatment with physical therapy and botulinum toxin type A

Parameter	Before therapy	After 1 month	Afetr 3 months	After 6 months
	mean ± SD	mean ± SD	mean ± SD	mean ± SD
Amplitude of movement				
rotation	2.4 ± 0.8	1.6 ± 0.7*	1.7 ± 0.9†	1.9 ± 1.2†
shift	2.6 ± 0.7	1.4 ± 0.9*	1.6 ± 1.0*	2.0 ± 1.0†
antero/retrocollis	2.7 ± 0.6	1.5 ± 1.0*	1.4 ± 0.9*	2.1 ± 0.9†
Duration of movement				
duration	1.9 ± 0.3	1.1 ± 0.2*	1.2 ± 0.3†	1.7 ± 0.2
Shoulder elevation				
elevation	2.2 ± 0.6	1.1 ± 0.6*	1.5 ± 0.4†	1.3 ± 0.9†
Head tremor				
intensity	1.7 ± 0.2	1.2 ± 0.2*	1.3 ± 0.3†	1.7 ± 0.2
duration	1.6 ± 0.3	1.2 ± 0.3*	1.4 ± 0.2†	1.5 ± 0.3

SD – standard deviation; *$p < 0.01$; †$p < 0.05$.

The treatment of CD using BT must be individual, according to pharmacokinetics and anatomy of the region. In some cases, electromyography (EMG) can be used to deliver BT precisely. The effect of BT in CD depends on the presence of contractures, and on the medical skills. There are no universal opinions concerning application site, doses, and efficiency of certain BT serotypes. On the other side, the symptoms and status of CD can be different [7–10]. Higher doses of BT and more local injections are needed for complex forms of CD. Initial dose of 500 IU of Dysport® can be increased if needed [16]. In our patients initial dose of 500 IU was sufficient to provide good therapeutic response.

The duration of effect is from twelve to sixteen weeks. In our study, the effect was maintained six months after the treatment which can be attributed to the exercises that patients practiced after the BTA application. The aim of the exercises was to achieve postural reducation and voluntary control of the head and neck position as well as passive muscular elongation for prevention of contracture.

Reported side effects after BTA include local pain, dryness of mouth, muscle weakness, and general weakness. In this study important side effects were not noticed.

Long-term application of BT indicated continuous improvement in 63% in a five-year period. The primary resistance was verified in 10%, while secondary one amounted to 8% [17, 18]. Reduced long-term efficiency of BT is explained by neutralizing antibodies [19–21]. They were found in 32% of children with cerebral pulsy usually after eight weeks of treatment [9].

The efficiency of BT in CD was verified in few double blind studies. They used clinical and video surveillance of symptoms, EMG, Tsui scale, and other scales [22, 23].

In this study, we used TWSTRS and Tsui scale that showed comparable values for follow-up in CD. Since TWSTRS includes disability and pain subscale, it gives important indicators of daily activities in CD and is therefore more valuable in clinical investigations.

TWSTRS showed good reliability in all the subscales, with bigger variability depending on the gravity of disease. Disability subscale is more sensitive than the subscales for pain and for severity of the disease as well [4, 23].

Tsui scale is used to measure the position of the head and shoulders, duration of movement, and head tremor in CD. Inter-test reliability was good, but the validity of this scale was not studied. Cervical Dystonia Impact Profile (CDIP-58) measures the 58 health parameters in CD, but it has not been widely used in investigations [4, 23].

Conclusion

TWSTRS and Tsui scale have confirmed highly significant improvement of all the parameters of cervical dystonia treated with botulinum toxin A and physical therapy after one and three months and significant improvement after six months.

The results were better and of longer duration compared to patients who were treated with physical therapy only. Future studies with larger number of patients and longer follow-up are necessary to confirm these initial positive effects.

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