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Original Article P&ME

Effect of botulinum toxin type-A in patients with focal spasticity

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ABSTRACT

OBJECTIVE: To investigate the effect of botulinum toxin type-A (BTX-A) on spasticity and function in patients with focal spasticity.

METHODS: Patients attended to the outpatient clinic of physical medicine and rehabilitation department with a diagnosis of focal spasticity and had BTX-A injections because of spasticty were evaluated for the study. Demographic data, exercise status, orthoses, drugs used for spasticity, functional status, stages of spasticity of muscles before and after 1st and 3rd months of BTX-A injection according to Modified Ashworth Scale (MAS) were evaluated retrospectively. MedCalc 11.6 statistical program was used for statistical analyses. Statistical significance was defined as $p<0.05$.

RESULTS: Forty-nine patients with focal spasticity were recruited for the study (35 men, 14 women). Mean age of the patients was 21.59±20.09 years. The patients had cerebral palsy (CP, n=28), 19 had hemiplegia (n=19) and paraplegia (n=2). Forty-three patients were using orthoses and exercising regularly. Mean Pediatric Functional Independence Measurement (WeeFIM) scores of the patients with CP was 54.82±28.91 and according to the Gross Motor Function Classification System (GMFCS) the patients were in stages 2 (14%), 3 (46%), 4 (11%) and 5 (29%). Mean Functional Independence Measure (FIM) of hemiplegic and paraplegic patients was 80.80±20.88. Brunnstrom staging scores for upper extremity (3.52±0.96), hands (2.68±0.82), lower extremity (4.57±1.01) were calculated. MAS muscles demonstrated statistically significant decrease in spasticity at the end of first and third months ($p<0.05$).

CONCLUSION: We saw a significant decrease in the spasticity of upper and lower extremities in patients with focal spasiticity who received BTX-A injections. We suggest that if BTX-A injections are supported with orthoses and exercise programs, then functional status of the patients would be better.

Key words: Botulinum toxin type-A; cerebral plasy; hemiplegia; spasticity.

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Spasticity arises as a result of destructive changes in medulla spinalis or serebrum caused by trauma, stroke, hypoxia, inflammatory, and demyselinizing diseases, degenerative or familial diseases or compression by mass lesions. Muscle contraction amplitude decreases, muscle tone, and rigidity increases, and velocity dependent resistance during passive joint movements occur because normal inhibition of lower motor neurons which is required for the maintenance of physiological muscle tone is not achieved resulting in predominancy of upper motor neuron functions [1-3].

Spasticity is a complex disorder which may lead to serious disability [4]. Primary aim in its treatment is to achieve functional improvement. Among treatment targets increasing mobility, decreasing pain, and spasms, increasing ROM of joints, facilitating use of ortheses, and positioning, providing cosmetic benefit, prevention or postponing surgery can be enumerated [5, 6]. Nowadays prophylactic treatment modalities applied for the treatment of spasticity include appropriate positioning, stretching, and exercises, physical therapy, oral antispastic drugs (baclofen, diazepam, tizanidine, and dantrolene), neuromuscular blockade with phenol or BTX-A, intratechal baclofen, and surgical interventions [7, 8].

BTX-A is the most potent neurotoxin produced by Clostridium botulinum. Via inhibition of acetylcholine release from presynaptic terminals of peripheral cholinergic nerves BTX-A prevents nervous signal transmission [9, 10]. Nearly two or three moınths later, new nerve terminals develos through axonal budding, and nervous signal transmission resumes. Various studies have demonstrated that recovery of neuromuscular transmission, and secretion of acetylcholine are achieved nearly 91 days after BTX-A injection. It exerts its effect within the first week which peaks at 4.-6. weeks, and disappears generally within 3-4 months [11]. Thanks to its long-term, but reversible effect, ease of its application, appropriateness, and established safety, in addition to its favourable side effect profile, BTX-A has become the first choice in the pharmacological treatment of focal spasticity [12].

In this study the effect of BTX-A injections on spasticity in patients with focal spasticity has been retrospectively investigated.

MATERIALS AND METHODS

After retrieval of the ethics committee approval, the patients who were followed up, and received BTX-A injections in the outpatient clinic of Physical Medicine, and Rehabilitation Department with the diagnosis of focal spasticity were retrospectively evaluated. The patients with generalized spasticity, and those who developed contractures were excluded from the study. Patients' demographic data, their compliance to exercise therapy, orthoses, and antispastic drugs used, and their functional status were retrieved, and recorded via screening their medical files, The severity of spasticity evaluated for BTX-A injected muscle groups were evaluated before, and 1, and 3 months after injections

MAS criteria'

0: No increase in muscle tone

1: Slight increase in muscle tone

1+: Minimal resistance at the end of the range of motion (ROM) of the affected mucle when the affected part(s) is moved in flexion or extension

2: More marked, but still slight increase in muscle tone; Minimal resistance felt throughout less than half of the ROM of the joint

3: Considerable increase in the muscle tone, difficulty during passive movements

4: Affected muscle part(s) are rigid in flexion or extension [7].

Study population consisted of the patients who received BTX-A injections, and diagnosed as focal spasticity, cerebral palsy (CP), hemiplegia, and paraplegia. Disease severity of CP patients according to Pediatric Functional Independence Measure (WeeFIM) scores, and their Gross Motor Function Classification levels, and also Functional Independence Measure (FIM), and Brunnstrom staging scores of the hemiplegic, and paraplegic patients were recorded, and all patients were included in the rehabilitation program.

For statistical Analysis MedCalc 11.6 statistical

TABLE 1. Demographic data

	n	%
Gender		
Female	14	28.57
Male	35	71.42
Diagnosis		
Cerebral Palsy	28	51.14
Hemiplegia	19	38.77
Paraplegia	2	4.08
Orthoses		
Users	43	87.75
Nonusers	6	12.24
Antispastics		
Users	18	36.73
Nonusers	31	63.26
Exercise program		
Compliants	43	87.75
Noncompliants	6	12.24

program was used. $p<0.05$ was accepted as the level of significance.

RESULTS

A total of 49 patients were included in the study. Demographic characteristics of the patients are demonstrated in Table 1. The study population consisted of 35 male, and 14 female patients. Mean age of the patients was 21.59±20.09 years. The patients were followed up with diagnosis of CP (n=28), hemiplegia (n=19), and paraplegia (n=2). Forty-three patients were using orthoses, and exercising to maintain their positioning or range of motion, and functionality of the affected joint.

Mean WEEFIM score of the patients with CP was 54.82±28.91. GMFCS. scores of the patients with CP are shown in Graphic 1. Mean FIM score of patients with hemiplegia, and paraplegia was 80.80± 20.88 Mean Brunnstrom staging scores of the patients were 3.52±0.96 for the affected upper extremity, 2.68±0.82 for the hand, and 4.57±1.01 for the lower extremity. Pre-, and post-treatment 1. (T1), and 3. (T3) month- MAS scores of the patients were also evaluated. Pre-, and post-treatment T1 spasticity levels were statistically significantly different ($p<0.05$). Besides, post-treatment 1 (T1), and 3. (T3) month spasticity scores were also statistically significantly different ($p<0.05$) (Table 2).

DISCUSSION

This retrospective study was performed to demonstrate the effect of BTX-A injection on patients with focal spasticity 1, and 3 months after injection. The results have demonstrated that BTX-A injection prominently decreased muscle tone.

Spasticity is a complex disorder which might lead to serious disability. BTX-A is used for multifocal, and focal spasticities. For the determina-

TABLE 2. BTX-A injected muscles, and their MAS (Modified Ashworth Scale) values

Muscles	(n)	Onset of treatment MEAN±SD	1. Month MEAN±SD	3. Month MEAN±SD	p
Biceps	18	2.4±0.61	1.5±0.7	1.94±0.63	<0.05
Flexor carpi radialis	14	2.42±0.85	1.35±0.84	1.71±1.06	<0.05
Flexor carpi ulnaris	13	2.61±0.5	1.46±0.77	1.69±0.75	<0.05
Flexor digitorum superficialis	12	2.58±0.51	1.5±0.75	1.75±0.45	<0.05
Flexor digitorum profundus	11	2.63±0.5	1.63±0.67	1.72±0.46	<0.05
Adductor muscles of the hip	18	2.38±0.69	1.33±0.76	1.72±1.01	<0.05
Hamstring		2.38±0.65	1.33±0.76	2.23±0.92	<0.05
Gastrosoleus	35	2.48±0.56	1.48±0.61	1.94±0.72	<0.05

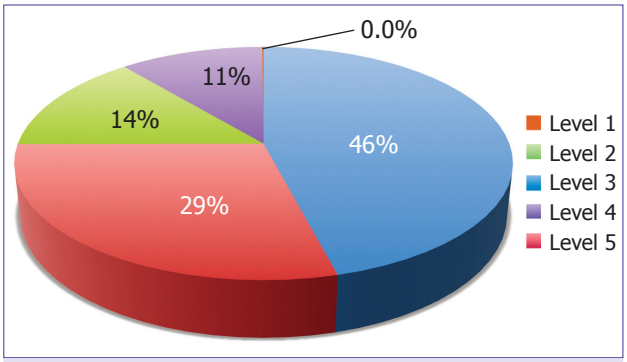

FIGURE 1. Distribution of the patients with cerebral palsy based on their GMFCS (Gross Motor Function Classification) scores.

tion of spasticity, and evaluation of its progression, physical, quantitative, and standardized scales have been used. Quantitative methods are preferred in randomized studies. Among them MAS is the most frequently used scale [8]. Slovek et al. injected a median dose of 255 IU botox to 18 stroke patients with upper extremity spasticity, and detected a significant regression in MAS values [13]. Simpson et al. investigated effectiveness of BTX-A on upper extremity spasticities in their randomized double-blind, placebo controlled studies, and compared BTX-A 75/150/300 IU doses with placebo. The authors detected significant decrease in muscle tone 6 weeks after application of higher doses of BTX-A [14]. In their randomized controlled studies, Scholtes et al. demonstrated the effect of BTX-A on muscle length, and walking parameters, and decrease in spasticity starting from the first week after injection. [15]. Brashear et al. injected 200-240 U botulinum toxin into wrist, and finger flexors of 126 patients who developed post-stroke spasticity, and detected significant regression in MAS values, improvement in hygiene, and also movements done during wearing clothes, and pain relief without any side effects [16]. Hesse et al. applied 400 units BTX-A to 12 patients with chronic lower extremity extensor spasticity, and and detected a significant regression of MAS values of 10 patients within 2 weeks [17]. Karaçam et al. analyzed 15 patients who developed post-stroke focal spasticity, and measures of spasticity (MAS), muscle strength score, disability scale, visual analogue scale, and Barthel index scores obtained at control visits performed at 1., and 3. months were compared With this study they obtained a serious decrease in MAS, and disability scores. Another striking feature of the study is that effectiveness of BTX-A still continued at 3. month controls [7]. In some literature studies decrease in the effectiveness of BTX-A was reported at. 3. month controls, and this phenomenon was associated with severity of spasticity, inadequate doses, and inability to comply regularly with the rehabilitation program [3, 13, 18]. In this study, decreases in the severity of spasticity were detected at 1, and 3. months based on MAS values of the patients who received BTX-A injections to their upper, and lower extremities, At 3. month controls of the patients, persistence of BTX-A effects can be associated with compliance of most of the patients to their exercise programs, and usage of appropriate doses. Physical therapy applications, therapeutic exercises, use of orthoses or plastering, electrical stimulation of BTX-A injected muscles, and biofeedback can be used after BTX-A injections [19]. Therapeutic exercises include traction/ stretching of BTX-A injected muscles, if active movements were noticed, then strength of antagonistic muscles were strenghtened, and neurofascilitative exercises were prescribed. Our patients were prescribed stretching exercises for BTX-A injected muscles, and if active muscle movements were noted, then these patients were included in the antagonistic muscle- strenghtening programs. Our 43 patients completed their exercise program.

CONCLUSION

Because of adverse effects of oral agents, in recent years for the treatment of spasticity, BTX-A injections have been used. Though various viewpoints have been proposed about effectiveness, and duration of BTX-A treatment, consensus opinion asserts that its effect is not sustainable Whatever the treatment choice for spasticity is, it should be supported by a neurohabilitative program.

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