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A Glance into Botulinum Toxin Outpatient Clinic in Movement Disorders Practice: Self Experience

Hareket Bozuklukları Pratiğinde Botulinum Toksin Polikliniğine Bakış: Kişisel Deneyim

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ABSTRACT

Aim: Aim of this study is to determine socio-demographic and disease features of patients who underwent Botulinum toxin injections, and to present our clinical experience via documenting intervals of Botulinum toxin injections and effect-side effect profiles.
Material and Methods: Socio-demographic features of patients and characteristic features of Botulinum toxin treatment were recorded. The diagnosis of the patients who underwent Botulinum toxin injections, disease durations and the onset of Botulinum toxin treatments were investigated. Possible side-effects were recorded.
Results: Thirty-two patients (20 men, 12 women) with the diagnosis of various types of movement disorders were enrolled the study. Mean age of patients was 60.65±14.40 years (range= 22-83 years). Diagnosis of the patients who underwent Botulinum toxin injections were cervical dystonia, blepharospasm, clonic hemifacial spasm, focal hand dystonia/writer's cramp, oromandibular dystonia, and dystonic tremor. All patients had repetitive Botulinum toxin injections. There were no remarkable adverse effects, other than mild temporary bruises in injection site in two patients with blepharospasm.
Conclusion: Botulinum toxin is an important treatment option in patients with focal dystonia. Botulinum toxin as a neurotoxin of *Clostridium botulinum* bacteria, suppresses muscle contractions via inhibiting acetylcholine release to the synaptic gap. This reversible effect lasts three to four months due to the neuronal sprouting. It is important to share clinical experiences, data of Botulinum toxin outpatient clinics or clinics from the movement disorders perspective to increase awareness of Botulinum toxin effectivity in patients with movement disorders, focal dystonia particularly.
Keywords: Botulinum toxin; movement disorders; focal distonia.

ÖZ

Amaç: Bu çalışmanın amacı Botulinum toksin enjeksiyonu uygulanan hastaların sosyodemografik özellikleri ve hastalık özelliklerinin belirlenmesi, ve Botulinum toksin uygulama aralıkları ile etki ve yan etki profillerini dokümante ederek klinik deneyimimizin sunulmasıdır.
Gereç ve Yöntemler: Hastaların sosyodemografik özellikleri ve Botulinum toksin tedavisinin karakteristik özellikleri kaydedilmiştir. Botulinum toksin enjeksiyonu yapılan hastaların hastalık tanıları, hastalık süreleri ve Botulinum toksin tedavisine başlama süreleri incelenmiştir. Olası yan etkiler kaydedilmiştir.
Bulgular: Çeşitli hareket hastalıkları tanısı almış otuz iki hasta (20 erkek, 12 kadın) çalışmaya dahil edilmiştir. Hastaların yaş ortalaması 60.65±14.40 yaştır (aralık= 22-83 yaş). Botulinum toksin enjeksiyonu uygulanan hastaların tanıları servikal distoni, blefarospazm, klonik hemifasiyal spazm, fokal el distonisi/yazıcı krampı, oromandibular distoni ve distonik tremordur. Tüm hastalara tekrarlayan Botulinum nörotoksin enjeksiyonları yapılmıştır. İki blefarospazm hastasında enjeksiyon bölgesinde izlenen hafif morluklar dışında, hastalarda belirgin yan etki görülmemiştir.
Sonuç: Botulinum toksin fokal distonili hastalarda önemli bir tedavi seçeneğidir. *Clostridium botulinum* bakterisinin nörotoksini olan Botulinum nörotoksin, sinaptik aralığa asetilkolin salınımını engelleyerek kas kasılmasını baskılamak üzere çalışır. Geri dönüşümlü olan bir etki ile nöronal filizlenmenin süresiyle ilişkili olarak yaklaşık üç ila dört ay kadar sürmektedir. Özellikle fokal distoni gibi hareket bozuklukları hastalarında Botulinum toksin etkinliğine ilişkin farkındalığı arttırmak amacıyla ve hareket hastalıkları perspektifinden Botulinum toksin poliklinik veya kliniklerinin klinik deneyimlerini ve verilerini paylaşmak önem arz etmektedir.
Anahtar kelimeler: Botulinum toksin; hareket bozuklukları; fokal distoni.

INTRODUCTION

Botulinum toxin (BoNT) is the most potent neurotoxin that is produced by gram-positive anaerobic bacteria known a *Clostridium botulinum*. It contains a peptide composed of a 100-kDa heavy chain and a 50-kDa light chain, which shows a mechanism of action in the terminals of cholinergic neurons at the neuromuscular junction via blocking the release of acetylcholine at the nerve terminals, and leading to a reversible paralysis in the skeletal muscle (1).

Since the effect of BoNT is reversible due to the reestablishment of the axonal sprouting on the nerve terminals of neuromuscular junction leading to acetylcholine release, and restore muscle contraction, periodic administrations of BONT is needed in order to maintain therapeutic effect (2,3). Although there are eight different serotypes as A to H, currently type A and B are the ones in market with the Food Drug Administration (FDA) approval in clinical use (1,4). These are commercially known as onabotulinum toxin-A (®Botox), abobotulinum toxin-A (®Dysport), incobotulinum toxin-A (®Xeomin), and rimabotulinum toxin-B (®Myobloc) in markets (5,6).

It has a wide range of use in ophthalmological, gastrointestinal, urological, orthopedic, dermatological, secretory, and painful disorders, as well as neurological diseases (7). In terms of neurological disorders, BoNT is a well-known treatment option in dystonia, which is a movement disorder syndrome characterized with sustained muscle contractions, frequently causing twisted and repetitive movements, or abnormal postures (8). Moreover in movement disorders practice, it is considered as an effective treatment in focal dystonia such as cervical dystonia, blepharospasm, clonic hemifacial spasm, task specific/focal hand dystonia and more (9-12).

Since BoNT has emerged as a powerful, multipurpose therapeutic agent leading to a dramatic improvement with an increase in the quality of life of patients with dystonia in movement disorders practice of neurology, in particular, the aim of this study was to present and document our self-experience of BoNT injections in our BoNT outpatient clinic, and discuss in the light of literature knowledge from the movement disorders perspective.

MATERIAL AND METHODS

In this retrospective study, patients with the diagnosis of dystonia who underwent BoNT injections in Duzce University Medical Faculty Hospital BoNT outpatient clinic of the Neurology Department by the same examiner between 1 January 2018 and 30 April 2019 were enrolled the study. The patients who underwent BoNT injections apart from the diagnosis dystonia and movement disorders were excluded. All participants were informed about the content of the procedure and gave their written approval before BoNT injections. The study was approved with the local ethical committee of Duzce University with the date and number as 27/05/2019 and 2019/114, respectively.

Socio-demographic features of the patients including age, gender, occupation, dominant-hand, marital status from retrospective analysis of the patients' data were recorded, as well as the type of movement disorders diagnosis that needed BoNT injections, and the disease durations. The characteristics of the BoNT injections including the duration of treatment, the number of injections, dilution parameters and side effects, if any, were also documented.

Statistical Analysis

Data were organized in an SPSS Version 15.0 (Statistical Package for Social Sciences for Windows) database. Statistical analyses were performed with the descriptive analysis, and the comparison of the groups was performed with parametric and non-parametric tests. Descriptive statistics calculated as mean ± SD or median (mean-max); and frequency and percentage as appropriate.

RESULTS

Thirty-two patients (20 men, 12 women) with the diagnosis of various types of movement disorders were enrolled the study. Mean age of the patients was 60.65±14.40 years (range= 22-83 years).

All were right-handed. Socio-demographic features of the patients are shown in Table 1. The types of movement disorders were focal dystonia including blepharospasm, clonic hemifacial spasm, oromandibular dystonia, and task specific dystonia which was called writer's cramp. Dystonic tremor was another diagnosis and one patient had a combined clinical manifestation of blepharospasm and cervical dystonia. The diagnosis of the patients in terms of movement disorders can be seen in Table 2.

Table 1. Socio-demographic features of the patients

	n (%)
Gender	
Male	20 (62.5)
Female	12 (37.5)
Marital status	
Single	31 (96.9)
Married	1 (3.1)
Education	
Not literate	5 (15.6)
Literate	3 (9.4)
Primary school (5 years)	19 (59.4)
Middle school (+3 years)	0 (0.0)
High school (+3 years)	2 (6.3)
College	3 (9.4)
Occupation	
Housewife	18 (56.3)
Retired	7 (21.9)
Tradesman	1 (3.1)
Teacher	1 (3.1)
Farmer	1 (3.1)
Officer	2 (6.3)
Worker	2 (6.3)

Table 2. Diagnosis of the patients

Diagnosis	**n (%)**
Cervical dystonia	4 (12.5)
Blepharospasm	3 (9.4)
Blepharospasm and cervical dystonia	1 (3.1)
Clonic hemifasial spasm	20 (62.5)
Task spesiphic dystonia/writer's cramp	1 (3.1)
Oromandibular dystonia	1 (3.1)
Dystonic tremor	2 (6.3)

Mean duration of disease was 6.35±4.95 years (range= 1-22 years). Mean duration of BoNT treatment among the patients was 3.48±2.70 years (range= 1-13 years). Within this period, they underwent repetitive BoNT treatments. Median number of BoNT injections was 3 (range= 1-7 injections).

In our clinic onabotulinum toxin-A (®Botox, Allergan) was used with the dilution of 2 ml of saline solution. Commonly injected muscles with the appropriate dosages, based on the diagnosis, indications and clinical needs were orbicularis oculi, stenocleidomastoid, splenius capitis, levator scapula, and the flexor muscles of the hand in the patient with writer's cramp, and masseter in the patient with jaw closing oromandibular dystonia. None of the patients reported any remarkable side-effects, other than mild temporary bruises in the injection site in 2 patients with blepharospasm.

DISCUSSION

BoNT is a favourable therapeutic agent in movement disorders clinics and outpatient clinics for focal dystonia, in particular (13). The term "focal dystonia" includes a wide range of disorders such as blepharospasm, cervical dystonia, clonic hemifacial spasm, focal hand dystonia, and there are several drugs like benzodiazepines, anticholinergic, and baclofen that are commonly used in the pharmacological treatment of dystonia. However, BoNT injections are the gold standard treatment options in focal dystonia, so far (14).

Targeting the acetylcholine release with consequently reduced overactive muscle contraction in the dystonic muscles at the site of injection is the main mechanism of action of BoNT leading to a reversible improvement, which makes BoNT most effective and widely used treatment in focal dystonia (13,14). The success of treatment depends on accurate diagnosis and injections that depends on the precise determination of the involved muscles, and the experience and the skills of the clinician applying the injections with appropriate doses and techniques, in which BoNT dosing and muscle targeting are mainly based on consensus and experience (15).

Thus the aim of this study was to document our clinical experience in BoNT injections from the perspective of movement disorders practice in the patients with the diagnosis of focal dystonia in various types. Similar to our data and results, previous studies reveal that the type of dystonia is commonly focal in patients who underwent BoNT injections such as blepharopasm, cervical dystonia, focal hand dystonia, and clonic hemifacial spasm (8-10,12).

As a well-known entity, BoNT has a reversible functional denervation lasting up to 3 months due to the sprouting of nerve terminals and formation of new synaptic contacts (16). Thus, similar to our data, patients need repetitive injections as the function of the injected muscles recover (12,15-17).

Most common adverse effects reported in the previous studies for BoNT injections in the movement disorders practice are mild pain and/or bruises in the injection side, as we two of our patients with blepharospasm experienced. The most unwanted adverse effect is the paralysis of the adjacent muscle caused by the spread of toxin which is also temporary. In patients with cervical dystonia, dysphagia is a frightening side-effect when injecting the neck muscles. Moreover, pitosis may be seen in 1-3% of the patients as a result of paralysis due to ocular musculature injections via migration of toxin to the levator palpebrae superioris muscle in the treatment of clonic hemifacial spasm and/or blepharospasm in movement disorders practice (16-17). However it usually resolves within several weeks or months. Infrequently, adverse effects such as brachial plexopathy, and influenza-like illness are also reported. However, it is generally a well-tolerated therapy with few side effects when performed accurately by experienced clinicians (17).

CONCLUSIONS

Owing to its well-known therapeutic effects in focal dystonia, BoNT is an important treatment option in preventing the involuntary, disabling muscle contractions in dystonia, which can often deteriorate the daily living activities of patients, and lead them to be socially isolated. On this aspect, it is important to share clinical experiences, and data of BoNT outpatient clinics from the movement disorders perspective in order to increase the utility, and awareness of BoNT affectivity in patients with movement disorders, focal dystonia in particular.

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