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Observing Adverse Effects of Botulinum Toxin Injection in Cervical Dystonia Pateints

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Abstract:

Background: *Cervical dystonia is the most common adult onset focal dystonias and botulinum toxin injection is an effective treatment for this condition.* ***Objective:*** *The objective of the study was to observe immediate (Up to 4 Hours after injection) and Delayed (14 Days after injection) adverse effect of botulinum toxin in cervical dystonia patients.* ***Methology:*** *All cervical dystonia patients attending the Neurology Clinic and aggreed to be injected with botulinum toxin for treatment, Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai, India, from August 2022 to May 2023, were included in the study. 36 patients with cervical dystonia were injected with Botox (Onabotulinum Toxin A, by Allergan). Injections were given by a single expert and dosing was determind by the expert.* ***Results:*** *Out of 36 patients 24 were female(66.66%) and 12 were male(33.33%). Highest number that is 12 out of 36 patients had onset of symptoms between the age of 41 to 60 years of age(33.33%).17 out of 36 patients had torticollis(68%), 9 had retrocolis(25%), 5 had lateroclis(13.88%) and 5 had anteroclis(13.88%).21 (58.34%) out of 36 patients had duration of symptoms more than 5 years.27 patients (75%)out 36 had received treatment with botulinum toxin previously and rest 9 patients (25%)never received botulinum toxin.4 patients(11.11%) had excessive bleeding from injection sites, 3 patients(8.33%)complained of pain but no patient developed anaphylaxis within 4 hours of injection(0). Excessive muscle weakness was observed in 4 patients (11.11%) 14 days after injection followed by dysphasia in 1(2.77%)and persistent hematoma in 1 patient(2.77%) at injection sites.* ***Conclusions:*** *Botulinum toxin is an effective method of treating focal dystonia and in expert hands side effects are minimal.*

Keywords: *Cervical dystonia, botulinum toxin.*

Introduction:

Cervical dystonia (CD) is characterized by excessive contraction of muscles of the neck leading to abnormal head movements and neck pain[1]. It is the most common and readily recognized of the adult-onset dystonias.[2] Cervical dystonia has distinctive features that make it easy to diagnose for clinicians who have experience with the disorder.

In contrast to many disorders, demographic factors are of limited help in diagnosing cervical dystonia. The disorder can manifest at any age, but it is more common in women, and its onset is most often in the 30s and 40s [3,4]. Sudden onset or development of the disorder in childhood or adolescence should raise the index of suspicion for other disorders. Hepatolenticular degeneration (Wilson's disease)[1], structural brain or spinal cord lesions, or hereditary forms of torsion (generalized) dystonia should be considered.[3,4]

As might be expected, most patients with cervical dystonia have a gradual onset and progression of symptoms. Sometimes patients can recall a self-limited period in the past when they had mild symptoms of the disorder that resolved without treatment[3,4,5].

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Most patients with cervical dystonia also have sensory tricks that paradoxically alleviate symptoms[1]. Most commonly, these tricks involve touching or holding the chin, but they can be related actions, such as leaning the head against the wall, bending forward, or lying down. Sometimes seemingly unrelated acts, such as yawning or shouting, seem to help.[6,7]

As indicated previously, movement is a key finding in cervical dystonia. Another prominent finding is evidence of active muscle contraction in the form of muscle thickening and hypertrophy. An expanded neck size can occur, but this finding is less common now that patients are treated with botulinum toxin earlier in the course of their disease. Asymmetry of the sternocleidomastoid is often present in untreated patients. The beneficial effects of sensory tricks or lying down are often apparent on examination, as are changes in the dystonia with different postures or walking. Sometimes shoulder elevation, mild tremor, or dystonic movements in other parts of the body are observed.

Cervical dystonia can be classified according to the dominant head position, with the most common type involving horizontal turning, the so called rotatory (or simple) torticollis. Other common patterns include laterocollis (tilt to one side), retrocollis (tilt upwards, resulting in neck extension), and anterocollis (tilt downwards, resulting in neck flexion).[8]

Although rarely needed as a diagnostic tool in cervical dystonia, electromyography (EMG) can help exclude the diagnosis in patients in whom it is in question and provides useful data for mapping out an injection dosing and distribution plan for patients who need botulinum toxin. At rest, minimal EMG activity is detectable in cervical muscles in patients without cervical dystonia[9].

Different classes of therapeutic agents have established some track record of success in managing patients with cervical dystonia. The first is anticholinergic medications, such as trihexyphenidyl or benztropine[10,11,12].

Benzodiazepines, particularly clonazepam, although associated with fewer side effects than anticholinergic medications, show a fairly similar efficacy profile[11]. Rare patients with cervical dystonia can respond impressively to levodopa.

Many medications, ranging from anticonvulsants to antispasticity agents, have been reported to be successful in case reports or small case series[12].

At this time, there are several commercially available botulinum toxin products that vary in unit strength and dosing[13,14,15].

Botulinum toxin (BoNTA) presynaptically blocks transmission at the neuromuscular junction and is regarded as an effective treatment option for the management of focal spasticity. Delivered by intramuscular injection into the affected muscle, BoNTA causes local and temporary paresis of the muscle and may also provide an analgesic effect lasting for three to four months.[16]

Although BoNTA is accepted as safe for therapeutic use, both local and systemic adverse events (AEs) have been reported in the literature. Reported AEs related to BoNTA include the symptoms in different systems such as musculoskeletal (pain and weakness), neurologic, visual, oropharyngeal, respiratory, immune system, bowel and bladder, cardiovascular, resulting in extreme cases in anaphylaxis, and spontaneous death.[17,18]

Methodology:

All cervical dystonia patients attending the Neurology Clinic and aggreed to be injected with botulinum toxin for treatment, Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai, India, from August 2022 to May 2023, were included in the study. Total 39 patients were included but 3 did not return for follow up. All 36 patients with cervical dystonia were injected with Botox (Onabotulinum Toxin A, by Allergan). Injections were given by a single expert and dosing was determind by the expert. A pre-designed proforma was filled, which included a detailed history, screening for immediate adverse effects(Up to 4 hours after injection) and delayed adverse effects(2 weeks after injection). Data was analyzed by statistical package for social science programme(SPSS).

Results:

Out of 36 patients 24 were female(66.66%) and 12 were male(33.33%).(Table 1)

12 out of 36 patients had onset of symptoms between the age of 41 to 60 years of age(33.33%), followed by 11 paients (30.55%)had onset of symptoms between the age of 21 to 40 years of age (Table I).

Table-I

Age of onset of symptoms and sex distribution of patients

Age at onset (years)	Male	Female	Total	Percentage
0-20	3	3	6	16.66
21-40	4	7	11	30.55
41-60	4	8	12	33.33
>60	1	6	7	19.44

17 out of 36 patients had torticollis(68%), 9 had retrocolis(25%), 5 had lateroclis(13.88%) and 5 had anteroclis(13.88%). (Table 2)

21 (58.34%) out of 36 patients had duration of symptoms more than 5 years and 15 patients (41.66%) had duration less then 5 years.(Table 3)

27 patients (75%) out 36 had received treatment with botulinum toxin previously and rest 9 patients (25%) never received botulinum toxin.(Table 4)

4 patients (11.11%) had excessive bleeding from injection sites, 3 patients (8.33%) complained of pain but no patient developed anaphylaxis within 4 hours of injection(0). (Table 5)

Excessive muscle weakness was observed in 4 patients (11.11%014 days after injection followed by dysphasia in 1(2.77%0and persistent hematoma in 1 patient(2.77%) at injection site.(Table 6).

Table-II

Clinical subtypes of Cervical Dystonia

Clinical subtypes	Total	Percentage
Torticollis	17	68
Latero- collis	5	13.88
Retrocollis	9	25
Anterocollis	5	13.88

Table-III

Duration of Cervical Dystonia

Duration of illness (years)	Male	Female	Total	Percentage
<5	4	11	15	41.66
>5	8	13	21	58.34

TableIV

History of previous treatment with Botulinum Toxin

Previous Treatment with Botulinum Toxin	Total	Percentage
Yes	27	75
No	9	25

Table-V

Immediate adverse effects after injection

Immediate adverse effect(Up to 4 Hours)	Total	Percentage
Pain	3	8.33
Bleeding	4	11.11
Anaphylaxis	0	0

Table-VI

Delayed adverse effects after injection

Delayed Adverse effects(Up to 14 days)	Total	Percentage
Excessive muscle weakness	4	11.11
Dysphagia	1	2.77
Respiratory difficulties	0	0
Dysphonia	0	0
Persistent hematoma	1	2.77

Discussion:

Several large clinical series have confirmed a female preponderance in CD.(19,20]. In this study 24 patients out of 36 (66.66%) were female and rest 12 were male(33.33%)

the peak age at CD onset reported by the various studies is in the fourth to fifth decade, with a mean age of 42 years (21]this is consistent in this study where 12 out of 36 patients had onset of symptoms between the age of 41 to 60 years of age(33.33%)

In this study commonest form of cervical dystonia was Torticolis (68%)followed by Retroclis(25%). This findings are consistent with different other studies. (22]

In this study 21 out of 36 patients (58.34%) had duration of illness for more than 5 years and 27 patients (75%) had previous treatment with botulinum toxin. This disorder is poorly recognised and results in delay in diagnosis and treatmment. One Australian study found a mean delay to diagnosis of 6.8 years. (23]

In this study bleeding from the injection sites were encountered in 4 patients(11.11%), pain at the injection sites in 3 patients(8.33%) and no patient suffered from anaphylactic reaction immediately after injection of botulinum toxin.

In this study excessive muscle weakness was observed in 4 patients 14 days after injection followed by dysphasia in 1and persistent hematoma in 1 patients at injection site.

Dysphagia is the most frequently cited adverse effect of BoNT, reported in 5%–42% of patients, followed by muscle weakness in 3%–4%, injection pain 1%–9%, generalized weakness 0.3%, speech difficulties 0.3%.(24]

Conclusions:

Botulinum toxin has been shown, through numerous trials, to be safe and effective in the treatment of CD. These benefits, which clearly translate into improved quality of life, are usually sustained indefinitely. Although there are some serious adverse effects but in expert hands botulinum toxin is safe for patients.

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