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**Original Research Article**

# Effectiveness, safety and tolerability of botulinum toxin in focal hyperhidrosis and dynamic facial wrinkles

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## ABSTRACT

**Background:** Botulinum toxin is a potent neurotoxin that inhibits the release of acetylcholine at the neuromuscular junction thereby causing localized muscle relaxation which smoothen the overlying skin and reduces dynamic facial wrinkles. Also clinical studies suggest that intra dermal injections of botulinum toxin are effective in the treatment of palmar hyperhidrosis by blocking the excessive sympathetic cholinergic sudomotor nerve traffic to the palmar surface of the hands.
**Methods:** We treated twenty patients with palmar hyperhidrosis and fifteen patients with dynamic facial wrinkles with intra dermal botulinum toxin type A.
**Results:** Among patients treated, complete response was seen in 90% of patients with hyperhidrosis and 70% for patients with facial wrinkles. The relapse of symptoms was highly variable among patients and the average relapse was seen at 14 weeks for both the indications. No major side effects noted.
**Conclusions:** Botox is an effective and highly tolerable treatment for both hyperhidrosis and facial wrinkles.

**Keywords:** Intra dermal botulinum toxin, Palmar hyperhidrosis, Dynamic facial wrinkles

## INTRODUCTION

Botulinum toxin was initially discovered to be produced by a bacterium that grows in improperly prepared meat products. Kerner, a physician, first conceived a possible therapeutic use of botulinum toxin and coined the name botulism.[1] Emile van Ermengem named the bacterium, Clostridium botulinum.[2] In 1928, Tessmer Snipe and Hermann Sommer were the first to purify the toxin.[3] In 1949, Burgen et al discovered, through an elegant experiment, that botulinum toxin blocks neuromuscular transmission by decreasing acetylcholine release.[4] Botulinum finds several applications in the field of general dermatology as in treatment of hyperhidrosis – axillary, palmar and plantar hyperhidrosis, gustatory sweating syndrome and in aesthetic dermatology for dynamic facial wrinkles. Our aim was to study the effectiveness of botulinum toxin in palmar hyperhidrosis and dynamic facial wrinkles and to analyze the safety and tolerability profile of it among the treated patients.

## METHODS

### *Study design*

Prospective non-randomized interventional study.

### *Study place and period*

Outpatient Department of Dermatology, Stanley Medical College between November 2010 and December 2012.

***Selection criteria***

*Inclusion criteria*

We included 20 patients with palmoplantar hyperhidrosis and 7 patients with horizontal frontal line and 3 with crow's feet. All were subjected to the pre-procedure consultation, assessment and relevant investigations.

*Exclusion criteria*

We excluded patients with neuromuscular disorders, pregnant and lactating women, patients receiving drugs with neuromuscular blocking properties like amino glycosides, spectinomycin in the previous 3 days and patients with known hypersensitivity to BTX-A.

Statistical analysis was done using SPSS version 22.0 was used to analyze the data.

***Ethical approval***

Obtained from Institution Ethical Committee, SMC.

***Procedure***

Minors starch iodine test and photographic recording was done to assess the severity of hyperhidrosis and wrinkles respectively.

The BTX-A containing vial was reconstituted with 2.5ml of normal saline. It was drawn in 100 units insulin syringe so that 1 unit marking in the syringe corresponds to 1 unit of BTX-A. Intra dermal test for BTX-A is given over volar aspect of left forearm. Anaesthesia was achieved using topical anaesthetic (EMLA) applied over the injection sites under occlusion. For hyperhidrosis the dominant hand was chosen for injection and the palm was divided into squares with area of 2 $cm^2$ each and 2 units of BTX-A is injected intra dermally into their centre. In the palmar aspect of fingers 2 units is injected into the centre of each phalanx.

Forehead lines were injected with 2units in two rows of equally spaced points which are 2 cm apart are marked on the forehead. The lower row being 1 cm above the brow and the inter-row distance was 2 cm.

For Crow's feet, 3 injection sites on each side were chosen with the first being 1cm away from the bony margin from lateral canthi and two other points 1 cm above and below the first point and just medial to it are marked a as shown in the pictures.

Immediately after the procedure ice packs are placed over the injection sites for 3–5 minutes.

Patients were advice to avoid lying down for 4 hours in patients treated for wrinkles and to avoid any rigorous activity of the injected hand. Follow up was done at $10^{th}$ day, $4^{th}$ week, $8^{th}$ week, $16^{th}$ week and $24^{th}$ week and once in 3 months after that. The response were assessed using the following criteria.

***Hyperhidrosis***

*Complete response* - more than 75% reduction in sweating.

*Partial response* - between 35% to 75% reduction in sweating.

*No response* - less than 35% reduction in sweating.

***Wrinkles***

*Complete response* – more than 75% reduction in visible wrinkles.

*Partial response* - between 35% to 75% reduction in visible wrinkles.

*No response* - no significant reduction in visible wrinkles.

***Relapse rate***

In both the conditions relapse was taken as complete recurrence of symptoms similar to that before treatment.

## RESULTS

Out of the total 30 patients, 21 were females and only 7 were males (Figure 1).

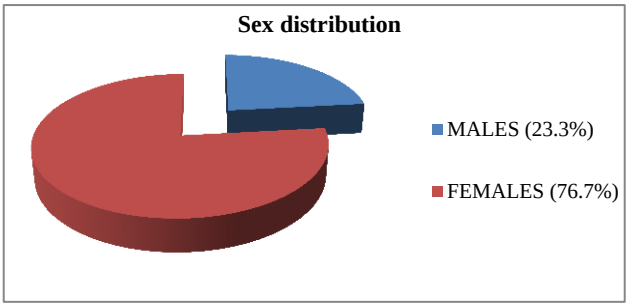


**Figure 1: Showing sex wise distribution of study group.**

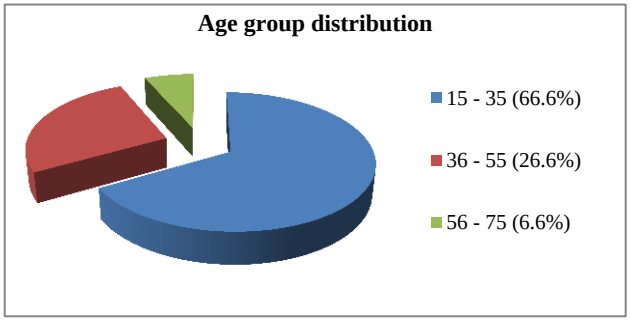


**Figure 2: Showing age group distribution of study population.**

More cosmetic awareness among women when compared to men could have resulted in women dominating the study population.

The commonest age group was 15 to 35 and the mean age of the study population was 35.5 (Figure 2).

**Table 1: Response rate to treatment given.**

| | Hyperhidrosis | Wrinkles |
|---|---|---|
| **Complete response** | 18/20 (90%) | 7/10 (70%) |
| **Partial response** | 2/20 (10%) | 3/10 (30%) |

Majority of the treated patients had good response to the treatment in both the groups. Complete response to treatment was seen in 90% and 70% of those treated for hyperhidrosis and wrinkles respectively (Table 1).

**Figure 3: Palmar hyperhidrosis right hand was treated minor statrch iodine test done before treatment.**

**Figure 4: 10th day after treatment showing complete response.**

**Figure 5: Crows feet – before treatment.**

**Table 2: Relapse rate during follow up.**

| | 4th week | 8th week | 16th week | 24th week |
|---|---|---|---|---|
| **Relapse rate for hyperhidrosis** | 2/20 (10%) | 3/20 (15%) | 5/20 (25%) | 16/20 (80%) |
| **Relapse rate for wrinkles** | 1/10 (10%) | 2/10 (20%) | 4/10 (40%) | 6/10 (60%) |

**Table 3: Complications observed.**

| Complications | No. of patients |
|---|---|
| **Pain over the treated site** | 3 |
| **Hematoma over the site** | 2 |
| **Hand muscle weakness** | 3 |

The relapse rate was 16/20 (80%) and 6/10 (60%) in hyperhidrosis and wrinkles respectively at the end of 24 weeks. Relapse of symptoms started appear significantly at 4 weeks follow up in both the conditions (Table 2).

Two patients developed hematoma at the site of injection. Three had developed hand weakness following treatment for hyperhidrosis (Table 3).

No major complications like anaphylaxis, ptosis, paralysis of facial or hand muscles were observed.

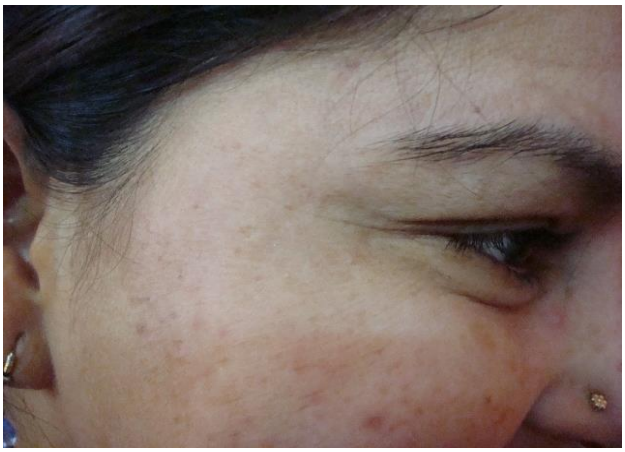

**Figure 6: Complete response after treatment.**

## DISCUSSION

### *Hyperhidrosis*

Our study showed that complete response to intra dermal Botox was seen in 90% (18/20) and partial response in 10% (2/20) patients treated for hyperhidrosis. In an earlier study done by Connolly and de Berker, 20 subjects having recalcitrant palmar and digital hyperhidrosis were treated with botulinum toxin type A, 50–65 U in one hand.[5] Treatment reduced sweat production significantly in the treated areas, with effect lasting from 4 to 9 months, although reduced sweating persisted in all patients for the 12-month evaluation period.

A study by Wollina and Karamfilov compared the effectiveness of BTX-A given in one hand compared with no treatment in the other control hand. Assessments included subjective and objective measurements, using gravimetric scales and Minor's iodine starch test. This study showed a significant improvement in 15/20 (75%) patients treated for palmar hyperhidrosis, with no serious adverse events. (Evidence levels: III)[6]. It has been expressed that botulinum toxin type A injections in the palm may impede the release of acetylcholine at the neuromuscular junctions, thereby decreasing muscle tone and function in the hand; however, this has not been found to be true (Evidence level: IIb). Lowe et al investigated the effectiveness of BTX-A vs. placebo in the treatment of palmar hyperhidrosis in 19 patients and concluded that patients experienced a significant improvement in palmar hyperhidrosis without a concomitant decrease in grip strength, finger dexterity, or the occurrence of any adverse events (Evidence level: Ib).[7]

Our study results correlated well with the above studies in that all patients treated had good response which lasted for an average of 14 weeks with no serious adverse events though transient hand weakness were noted in 50% of those treated.

### *Wrinkles*

In our study complete response was seen in 7/10(70%) and partial response in 3/10(30%) in those treated for wrinkles. Study done by Blitzer and Brin has shown the effectiveness of botulinum injections for hyper functional lines. These studies confer certain characteristics of successfully treated patients. The ideal patients are the ones with thin skin, fine wrinkles, lines that are exacerbated by muscle contraction, and hyper functional lines that can be spread out with their fingers. Blitzer et al described a "glabellar-spread test" in which the physician is able to spread out the hyper functional glabellar lines to project the maximum benefit that a paralytic injection could achieve.[8]

The relapse rate was 16/20 (80%) and 6/10 (60%) in hyperhidrosis and wrinkles respectively at the end of 24 weeks.

### *Complications*

The most dreaded complication is temporary paralysis of nearby facial musculature. Nearly 1-3% of patients may experience a temporary upper lid or brow ptosis; the most serious complication to the patient is upper lid ptosis.[7] This results when there is migration of the botulinum toxin to the levator palpebrae superioris muscle. The ptosis usually persists for 2-6 weeks. It can be treated with topical apraclonidine. This is an alpha-adrenergic agent that stimulates the Muller muscle and immediately elevates the upper eyelid. This treatment can usually raise the eyelid 1-3 mm. Treatment with 1-2 drops 3 times per day continues until the ptosis resolves.

Bruising usually occurs if a small vein is lacerated or a patient is on aspirin, vitamin E, or NSAIDs. Strictly patients should stop taking these products 2 weeks before the procedure. Headaches can occur after injections; however, in one study done by Carruthers et al, this did not exceed the placebo group.[9] This is due to the trauma of the injection and not something inherent in the toxin. In fact, botulinum toxin injections are quite safe. To date, no significant long-term complication of botulinum toxin injections has been identified.[10]

In our study only minor side effects like pain after injection, hematoma, and mild hand muscle weakness were noted. No major complications like anaphylaxis, ptosis, paralysis of facial or hand muscles were observed.

### *Study limitation*

One of the study limitations is the possible first stage selection bias, which cannot be ruled out and case control could not be done and it is a simple observational study.

## CONCLUSION

From our study we conclude that Botox is a valuable treatment for both hyperhidrosis and facial wrinkles and is effective in a single sitting. Since Botox is costly it should offered to patients with hyperhidrosis when they don't respond to other modalities of treatment or when a quick response is needed ahead of socially important situations like an examination, wedding etc., Pain during injection can be addressed through application of ice packs, use of the Dermojet delivery system or anesthetic procedures. Hence BTX is a safe, in-office procedure which can be performed without hospitalisation when done by a well-trained dermatologist with expertise.

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*Ethical approval: The study was approved by the institutional ethics committee, SMC*

## REFERENCES

1. Erbguth FJ. Historical notes on botulism, Clostridium botulinum, botulinum toxin, and the idea of the therapeutic use of the toxin. J Movement Disorders. 2004;20:12–6.
2. vanErmengem EP. Uebereinenneuenanaëroben Bacillus und seine BeziehungenzumBotulismus (in German). Zeitschriftfür Hygiene und Infektionskrankheiten. 1985;26:1–56.
3. Tessmer SP, Sommer H. Studies on Botulinus Toxin. Acid Precipitation of Botulinus Toxin. J Infect Dis. 1943;2:152–60.
4. Burgen ASV, Dickens F, Zatman LJ. The Journal of Physiology. 1949;10:10–24
5. Connolly M, de Berker D. Management of primary hyperhidrosis: a summary of the different treatment modalities.Am J Clin Dermatol. 2003;4:861-97.
6. Wollina U, Karamfilov T. Botulinum toxin A for palmar hyperhidrosis. J Eur Acad Dermatol Venereol. 2001;15(6):555-8.
7. Lowe N, Lask G, Yamauchi P. Efficacy and safety of botulinum toxins A and B, for the reduction of glabellarrhytids in female subjects. JAAD. 2002;28(9):822-7.
8. Blitzer A, Brin MF, Keen MS, Aviv JE. Botulinum toxin, for the treatment of hyperfunctional lines of the face. Arch Otolaryngol Head Neck Surg. 1993;119:1018-22.
9. Carruthers J, Stubbs HA. Botulinum toxin for benign essential blepharospasm, hemifacial spasm and age-related lower eyelid ectropion. Can J Neurol Sci. 1987;14:42-5.
10. Fagien S. Botox for the treatment of dynamic and hyperkinetic facial lines and furrows - Adjunctive use in facial aesthetic surgery. Plast Reconstr Surg. 2003;112:40-52.

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