

## Botulinum Toxin Type A injection versus placebo Treatment of Primary Palmar Hyperhidrosis

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### ABSTRACT

**Background:** When the hands, axillae and soles of the feet are excessively perspired, it can be debilitating. Type A botulinum toxin-A (BTX-A) prevents sweating by preventing sweat glands from releasing acetylcholine.

**Objective:** This study aimed to assess role of Botulinum toxin type A injection versus placebo treatment of primary palmar hyperhidrosis.

**Patients and Methods:** twenty four patients presented with primary palmar hyperhidrosis (PPH) were collected from Dermatology Outpatient Clinics, Zagazig University Hospital. Their left hands were treated by placebo and their right hands were treated using BTX-A injection.

**Results:** Improvement of HDSS (score 4) regarding treatment modalities. HDSS (score 4) before treatment improved after to be 6.7%, 66.7%, 8.3%, 8.3% score 1, score 2, score 3, score 4 in right side treated with Botulinum toxin type A injection, versus 16.7%, 33.3%, 20.8%, in left side treated with placebo treatment. There was significant high percent of excellent response for Botulinum toxin type A injection among females and patients with delay onset of disease ( $p < 0.05$ ).

**Conclusion:** BTX injections appear to be more effective than placebo. It's still one of the most popular noninvasive cosmetic procedures, and neurotoxin. BTX is still an effective and predictable agent.

**Keywords:** Botulinum toxin, Primary palmar hyperhidrosis.

### INTRODUCTION

When the hands, axillae and soles of the feet are excessively perspired, it can be debilitating. Those with palmar hyperhidrosis may find it difficult to write because the page becomes wet. They may have difficulty writing with a pen or pencil. Sports that require a strong grip, as well as playing musical instruments, may be out of the question. It is possible for the patient to become isolated and socially awkward. People who suffer from hyperhidrosis often seek treatment for their palms and axillae, which are the most affected areas <sup>(1)</sup>.

Palmar hyperhidrosis is a condition in which the palms sweat excessively, above and beyond the amount necessary to keep the body cool. Adults are more likely to suffer from it than children. Disruptive to the patient's social or work life, it can be emotionally challenging, socially embarrassing and professionally disruptive. In extreme cases, sweat drips from the hands and gives the impression of nervousness. The most common explanation is that it stems from stress or other emotional factors, but this is not always the case <sup>(2)</sup>.

Most commonly, aluminium chloride hexahydrate (ACH) is applied to the skin to alleviate symptoms of mild to moderate severity. It is a first-line treatment because of its wide availability, cost-effectiveness, and ease of use. Water, alcohol, ether, and glycerol all contain ACH in concentrations ranging from 6.25% to 40%. ACH concentrations in over-the-counter (OTC) antiperspirants are limited to 12.5%. Aluminum chloride in ethyl alcohol, 6.25% aluminum tetrachloride, and 12% aluminum chloride in sodium carbonate-water are all commonly prescribed formulations <sup>(3,4)</sup>.

The acetylcholine release in sweat glands is blocked by botulinum toxin type A (BTX-A). Excessive sweating in primary axillary and palmo-plantar hyperhidrosis was reduced by intradermal BTX-A injections. Topical anesthesia makes it simple to administer intradermal BTX-A to the axillary skin. The majority of patients who undergo intradermal BTX-A for palmo-plantar sweating necessitate regional nerve block anesthesia <sup>(5,6)</sup>.

### PATIENTS AND METHODS

In this comparative study, twenty four patients presented with primary palmar hyperhidrosis (PPH). They were collected from Dermatology Outpatient Clinics, Zagazig University Hospital. These volunteers were randomly divided into two groups, split hand that received four treatments at 2-week intervals.

**Group A** included left hands of the 24 patients with excessive palmar perspiration and excessive sweating treated with placebo treatment, and **group B** that included right hands of the 24 patients with excessive palmar perspiration and excessive sweating treated with BTX-A injection.

#### Inclusion criteria:

1. Aged up to 50.
2. Male and females.
3. Diagnosed with moderate and severe primary palmar hyperhidrosis (PPH) and meeting diagnostic criteria. The symptoms of severe palmar hyperhidrosis include base score of 3 or 4 on the Hyperhidrosis Disease Severity Scale and a minimum sweat production gravimetric

measurement of 0.15 g/5 min/hand for spontaneously resting people.

4. More than a year of excessive palmer perspiration and excessive sweating.
5. Patients with a sweating severity score of three or four (HDSS).

**Exclusion criteria:**

1. Lactation and pregnancy.
2. The disease of the motor neurons.
3. Organically ill patients, such as those with hyperthyroidism.
4. Botulinum toxin sensitivity has been established.
5. Those with HDSS 1, 2, and hyperhidrosis, both generalized and localized.

**All patients were subjected to the following:**

**History taking:**

Personal history (age, sex, marital status, education, age onset of disease, duration of disease and medication). Present history with search for possible causes of 2<sup>ry</sup> hyperhidrosis and manifestations of other system affection, previous experience with medicine and surgery. Family history, paying particular attention to any other members of the family who have the same condition as you do, as well as any evidence of blood relation between the parents.

**Full physical examination:**

General examination including weight, vital signs, body built overall activity and chest examination. Local examination of palms with clinical assessment of severity of hyperhidrosis according to HDSS grade 1 to 4 for postoperative assessment of improvement of symptoms. Severe hyperhidrosis was indicated by a score of 3 or 4, while mild or moderate hyperhidrosis was indicated by a score of 1 or 2. One point improvement in HDSS score results in a 50% reduction in sweat production, while two points results in an 80% reduction.

A successful treatment was defined as an improvement from a score 4 or 3 to a score 2 or 1. Regular pre-op lab testing, including a complete blood count, profile of coagulation, liver and kidney function tests. The P.A. and lateral views of a plain chest and cervical x-ray are used to rule out abnormalities in the cervical ribs and lungs. In order to rule out secondary hyperhidrosis that can be treated medically, a thyroid

function panel, serum glucose levels, and uric acid levels were performed. If necessary, a psychiatric evaluation was conducted.

**Sweating assessment:**

It was decided to perform a Minor's starch iodine test in order to find out if there were any sweaty patches on the hands. After a few seconds, starch was sprinkled on top of the iodine solution (1-5 %). In the presence of sweat, starch and iodine combine, resulting in a purple sediment that can be seen in photographs. We treat each patient right hand by botox (for two sessions and two weeks between each session). In the first session, we used botox 50 IU and in second one, we used 75 IU. The left hand was treated by aluminium chloride 20% after fractional CO<sub>2</sub> laser, then we follow the patient for 6 months. The first follow up was after one month and the second follow up was after 3 months then after 6 months from the last session.

**Right hand:** It was administered as a 50-unit injection of 4 units/0.1 milliliter of BTX-A in 0.9% saline solution.

**Left hand:** placebo injection

**Ethical consent:**

**An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.**

**Statistical analysis**

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution using Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ( $\chi^2$ ) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean  $\pm$  SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value  $\leq$  0.05 was considered significant.

**RESULTS**

Table (1) showed hyperhidrosis disease severity scale among the 2 studied groups (details of the table).

**Table (1):** Hyperhidrosis disease severity scale (HDSS), throughout study phases (n=24)

Variables	HDSS	Time				P1
		Before treatment		After treatment		
		No.	%	No.	%	
<b>Group I</b>	1	0	0.0	8	33.3	0.0001 (HS)
	2	0	0.0	12	50.0	
	3	9	37.5	2	8.3	
	4	15	62.5	2	8.3	
<b>Group II</b>	1	0	0.0	9	37.5	0.0001 (HS)
	2	0	0.0	10	41.7	
	3	7	29.2	5	20.8	
	4	17	70.8	0	0.0	
P		0.54		0.26		

**P1** : Marginal Homogeneity Test (within group), **p** : chi square test (between groups), **(HS) p<0.001** highly significant  
**Group I:** Botulinum Toxin Type A injection .**Group II:** placebo injection

Table (2) showed improvement of HDSS score 3 regarding treatment modalities. HDSS (score 3) before treatment improved to be HDSS (score 1 & 2). The difference was statistically insignificant of treatment modalities (p > 0.05). There was improvement of HDSS score 4 regarding treatment modalities. HDSS (score 4) before treatment improved after to be 6.7%, 66.7%, 8.3% and 8.3% score 1, score 2, score 3 and score 4 respectively in right side treated with Botulinum toxin type A injection ,versus 16.7%, 33.3% and 20.8%, in left side treated with placebo treatment.

**Table (2):** Comparison both groups regarding HDSS before and after treatment (n=24)

Variables		Studied patients				$\chi^2$	P
		Group I (RT side)		Group II (LF side)			
		Before ttt n.(%)	After ttt n.(%)%	Before ttt n.(%)	After ttt n.(%)		
<b>HDSS before treatment (score 3)</b>	Score1	-	7(29.1)	-	(5)20.8	F	0.99
	Score2	-	2(8.3)	-	(2)8.3		
	<b>Score3</b>	<b>9(37.4)</b>	0.0	<b>7(29.1)</b>	0.0		
<b>HDSS before treatment (score4)</b>	Score1	-	1(6.7)	-	4(16.7)	5.2	0.16
	Score2	-	10(66.7)	-	8(33.3)		
	Score3	-	2(8.3)	-	5(20.8)		
	<b>Score4</b>	<b>15(62.6)</b>	2(8.3)	<b>17(70.9)</b>	0		

$\chi^2$  Chi square test      f= Fisher exact test      **p>0.05:** Non-significant      **Group I:** injection of Botulinum Toxin Type A      **Group II:** placebo injection

(Table 3) showed that there was significant high percent of excellent response for Botulinum toxin type A injection among females and patients with delay onset of disease (p < 0.05).

**Table (3):** Relation between patients' therapeutic response for Botulinum toxin type A injection and their demographic and basic clinical characters

Variables		Therapeutic response Fractional CO2 Laser Assisted Botulinum Toxin Type A			KW/ $\chi^2$	p-value	
		Excellent n.16	Good n.6	No n.2			
Age per years	Median (range)	16.5(12-35)	17(16-23)	12(12-12)	3.8	0.15	
Sex	males	N	2	4	2	10.1	.006(S)
		%	12.5%	66.7%	100.0%		
females	N	14	2	0			
	%	87.5%	33.3%	0.0%			
Family history	Positive	N	6	4	2	3.7	0.16
		%	37.5%	66.7%	100.0%		
	negative	N	10	2	0		
		%	62.5%	33.3%	0.0%		
Age at disease onset	Median (range)	7(5-10)	5 (3-7)	4(4-4)	7.8	0.02 (S)	
Disease duration /years	(Median (range)	11.5(3-28)	13 (12-16)	8(8-8)	3.7	0.16	
HDSS	3	N	5	4	0	3.6	0.16
		%	31.3%	66.7%	0.0%		
	4	N	11	2	2		
		%	68.8%	33.3%	100.0%		

KW= Kruskal Wallis Test,  $\chi^2$  Chi square test, p > 0.05: Non-significant, p < 0.05: significant

## DISCUSSION

An excessive amount of sweating in the palms is the most common symptom of palmar hyperhidrosis. The cause is unknown and the incidence is 2.8%. There is a significant impact on younger patients' mental and social well-being. Medical or topical treatment has little effect on these symptoms. As many as one percent of the general population is thought to be affected by the condition, which is linked to significant physical, psychological, and occupational impairments<sup>(7)</sup>.

Axillary and palmar hyperhidrosis can be effectively treated with Botulinum toxin type A (Botox), which is a neurotoxin produced by Clostridium botulinum, [Botulinum toxin-A (BTX-A)]. It blocks acetylcholine release at neuromuscular junctions, resulting in muscle relaxation and paralysis<sup>(8,9)</sup>.

The analgesic properties of BTX-A have been demonstrated in animal studies by a number of different mechanisms. It blocks the release of calcitonin-derived peptide and other neuropeptides, as well as the release of pain mediators from motor and sensory neurons. Additionally, it was reported that BTX-A alone is ineffective in treating idiopathic palmar hyperhidrosis<sup>(10)</sup>.

All patients underwent a thorough examination, including a medical history interview, physical examination, and a battery of tests including thyroid function and blood glucose levels. It was decided to perform a Minor's starch iodine test in order to find out

if there were any sweaty patches on the hands. According to hyperhidrosis disease severity scoring system, we used clinical assessment to determine the severity of the condition (HDSS). Before treatment, iodine starch tests were positive in all patients. After treatment, this number dropped to 16.7% for both sides. HDSS was administered to 33.3% of patients with a score of 3 and 66.7% of patients with a score of 4 prior to treatment.

**Rajagopal and Mallya<sup>(11)</sup>** a total of 60 cases of HDSS 4 and HDSS 3 were found in the study, which was evenly distributed between the two arms. We found statistically significant long disease-free periods for palmar hyperhidrosis among hands treated with fractional CO<sub>2</sub> Laser assisted botulinum toxin type A (p = 0.0001).

**Rajagopal and Mallya<sup>(11)</sup>** showed that the relapse rate between hands treated with NA/BoNT/A and hands treated with WB/BoNT/A was similar. For the sake of patient safety, botulinum toxin type A appears to reduce muscle weakness, which patients prefer because it expedites the hand's functional recovery. Botulinum toxin type A has a higher-than-average percentage of excellent responses in females and patients with late-onset disease, according to our research (p 0.05).

**Rajagopal and Mallya<sup>(11)</sup>** found that the response began 2 weeks after injections and was maintained for 4 months after injections in the 24 cases

that showed improvement. After that, there was some recurrence, but it was much less than it had been prior to therapy. Six months after the initial injections, patients received additional injections where 11 cases showed improvement. The response was seen three weeks from the treatment and lasted as long as the medicine was applied. One month after stopping treatment, a relapse was observed. They came to the conclusion that botulinum therapy produced better results than iontophoresis or topical therapy. In comparison to iontophoresis and topical therapy, botulinum toxin's residual effects lasted an average of four months. In comparison to botulinum therapy, iontophoresis and topical therapy were non-invasive and did not necessitate regional anesthesia<sup>(12)</sup>.

It's still common practice to use BTX as a noninvasive aesthetic treatment because the neurotoxin is both effective and predictable. BTX has a slew of uses that go far beyond the well-known cosmetic advantages. Because of its anhidrotic efficacy, acceptable safety profile and positive impact on patient quality of life. BTX has quickly become an effective multidisciplinary treatment for hyperhidrosis. This meta-analysis suggests that BTX injections are more effective than a placebo, based on the findings<sup>(13)</sup>.

## CONCLUSION

BTX injections appear to be more effective than placebo. It's still one of the most popular noninvasive cosmetic procedures, and neurotoxin BTX is still an effective and predictable agent.

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