Basrah Journal Of Surgery

Original Article

Bas J Surg, June, 20, 2014

EVALUATION OF BOTOX TREATMENT FOR PATIENTS WITH PRIMARY AXILLARY HYPERHIDROSIS IN BASRAH

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Abstract

Hyperhidrosis is a distressing condition that affects the social life of many patients. Botox has been discovered to treat this problem. This study aimed to evaluate the response of the patients to Botulinum toxin type A (BTX-A) and the time interval between injections during which the patient is free from symptoms.

The study evaluates subjectively the response of patients with axillary hyperhidrosis to Botox with 100% scale and Hyperhidrosis Disease Severity Scale (HDSS). The time interval between injections was also evaluated. The data were collected prospectively and analyzed.

This study included 21 patients with mean age of 27 years. Twenty of them were males. Of the 21 patients, 33% were subjected to multiple sessions. The response in 18 (85%) of patients was between 90-100%. The average time interval between injections was 211 days.

In conclusion, botulinum toxin type A (BTX-A) has significant benefit in treating patient with axillary hyperhidrosis with rapid onset and the average duration of symptom free period was 7 months.

Introduction

Primary axillary hyperhidrosis is defined as idiopathic, visible, excessive sweating that lasts for at least 6 months and has at least two of the following features: bilateral and relatively symmetric sweating, impairment of daily activities, cessation of focal sweating during sleep, the age of onset younger than 25 years, and positive family history of hyperhidrosis[1]. Hyperhidrosis affects about 3% of the population and it is commonly associated with hyperactivity of the sympathetic autonomous nervous system, which generates glandular hypertrophy and hypersecretion of the eccrine sweat glands in certain anatomical areas[2]. Hyperhidrosis can have a deeply detrimental effect on a patient's quality of life, resulting in dramatic impairments of daily activities, social interactions and occupational activities[3]. Two main types of treatment have been reported for primary hyperhidrosis:

Conservative treatment: Topical agents (aluminum hydrochloride-based antiperspirants): This treatment promotes the blockage of excreting ducts from eccrine glands. It has the advantage of being very accessible and can be used in association with other treatments[2,4].

Botulinum toxin: this treatment blocks the release of the neurotransmitter acetyl-choline, i.e., it blocks synaptic transmission, producing efficient chemical denervation of the gland and temporary cessation of excessive sweating. It is safe and effective and can improve quality of life. It is an easy treatment and can be administered under topical anesthesia, local anesthesia, or even sedation. It has the disadvantages of being costy in addition to the discomfort associated with multiple injections and a temporary therapeutic effect (with an average duration of 7 months)[5-8].

Surgical treatment: This include endoscopic thoracic sympathectomy, which is the only definitive surgical treatment for hyperhidrosis, of both palmar and axillary forms. This method

destroys the sympathetic ganglia by excision, clamping, transection or ablation with cautery or laser[9-11].

Other surgical procedures with reported efficacy include excision of axillary tissue and subcutaneous axillary curettage[12].

Subdermal axillary liposuction: this treatment causes rupture of the nervous supply to the sweat glands and removal or destruction of some of the sweat glands[13,14].

Another new surgical method is arthroscopic shaver technique, which remove a large percentage of gross eccrine gland volume and denervating the eccrine gland and simultaneously preserving vascularized dermal skin flaps[15].

The objective of this study was to observe the effects of subdermal botulinum toxin injection in treatment of patients with primary axillary hyperhidrosis and the duration of the results obtained with the treatment.

Patients & Methods

Twenty one patients with primary hyperhidrosis of the axilla were included in this study. The study was conducted from May 2011 to August 2013. All patients were injected with botulinum toxin. The patients were aged between 23 to 35 years (mean age 29 year). One patient was female and the others are males. All patients were followed up for more than one year after the treatment by phone and during the next visits, in 3, 6, and 12 months intervals.

In each visit, history was taken about the duration of symptoms, severity, family history of the same complaint, and previous treatment. Symptoms and signs of hyperthyroidism was analyzed if presents.

All patients had used previously topical agents, such as antiperspirants, but without benefits.

Iodine-starch test was performed in all patients to identify the maximum intensity of hyperhidrosis in the axilla (figure 1). The patient was positioned in 45" flexion of the hip with both arm abducted. Two percent iodine spray was used to wet the axillary area, then a thin film of starch was spread over it and left for 10-15 minutes. Areas of maximum sweating was changed to dark violet color (figure 2). These areas were marked with marking pen.

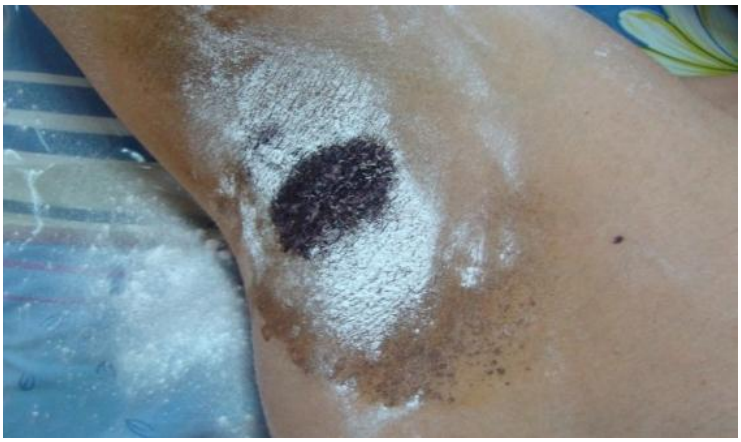

Fig. 1: Iodine starch test, iodine and starch is applied.

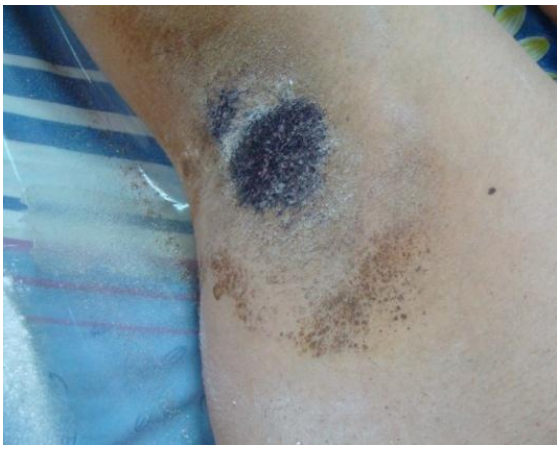

Fig.2: Iodine starch test, after 10 minutes the presence of sweating is indicated by the onset of a dark-blue color.

EMLA (eutectic mixture of lidocaine and prilocaine) cream as a local anesthetic was applied for some patients to reduce the pain of the intradermal injection of the Botox. The Botox, Botulax (HUGEL, Inc., Chuncheon-si, Gangwon-do, Korea) of 100 IU was reconstituted with 5ml of normal saline and divided into 5 syringes of 1ml and 31 gauge needle. This provide concentration of 2 U in every 0.1ml. The botox was injected subdermally in the marked area mainly. Part of the botox was injected in the periphery behind the marked area. Each axilla was injected with 2.5 ml (50 IU) of the reconstituted botox. In one patient the botox was reconstituted with 1ml xylocaine and 4ml normal saline to reduce pain of the injection. The time of the procedure ranged from 20 to 30 minutes with an average of 25 minutes per session.

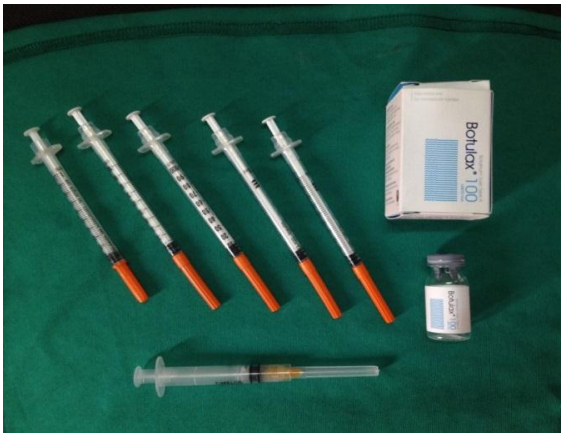

Fig. 3: 100 U of Botulax (HUGEL, Inc., Chuncheon-si, Gangwon-do, Korea)

The results were assessed during 12 months post injection with Hyperhidrosis Disease Severity Scale (HDSS). The HDSS is a validated 4-point scale on which the subject rates the tolerability of his or her axillary sweating and its interference with daily life (table I)[16]. The patients were asked to rate the severity of their hyperhidrosis. The results were also assessed by 100% scale by asking the patient how much success he or she got after the injection or how much the sweating has been reduced. The patients were then followed up after one month,

six months, and twelve months. The follow up mostly was by phone call. Some patients were injected twice or three times during the study.

Table I: Hyperhidrosis Disease Severity Scale (HDSS)

Score	Patient response
1	My underarm sweating is never noticeable and never interferes with my daily activities
2	My underarm sweating is tolerable but sometimes interferes with my daily activities
3	My underarm sweating is barely tolerable and frequently interferes with my daily activities
4	My underarm sweating is intolerable and always interferes with my daily activities

Results

Twenty one patients suffering from significant hyperhidrosis of the axillae were included in this study. All the cases were primary hyperhidrosis that was very embarrassing and frequently interfere with their daily activities and their score on HDSS was 3 or 4. Twenty cases (94.7%) were males and only one case (5.3%) was female. Patients ranged in age between 23years and 39 years (mean age 29).

Table II: Patient demographics

Patient demographics	
Mean age	29 year
Range	23-39 year
Gender	Number (%)
Male	20 (95%)
Female	1 (5%)

No patients were suffering from signs or symptoms of thyrotoxicosis. Four patients had family history of hyperhidrosis of the axilla. All the patients had previously used topical agents such as antiperspirants but without benefits. Two patients have another site of hyperhidrosis, one in his palms and the other in his lower breast. No one of them asked for treatment for these areas.

The response to the treatment started after three days with 50% reduction in sweating in all of the patients. After 4 weeks the response was 100% in 4 cases, 90-99 % in 11 cases, and 80-89% in two patients (table III). In three patients, the response was 75% and reinforcement was done after one month with 25 units in each axilla. The response was increased to 90-95% in them. The response of the female patient was 75% and did not return back for reinforcement. Nearly all the patients reported an improvement in their symptoms and quality of life as define d by a 2-point improvement in the HDSS scale within the first 4 weeks after treatment. Fifteen patients (71%) reported two points reduction while two patients (9%) reported three points reduction in HDSS in one month after the injection (table IV). The length of reduction in hyperhidrosis ranged from 5 to 9 months. The average length of reduction of symptoms was 7 months (table V). Of the 21 patients, only four patients (19%) returned for multiple injections. Three of them were injected three times and one patient was injected twice. The interval between injections was ranged between 152 to 439 days (average 283 days) as shown in table VI. The case with two injections is not included in this table.

Table III: Results

Response grade at one month	Number (%)
91-100%	15 (71%)
81-90%	2 (10%)
71-80%	4 (19%)
61-70%	0 (0%)
Response after one month	Number (%)
With reinforcement for 3 patients	
91-100%	18 (85%)
81-90%	2 (10%)
71-80%	1 (5%)
61-70%	0 (0%)

Table IV: Result of HDSS Reduction of HDSS at four weeks

	Number (%)
1 point	4 (19%)
2 points	15 (71%)
3 points	2 (10%)
Reduction of HDSS after four weeks	With reinforcement
1 point	1 (5%)
2 points	18 (85%)
3 points	2 (10%)

Table V: Duration of symptom relief

4-6 months	11 (52%)
6–8 months	6 (28%)
8–10 months	4 (20%)
10–12 months	0 (0%)

Table VI: Duration between injections

case no.	Duration between 1st and 2nd injection (days)	Duration between 2nd and 3rd injection (days)	Average (days)
1	212	152	182
2	351	439	395
3	208	336	272
			283

Only one case mentioned swelling at site of the injection without pain that subsided after two days (table VII). No hematoma was reported. Mild pain was subjected at time of injection that was decreased with the use of topical EMLA cream or xylocaine 2% mixed with the reconstituted botox. One patient developed compensatory hyperhidrosis in his lower breast.

Table VII: Side effects

No side effects	19 (90%)
Swelling at site of injection	1 (5%)
Compensatory trunk hyperhidrosis	1 (5%)

Discussion

Botulinum toxin type A (BTX-A) treatment for primary axillary hyperhidrosis is considered an intermediate between conservative treatment and surgical management by liposuction or by sympathetic block.

The efficacy of the treatment and the duration of action is important to be discussed with the patient. Botulinum toxin type A is safe, effective, durable with rapid action as the patients reported beginning of the action within few days of injection.

Several studies have mentioned the dose of botulinum toxin that is required for patients with axillary hyperhidrosis. A minimum botulinum toxin dose of 50 units per axilla is necessary to cause anhidrosis in healthy volunteers[7,8]. In our study , the dose of 50 U per axilla was enough in 16 cases. Only three patients required reinforcement with 25 U in each axilla after two weeks reaching to total dose of 75U in each site. Gilberto Marcos used 75U in each axilla in his study[1].

Evaluation of response to botox was done using simple 100% scale. The scale was easy for the patients to show their response to the botox treatment although it is subjective one. Jugbal et al. used subjective severity assessment based on a numerical rating scale ranging from 1 to 10[9]. The gold standard for quantitatively measuring a decrease in sweat production has been gravimetry. Gravimetric measurement is not practical or routine in clinical practice and is associated with high intra-patient variability over time. It therefore is not an ideal standard when used in isolation[6]. In our study, eighteen patients (85%) mentioned 90-100% response and two patients (9%) mentioned 80-89% response to the injections, with high satisfaction and improvement in social life. Only one case, that her response was 70%, she refused to return back for reinforcement which may be because she cannot tolerate the pain of injections.

In addition we use the HDSS scale to measure the patient satisfaction as our goal in treatment the hyperhidrosis is not to inhibit all the sweat production from the axilla but rather to improve the quality of life. The HDSS scale is easy to use in clinical practice and may show how the patients perceive their symptoms and disability. Mellisa et al and Stefan et al also use the HDSS scale in their studiesIn our study, within four week, 2 patients (9%) had three point reduction in HDSS, 15 patients (71%) had two point reduction, and 4 patient (19%) had one point reduction. In Stefano study, he reported a reduction of the HDSS at 4 weeks after the injections of three points in one patient (2%), of two points in 34 patients (68%), and of one point in 15 patients (30%)[18,8].

It is possible that seasonality and geography could have altered our results. The patients were seen in Basrah, which has four seasons. This seasonality did not appear to affect the time when patients returned for follow-up visits.

The use EMLA cream had reduced the severity of pain of the injections but lidocaine-reconstituted botulinum toxin A may be preferable for treating axillary hyperhidrosis[4]. We used the lidocaine reconstituted botox in only one case which shows same response. Some authors used local infiltration of Lidocaine or use sedation such as Midazolam or Fatanyl. We think that these methods are better used according the patient pain threshold or when he ask for that type of sedation.

The length of action or sweating free period was comparable to other studies. In the present study, it was 5 to 9 months (average 7 months). In Melisa study, the average duration of efficacy ranged from 4.7 to 8.7 months. In Gilberto Marco study, the length of reduction of Hyperhidrosis symptoms ranged from 4 to 12 months).

Four of our patients received multiple injections. The average time intervals between injections were 245 days.

Naumann study reported 7 months duration between botox treatment[8]. Talarico-Filho Sergio reported 260 days duration of action and Melissa reported that the efficacy was sustained for an average of 261 days by patients who required multiple injections[17,18]. This interval does not mean the onset of decrease of the therapeutic effect of the botox. The intervals between injections may be affected by multiple factors such as availability of the patient, financial considerations, availability of the treatment, etc. All these factors may delay the reinjection time and thus may produce seemingly longer duration of action. So it is better to consider the onset of decrease in symptoms free as a indicators of the duration of the botox, although it is subjective character. Dirk Dressler, in his study, mentioned that the duration of symptom free rather than the duration between the injection as a parameter for the effect of the botox[10]. The duration of action of the botox did not change with the increasing numbers of injections. Melissa study also shows no statistical difference in time interval with multiple treatments.

Conservative treatment with injections of Botulinum toxin type A has increased the degree of satisfaction and decreased the rate of complications or side effects[18].

Conclusion

Primary axillary hyperhidrosis is one of the conditions that cause embarrassment, isolation and low-self-esteem. The use of intradermal injection of botox is highly effective, with early onset of action, and durable method to treat this problem. It is minimally invasive and provides a high degree of satisfaction. It allows patients to return to their professional activities on the same day. It is a simple procedure with minimal pain that can be overcomed by local EMLA cream. Although it is costy but it improve the patient's emotional state and self-esteem, delay the reappearance of the symptoms of hyperhidrosis and enhance patient quality of life.

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