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Original articles

Botulinum toxin-A therapy for palmar and plantar hyperhidrosis

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Abstract

In an open study regarding focal hyperhidrosis, we injected 45-65 mouse units of botulinum toxin A (Btx-A) per palm and 100 per sole intracutaneously to 28 hands and 6 feet. We observed patients for up to 10 months to evaluate the efficacy and tolerability of Btx-A for palmar and plantar hyperhidrosis. The mean sweat production significantly declined for both palmar and plantar hyperhidrosis quantitatively on the first month of therapy ($P < 0.01$). One patient had transient muscle weakness and mild thenar atrophy interfering with her daily activities for 10 days. Injections were otherwise tolerated well by the patients. In this trial Btx-A injection is found to be an effective and safe method of treatment for palmar and plantar hyperhidrosis.

Key words : Hyperhidrosis ; treatment ; botulinum toxin ; palms ; soles.

Introduction

Focal hyperhidrosis is a result of over-activity of eccrin sweat glands innervated by cholinergic fibers of the sympathetic nervous system (1). It can involve palms, soles, axillae, and rarely face and trunk and may cause social, occupational and psychological problems (1). The most common form of focal hyperhidrosis is idiopathic focal hyperhidrosis which is suspected to be a result of central sympathetic system dysfunction (2, 3, 4). Available topical and systemic treatments are found to be ineffective in most of the cases, and thoracic sympathectomy can result in serious complications (5, 6). Btx-A is a protein which acts by blocking the release of presynaptic acetylcholine nerve fibers at the neuromuscular junction (7). The heavy chain of the molecule (100Da) provides affinity to cholinergic nerve endings and linked to the light chain (50Da) by a disulphide bond. After transportation of the toxin across the membrane of synapses, the disulphide bond is cleaved and the light chain interferes with the target protein, soluble N-ethylmaleimide-sensitive fusion attachment protein-25 (SNAP-25), which is involved in the exocytosis of aceltylcholine. Inhibition of aceltylcholine release blocks postganglionic cholinergic sympathetic fibers of eccrin glands, hence reduces sweat production. This was first observed in healthy volunteers in two studies which gave rise to a new indication of Btx-A (8, 9). In the last 5 years many studies have been performed including both open-label and double-blind placebo-controlled trials, in which patients suffering from excessive sweating in different parts of their body, predominantly axillary, were treated safely and successfully with local intracutaneous or subcutaneous injections of Btx-A (10, 11, 12, 13, 14).

Materials and methods

A total of 14 patients (11 women and 3 men aged 18-47 years, mean 27.64 and standard deviation [SD] 9.7) suffering from excessive sweating of their palms (all 14) and soles (3) and unresponsive to appropriate conventional topical or systemic therapies participated in the trial. The mean duration of hyperhidrosis was 13.29 and SD 8.2 years. Patients younger than 18 years of age, pregnant women and patients with symptomatic hyperhidrosis were excluded. The Ethics Committee of the Medical Faculty of Mersin University approved the study.

In this open study, all patients underwent a pretreatment evaluation of clinical assessment to exclude other diseases and none was found to be remarkable except for focal hyperhidrosis. Also, objective quantification of sweat production was evaluated before and at the first month of the injection and subjective rating of the individual sweating profile was assessed monthly. Hyperhidrotic areas were visualised by the iodine-starch test. In this test the skin is painted with 5% iodine/alcohol solution. After it has dried a fine potato starch powder is applied. Sweat causes the painted and powdered areas to turn to dark blue.

Hyperhidrosis was quantified by the Reinauer's method (15). The hyperhidrotic areas were dried and each brought into contact with a copy paper (Triton) for 1 minute ; and weight increases of the papers were evaluated as sweat production. This test was performed before and 1 month after the injections while the temperature (25°C) and

FIG. 1. — Palmar intradermal injection of Btx-A

humidity (70%) were held constant. All patients were questioned for their subjective impressions of sweat reduction and satisfaction prior to and monthly after the treatment. For sweat reduction a scale with 10% intervals (from 0% to 100%) was included in the questionnaire. Treatment satisfaction was rated as no, mild, moderate or total.

A relapse was defined as a 25% increase of sweat production assessed both by Reinauer's test and individual questionnaire compared to the ones performed one month after the treatment.

Median and ulnar nerve blocks for the palms were performed by injections of 4 ml %1 lidocaine HCl for each nerve at the wrist to reduce pain during multiple subcutaneous injections. For soles 7ml of %1 lidocaine HCl was injected for the tibial nerve into the area at the back of medial malleolus and 3 ml. for the sural nerve into the area between the Achilles tendon and lateral malleolus.

The palms and soles to be injected were divided into squares of 1,5 × 1,5 cm with a pen. Totally 100 mouse units [MU] of Btx-A (Botox, Allergan, Irvine, Calif, 100 MU) for each sole, 65 MU for patients with excessive palmar hyperhidrosis (4 out of 14 patients with more than 250 mg sweat production as a total of 2 palms by Reinauer's method) and 45 MU for each palm for the remainder 10 was injected intracutaneously by a 30-gauge needle, at the centre of the drawn squares, after diluting 100 MU of Btx-A with 4 ml of sterile 0.9% saline (2,5 MU in 0,1ml of diluent) (Fig. 1).

A paired t test was performed to compare the amount of sweat production quantitatively prior to and 1 month after the treatment. $P < 0.05$ was regarded to indicate statistical significance.

Results

All patients completed the study. The mean total sweat productions of 2 palms prior to and 1 month after the treatment in mg/minute were found to be 220.80 (SD : 73.77) and 43.43 (SD : 27.6) ; and total of 2 soles for the 3 patients with plantar hyperhidrosis 326.66 (SD : 71.28) and 50.33 (SD : 29.36), respectively (Fig. 2). The sweat production reductions were highly significant for both palmar and plantar hyperhidrosis quantitatively ($P < 0.01$). The mean average time to perceive reduction of sweating by the patients was 3.23 (SD : 1.26) days (min : 2 max : 6). Three patients experienced 90%, 4 patients 70%, 3 patients 60%, 3 patients 50%, and 1 patient 30% reduction in sweating 1 month after the treatment. At the end of the fourth month, 5 patients were fully, 7 moderately and 2 mildly satisfied by the treatment. Recurrence was observed in 3 months in 1, 4 months in 1, 5 months in 7, 6 months in 3 and 7 months in 2 patients for palmar hyperhidrosis (Mean : 5.29 ; SD : 1.07 months). Three patients who were treated for both palmar and plantar hyperhidrosis had equal recurrence period in the palms and soles (2 after 5, 1 after 4 months).

Injections were tolerated generally well. Two of the patients stated moderate pain during palmar and one during plantar injections. No hematomas were observed. One patient who was injected 65MU of Btx-A per palm, developed thenar and hypothenar muscle weakness in both hands which was measured by opposition strength. Weakness made a peak on the fifth day of injection, stated as + 3/5 in thenar and 4/5 in hypothenar muscles of both hands and lasted 4 weeks on neurological examination. This patient had difficulty in writing and brushing her hair for 10 days, between the fifth and fifteenth days of injection. At the end of the fourth week she had mild atrophy of thenar muscles which reduced gradually and disappeared on the eighth week. Two patients had less serious thenar weakness in both hands lasting 1 week and one of these patients did not complain of weakness. One of the 3 patients treated for plantar hyperhidrosis had mild muscle weakness of plantar flexors of both feet (predominantly right) which lasted 10 days on both examination and patient's statement. Another 2 of the 14 patients complained of mild weakness in their hands which they reported to not affect their daily activities, both lasted less than 10 days and none were determined on detailed neurologic examination. None of the patients experienced compensatory hyperhidrosis in another part of their body. No systemic or allergic side affects were observed or expressed.

Discussion

Btx-A was found to be effective and safe in both treating palmar and plantar hyperhidrosis in our study. One of our observations was the same recurrence period in the palms and soles for the 3 patients who were injected for both palmar and plantar hyperhidrosis. The duration of effect was equal in two different, but structurally similar parts of the body of these 3 patients.

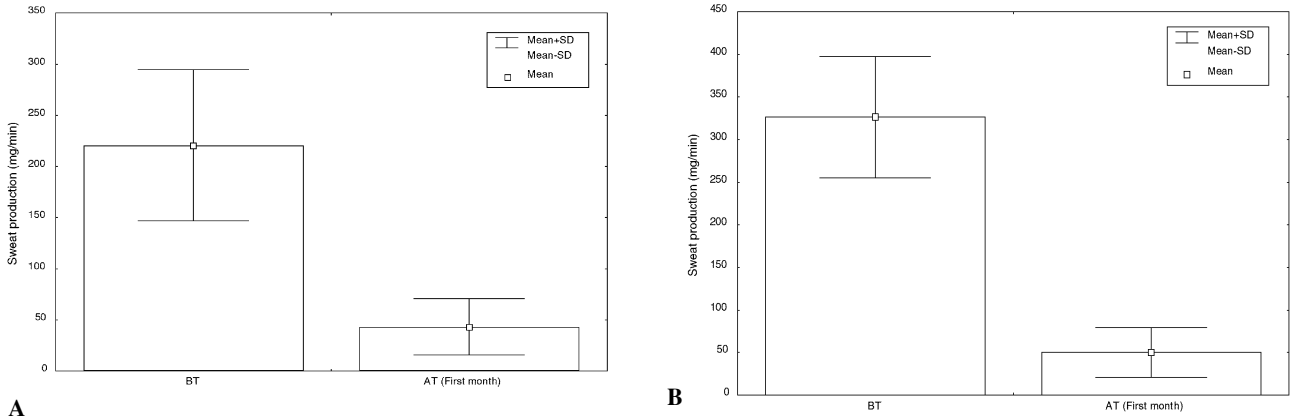

FIG. 2. — Total sweat production (mg/minute) of two palms (A) and two soles (B) before and at the first month of injection. BT : Before treatment ; AT : After treatment.

We can conclude that plantar injections are as safe and effective as palmar ones, but had the disadvantage of a longer time of application in our study. One of our patients had a transient disabling muscle weakness of hands and mild atrophy of thenar muscles who were injected 65 MU of Btx-A for each hand. There are a few patients who were reported to have disabling muscle weakness in the literature but none found to report muscle atrophy (16, 17). It is possible that some of the injections were made intramuscularly instead of intradermally for this patient or Btx-A diffused to the muscles from the dermis more than expected. Although it was transient ; to avoid undesirable muscle weakness and atrophy, the toxin can be injected carefully to the nondominant hand at the first session of injection to adjust the dosage for both the effectiveness and side-effects as is suggested by Naver *et al*. (17). A lower relapse rate has been reported for axillary hyperhidrosis by unusual high doses of Btx-A (18). We observed transient muscle weakness in 4 of our 14 patients (28.6%). Our ratio was higher than the ratios of previous reports (1, 17). Therefore higher doses of Btx-A for palmar and plantar hyperhidrosis than doses used in our study should be administered with caution and not be the subject of a new study unless a new application method preventing the diffusion of Btx-A to the muscles is found.

12 of our 14 patients were fully or moderately satisfied by the treatment, but to make an objective comment studies measuring life quality should be performed one of which is carried out by Naver *et al*.

In conclusion, although it seems to have a higher side effect profile compared to axillary, intracutaneous Btx-A injection for both palmar and plantar hyperhidrosis still appears to be a safe and effective treatment method and has a low and transient side-effect profile.

Abbreviations

Btx-A : Botulinum toxin A
Da : Dalton
SD : Standard Deviation

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